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, 2020

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 001-39782

4D Molecular Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**47-3506994**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
5858 Horton Street #455 Emeryville, CA	**94608**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (510) 505-2680

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	FDMT	The Nasdaq Global Select Market

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

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

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

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

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

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

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

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

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

The registrant was not a public company as of June 30, 2020, the last business day of its most recently completed second fiscal quarter, and therefore, cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date. The registrant's Common Stock began trading on the Nasdaq Global Select Market on December 11, 2020.

The number of shares of Registrant's Common Stock outstanding as of March 15, 2021 was 26,692,879.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to the 2021 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein. The proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2020.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our development activities, preclinical studies and clinical trials, including our clinical trials for 4D-310, 4D-125 and 4D-110;
- the timing of IND-enabling studies and results from such studies, including our IND-enabling studies in 4D-150 and 4D-710;
- the timing and success of lead optimization for our product candidates in lead optimization, including for 4D-135;
- the translation of our preclinical results and data into future clinical trials in humans;
- the timing of any manufacturing runs for materials to be used in patient trials;
- the number, size and design of our planned clinical trials, and what regulatory authorities may require to obtain marketing approval
- the potential effects of the COVID-19 pandemic on our preclinical and clinical programs and business;
- the timing or likelihood of regulatory filings and approvals;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the success of competing products or platform technologies that are or may become available;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain approval;
- future agreements with third parties in connection with the commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, if approved for commercial use, and our ability to serve those markets;
- existing regulations and regulatory developments in the United States and foreign countries;
- the expected potential benefits of strategic collaboration agreements, including our relationships with Roche and uniQure, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;

- potential claims relating to our intellectual property and third-party intellectual property;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the pricing and reimbursement of our product candidates, if approved;
- our ability to attract and retain key managerial, scientific and medical personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance; and
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

These forward-looking statements are based on management's current expectations, estimates, forecasts and projections about our business and the industry in which we operate and management's beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K. 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. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this Annual Report on Form 10-K.

PART I

Item 1. Business.

Overview

We are a clinical-stage gene therapy company pioneering the development of product candidates using our targeted and evolved AAV vectors. We seek to unlock the full potential of gene therapy using our platform, Therapeutic Vector Evolution, which combines the power of directed evolution with our approximately one billion synthetic capsid sequences to invent evolved vectors for use in targeted gene therapy products. Our targeted and evolved vectors are invented with the goals of being delivered through clinically routine, well-tolerated and minimally invasive routes of administration, of transducing diseased cells in target tissues efficiently, of having reduced immunogenicity and, where relevant, of having resistance to pre-existing antibodies. We believe these key features will help us to potentially create targeted gene therapy product candidates with improved therapeutic profiles, and to address a broad range of diseases from rare to large patient populations, including those that other gene therapies are unable to address. Each of our product candidates is created with one of our targeted and evolved AAV vectors. Our platform is designed to be modular, in that an evolved vector invented for a given set of diseases can be equipped with different transgene payloads to treat other diseases affecting the same tissue types. We believe this modularity will help inform the clinical development of subsequent product candidates using the same vector.

We have built a deep portfolio of gene therapy product candidates initially focused in three therapeutic areas: ophthalmology (intravitreal vector), cardiology (intravenous vector) and pulmonology (aerosol vector). We have three product candidates that are in clinical trials: 4D-125 for the treatment of X-linked retinitis pigmentosa (“XLRP”) in a Phase 1/2 clinical trial, 4D-110 for the treatment of choroideremia in a Phase 1 clinical trial, and 4D-310 for the treatment of Fabry disease in a Phase 1/2 clinical trial. Our two IND candidates are 4D-150 for the treatment of wet age-related macular degeneration (“wet AMD”), and 4D-710 for the treatment of cystic fibrosis lung disease. We expect to file the INDs and to initiate clinical trials for both of these programs in the second half of 2021.

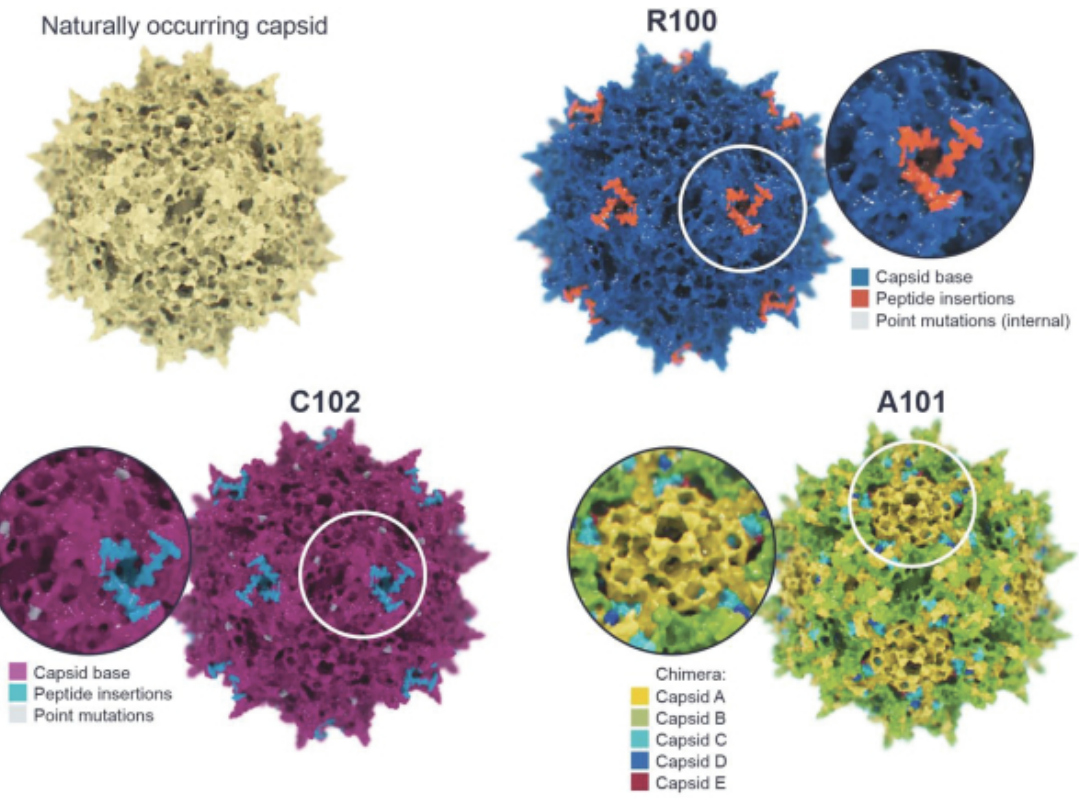
We believe our competitive advantages, combined with our highly experienced team, help to position our company to create, develop, manufacture and, if approved, effectively commercialize targeted gene therapies that could transform the lives of patients suffering from debilitating diseases.

Our Approach: Therapeutic Vector Evolution Platform

Gene therapy holds tremendous promise as a transformative therapeutic class. However, the majority of gene therapies have encountered limitations such as inflammation and toxicity, high dose requirements, limited efficacy and neutralization by pre-existing antibodies, due in part to their utilization of conventional AAV vectors that are naturally occurring and non-targeted. Through our Therapeutic Vector Evolution platform we apply the principles of directed evolution to invent targeted and evolved vectors for the delivery of genes to specific tissue types for diseases involving the same target tissue(s). Our product candidates are designed and engineered to utilize our targeted and evolved vectors to potentially address the limitations encountered with gene therapies utilizing conventional AAV vectors.

Leveraging a wide range of molecular biology techniques, we have developed a collection of 40 distinct libraries that are comprised of approximately one billion synthetic capsid sequences. We next define a Target Vector Profile that identifies the optimal vector features for the specific tissue type(s) and related set of diseases we seek to target, with the goal of overcoming limitations encountered by conventional AAVs. We then deploy Therapeutic Vector Evolution with our capsid libraries in NHPs and use competitive selection to identify targeted and evolved vectors from our libraries that demonstrate the strongest match to the Target Vector Profile. Our three lead vectors have unique structural changes as compared to the conventional naturally occurring AAV capsid as shown below.

Our three lead targeted and evolved vectors comprise numerous diverse and biologically important differences from the conventional AAV capsid, as illustrated in the computer generated representations of the three-dimensional capsid structures depicted below. The colorized areas illustrate these differences.



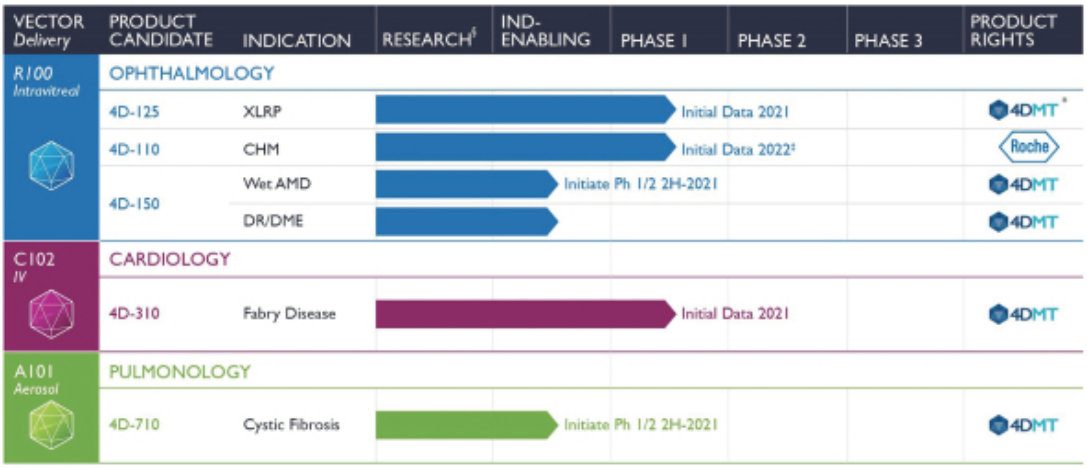
Based on preclinical data reported to date from our NHP and human cell models, including preclinical head-to-head comparisons with relevant conventional AAV vectors, we observed that our targeted and evolved vectors were well-tolerated and achieved enhanced delivery, increased transgene expression, reduced immunogenicity and/or improved antibody resistance when compared to conventional AAV vectors. We have not compared our targeted and evolved vectors to conventional AAV vectors in patients in clinical studies.

As we advance through clinical trials, we plan to evaluate the following potential design features of our targeted and evolved vectors and product candidates:

- Tolerability**:** Well-tolerated therapies with a low inflammation profile, low dose requirements and routine, safe routes of delivery
- Biologic activity**:** Effective delivery to targeted tissues, efficient transgene expression in targeted tissues, and/or resistance to neutralization by pre-existing antibodies
- Routine routes of administration**:** Routine, well-tolerated and minimally invasive routes of administration, including intravitreal, aerosol and intravenous delivery
- Antibody resistance: Resistance to neutralization by pre-existing antibodies, translating into improved efficacy, larger addressable patient populations, and the potential for re-dosing

Our Product Candidate Pipeline

We are developing a diverse pipeline of product candidates for both rare and large market diseases, including patient populations that other gene therapies are unable to address. Our initial product candidates are focused on the following therapeutic areas: ophthalmology, cardiology and pulmonology. Each of our product candidates leverages a targeted and evolved vector we invented through our Therapeutic Vector Evolution platform. Below is a summary of our product candidate pipeline and our next anticipated milestones:



* *4DMT is responsible for the development of this product candidate; Roche has an exclusive option to assume development and commercialization at its sole cost and expense. Such an option may be exercised prior to pivotal trial initiation.*

‡ Reporting in coordination with our partner Roche.

§ The Research stage involves (1) defining the Target Vector Profile then deploying Therapeutic Vector Evolution with our capsid libraries in non-human primates (NHPs) and using competitive selection to identify targeted and evolved vectors from our libraries that demonstrate the strongest match to the Target Vector Profile; then (2) optimizing our product candidates using the lead vector by conducting in vivo and in vitro evaluation of various transgene and promoter construct candidates in cell and animal models, and the selection of at least one product candidate to move forward into IND-enabling studies.

Ophthalmology Pipeline: Intravitreal Product Candidates

We are developing product candidates to treat tissues throughout the retina. Our targeted and evolved AAV vector, R100, was invented for routine intravitreal injection, leading to transgene expression across the entire surface area of the retina, and in the major cell layers of the retina.

We currently have four ophthalmology product candidates that utilize our proprietary intravitreal R100 vector:

1. 4D-125: 4D-125 is in an ongoing Phase 1/2 clinical trial in patients with XLRP due to mutations in the *RPGR* gene. We expect to report initial clinical data from this trial in the second half of 2021. We currently hold worldwide commercialization rights for 4D-125, and Roche holds an exclusive option to in-license the product prior to pivotal trial initiation.
2. 4D-110: 4D-110 is in an ongoing Phase 1 clinical trial in patients with choroideremia. In coordination with our partner Roche, we expect to report initial clinical data from this trial in 2022. We licensed exclusive worldwide rights to 4D-110 to Roche.
3. 4D-150: 4D-150 is in IND-enabling preclinical development for wet AMD and diabetic retinopathy, two large market ophthalmology indications. We wholly own this product candidate. We expect to file an IND and to initiate a Phase 1/2 clinical trial for 4D-150 in the second half of 2021.

4. 4D-135: 4D-135 is in preclinical development for autosomal dominant retinitis pigmentosa (“adRP”) due to mutations in the *RHO* gene. We wholly own this product candidate. We expect to initiate IND-enabling studies for 4D-135 in 2021.

Cardiology Pipeline: Intravenous Product Candidates

With our cardiology product candidates, all of which are wholly owned, we plan to treat patient populations in both primary cardiomyopathies, that involve the heart only, as well as cardiomyopathies that are secondary to systemic diseases, such as lysosomal storage diseases. Our cardiology product candidates utilize our targeted and evolved AAV vector, C102, which was invented for routine low dose intravenous administration and delivery to the heart, leading to transgene expression in heart muscle cells throughout the organ. For lysosomal storage diseases involving the heart and other organs, including Fabry disease, our product candidates are designed for transgene expression both within the heart and in other targeted tissues.

Our initial cardiology product candidate 4D-310 is in an ongoing Phase 1/2 clinical trial in adult patients with classic (severe) Fabry disease. 4D-310 is designed to address all critically affected organs, including the heart, kidney, and blood vessels through direct intracellular transgene expression. To our knowledge, 4D-310 is the only Fabry disease product candidate specifically designed to treat cardiomyocytes. We expect to report initial clinical data from this trial in the second half of 2021.

Pulmonology Pipeline: Aerosol Delivery Product Candidates

With our pulmonology product candidates, all of which are wholly owned, we plan to treat diseases that affect the lungs. Our pulmonology product candidates utilize our targeted and evolved vector, A101, which was invented for aerosol delivery to all major regions within the lung, including airways and alveoli, and successful penetration of the mucus barrier for transduction of lung airway cells, overcoming potential barriers such as pre-existing AAV antibodies and other inhibitory proteins within the mucus barrier. Our products utilizing A101 are designed for delivery as an aerosol to the lung epithelial cell surface resulting in efficient airway and alveolar cell transduction and transgene expression.

Our initial pulmonology product candidate 4D-710 is in IND-enabling preclinical development for cystic fibrosis lung disease. We expect to file an IND and to initiate a Phase 1/2 clinical trial for 4D-710 in the second half of 2021.

Our Team

Our experienced team consists of biotherapeutics developers, entrepreneurs, innovative gene therapy scientists and clinicians to execute our platform, product design and development and commercialization strategies. Collectively, our team has more than 100 years of combined experience in the field of viral vector gene therapy, including leadership of over 30 clinical trials from Phase 1 through Phase 3 and product approval. We are led by our Chief Executive Officer and co-founder, David Kirn, M.D., who has over 25 years of experience creating and growing therapeutic platform companies, including viral vector gene therapy and oncolytic virus technologies, and advising on the design, preclinical translation and clinical development of viral vector gene therapeutics for leading life science companies, such as Onyx Pharmaceuticals, Novartis International AG, Pfizer Inc., Bayer AG and Biogen Inc. Our Executive Chairman, John Milligan, Ph.D., is the former CEO and President of Gilead Sciences, where he spent over 29 years scaling the company and commercializing numerous transformative therapies across multiple disease areas. Our Chief Scientific Advisor and co-founder, David Schaffer, Ph.D., pioneered the application of directed evolution to the capsid of AAV vectors 20 years ago. Our Chief Operating Officer and Chief Technical Officer, Fred Kamal, Ph.D., has over 25 years of industry experience in product manufacturing and quality, including most recently with AveXis, Inc. where he was a key contributor to the development and biologics license application (“BLA”) for the AAV product Zolgensma (onasemnogene abeparvovec). Our Chief Medical Officer, Robert S. Fishman, M.D., brings over 20 years of clinical trial execution and product development expertise. Our board of directors also brings significant experience in biopharmaceutical commercial execution and strategic initiatives.

Our Strategy

Our vision is to unlock the full potential of gene therapy to address as many patient populations as possible in both rare and large market diseases. We have developed the following strategies and guiding principles to achieve our goals:

Invent targeted and evolved AAV vectors using the power of directed evolution to unlock the full potential of gene therapy with transformative gene therapy products

Our Therapeutic Vector Evolution platform allows us to move beyond conventional AAV vectors and has enabled us to develop proprietary targeted and evolved vectors based on a Target Vector Profile for any set of diseases we strive to treat. This platform empowers us to select the best (or "fittest") targeted and evolved vector, matching the Target Vector Profile for any set of related diseases, out of our 40 distinct libraries comprising approximately one billion synthetic capsid sequences. Our goal is to unlock the full potential of gene therapy by creating targeted gene therapies based on these vectors. As compared to gene therapy products utilizing conventional AAV vectors, we believe our targeted gene therapies, if approved, will enable treatment of broader patient populations within specific diseases, diseases currently not addressed by gene therapy and large market diseases.

Apply our modular product design and engineering to help inform the clinical development of subsequent product candidates using the same vectors used for prior product candidates

Our targeted gene therapy product candidates are modular, in that a single targeted and evolved vector can be equipped with different transgene payloads to enable treatment of multiple different diseases affecting the same tissue type(s). Our preclinical and clinical development will provide us with insights and clinical proof-of-concept for a given vector equipped with one transgene. Development of subsequent product candidates could also be more efficient, as manufacturing, preclinical, clinical and regulatory activities will be guided by experience with preceding product candidates using the same vector.

Develop and commercialize a diverse portfolio of transformative gene therapy products in a broad range of therapeutic areas with significant unmet needs, including rare and large patient populations

We are building a diverse portfolio of product candidates. We believe this diversity increases our likelihood of success in contrast to relying on a single vector or disease area as evidenced by our: (1) multiple proprietary vectors delivered by different routine, well-tolerated and minimally invasive routes of administration specific to the disease, (2) therapeutic area diversity including ophthalmology, cardiology and pulmonology; and (3) opportunity to address both rare and large patient populations not currently addressed with conventional AAV vectors. We seek to develop our wholly owned product candidates through market approval and to retain product marketing rights for key products, regions and strategic therapeutic areas.

Build a fully integrated biopharmaceutical company by advancing our capabilities in product development and commercialization, and expanding our manufacturing facilities and internal proprietary Good Manufacturing Practice ("GMP") capabilities

To become a fully integrated biopharmaceutical company, we are building robust internal capabilities including translational and clinical research and development, regulatory affairs, manufacturing and quality which can mitigate operational risks, reduce costs, and increase product development control and speed. In the future we intend to build commercialization capabilities, including sales and marketing.

We believe robust internal manufacturing capabilities are of particular importance in gene therapy due to the high complexity of producing these therapies. Our current in-house manufacturing capabilities include GMP manufacturing, production capabilities for IND-enabling GLP toxicology studies and

research candidate production (upstream, downstream and fill/finish). We intend to further maximize the robustness and internal control of our manufacturing processes from discovery and process development through to clinical-grade cGMP manufacturing and to scale these capabilities to support later stage clinical programs and indications where clinical trials require more patients and/or higher intravenous doses. In the future we intend to build manufacturing capacity sufficient to support commercialization of any product candidates that are approved.

Selectively execute strategic collaborations to maximize the potential value of our Therapeutic Vector Evolution platform

We intend to enter into patient advocacy foundation alliances and academic collaborations, and to evaluate potential strategic corporate partnerships. We believe that alliances with patient advocacy organizations, such as the Cystic Fibrosis Foundation, can be beneficial for funding, patient enrollment, regulatory strategy, product design and clinical development. In addition, we intend to further expand our enabling technologies and our intellectual property portfolio by pursuing new opportunities through our sponsored research agreements with our Chief Scientific Advisor Dr. Schaffer and U.C. Berkeley. We will continue to evaluate new opportunities to partner with biopharmaceutical companies that we believe enhance our ability to deliver value for stockholders and clinical benefits for patients.

Our Therapeutic Vector Evolution Platform

Gene Therapy Successes and Limitations of Current Conventional Non-Targeted AAV Vectors

Gene Therapy Overview

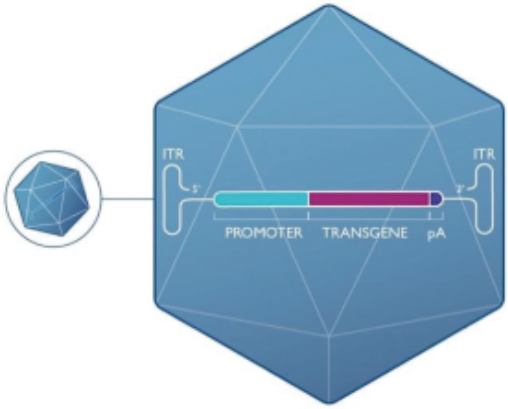
Gene therapy aims to address diseases caused by gene mutations and gene dysregulation. Gene therapies hold the promise of delivering transformative and durable benefit to the patient by addressing the underlying molecular root cause of genetic diseases, in many cases, by introducing a functional version of the patient's defective gene into their own cells. Gene therapy has shown the potential to halt the progression of rare diseases, as well as to enable or restore critical human functions. Gene therapies may be delivered to their target cells either *in vivo* or *ex vivo* and can be paired with other therapeutic approaches including cell therapy and gene editing.

The transformative potential of gene therapy has been demonstrated across multiple rare disease areas. There has been significant progress over the last decade in the field of gene and cell therapies, including with AAV based gene therapy. Further, the number of companies developing gene and cell therapy products has increased significantly over the last five years. There are currently a number of approved viral vector gene therapy products, including Zynteglo, Zolgensma, Luxturna, Imlygic and Strimvelis.

The physical construct of gene therapies are comprised of two essential components:

- Vector*:* A vehicle that packages and delivers the promoter and transgene into the body and transports them through the protective cell membrane and ultimately into the cell nucleus. As a result, the vector plays an essential role in delivery and transduction, the process of guiding the transgene into the cell with subsequent expression of the transgene product. The vector is foundational to the potential safety and efficacy of gene therapies, as the vector is ideally relied on to deliver the promoter and transgene to the diseased cells safely and in sufficient quantities to result in clinical benefit.
- Promoter and Transgene Payload*:* The promoter is the DNA region that controls and initiates transcription of the transgene in the desired cell type(s), while the transgene is the functional gene intended to be delivered into the target cell and expressed at the RNA and/or protein levels. Examples include enzymes, structural proteins, cell surface protein receptors, antibodies, gene editing machinery and inhibitory RNA molecules.

Generalized components of an AAV gene therapy include the vector and a therapeutic payload consisting of DNA encoding a promoter, transgene, polyadenylated ("pA") tail for stability, and inverted terminal repeats ("ITR") to support packaging and other functionality within the target cell.



Key Challenges with Conventional AAV Vectors

The fundamental gene therapy components used in current gene therapy candidates originated largely from academia, some as early as the 1960s, with limited improvements since their discovery. The majority of AAV gene therapy companies use conventional AAV vectors that are comprised of naturally occurring AAV capsids (protein shells) of a few specific subtypes, including AAV1, AAV2, AAV5, AAV8, AAV9, AAVhu68, AAVrh10, and AAVrh74. In some cases, minor changes have been made to these naturally occurring, non-targeted capsids in an attempt to enhance non-specific transduction. While gene therapy holds tremendous promise as a transformative therapeutic class, the demonstrated hurdles with conventional AAV vectors may limit the diseases and patient populations that can be effectively addressed.

We believe that there are four fundamental challenges that hinder gene therapies that utilize conventional AAV vectors which may adversely impact their product safety, efficacy and commercial potential:

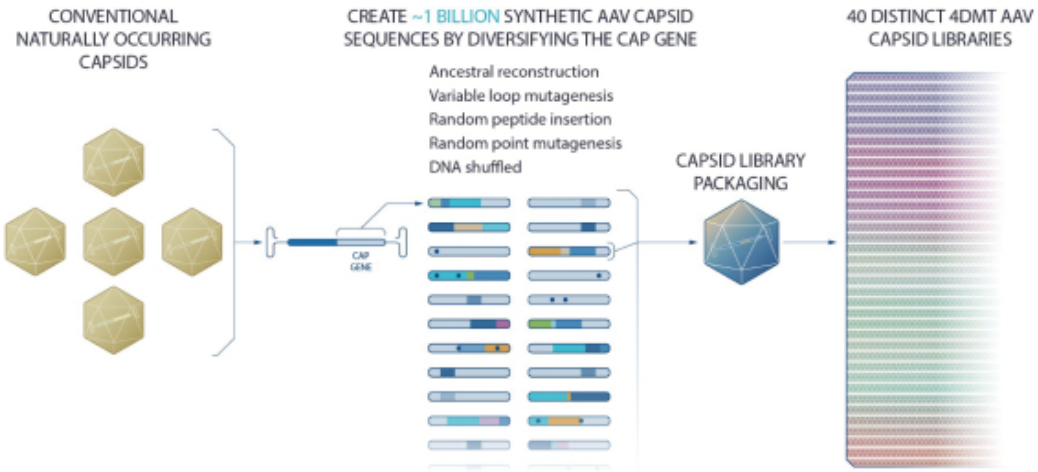
1. Lack of effective delivery to desired target tissues and/or cell types due to physical barriers: Conventional AAV vectors have not been engineered to circumvent natural barriers to viral vector delivery by various routes of delivery, such as the inner-limiting membrane of the retina or clearance by the liver, and they are not targeted to specific tissues or cells. As a result, products using these vectors may require suboptimal delivery mechanisms, such as subretinal injection compared with intravitreal dosing, or high doses, such as with intravenous administration for the treatment of muscle diseases, to achieve therapeutic benefit. These strategies may result in toxicities and even patient deaths, as well as commercialization challenges.
2. Lack of efficient transduction and transgene expression from target cells: To yield therapeutic benefit, the vector must efficiently deliver its transgene from the cell surface into the target cell nucleus, resulting in subsequent therapeutic transgene expression within the cell. Conventional AAV vectors are not engineered for efficient transduction of specific target cells. As a consequence, conventional AAV vectors may be associated with inefficient transduction and transgene expression which would limit efficacy.

3. Potential to cause toxicity due to inflammation: Conventional AAV vectors have been associated with inflammation-related toxicities in some patients. Potential contributing factors may include the lack of specificity with current conventional AAV vectors, the high intravenous doses required for delivery to target tissues systemically, and the ability of these conventional AAV vectors to transduce immune cells. For example, intravenous gene therapy programs in patients with DMD using doses of 2E14-3E14 vg/kg have been associated with acute inflammation and transient kidney dysfunction resulting in intermittent clinical holds from the FDA. Another high dose intravenous gene therapy program utilizing a conventional AAV vector, for patients with X-linked myotubular myopathy, resulted in serious adverse events including three patient deaths.
4. Neutralization by pre-existing antibodies: The human immune system has evolved to fight viruses, including conventional AAVs which are present in nature. Widespread exposure to these conventional AAVs has resulted in neutralizing antibodies in approximately 30% to 70% of the population depending on the vector serotype and patient population. These antibodies to conventional AAV vectors can limit gene therapy efficacy and the addressable patient population. In addition, re-dosing with the same conventional AAV vector is generally not feasible given the induction of neutralizing antibodies to the vector.

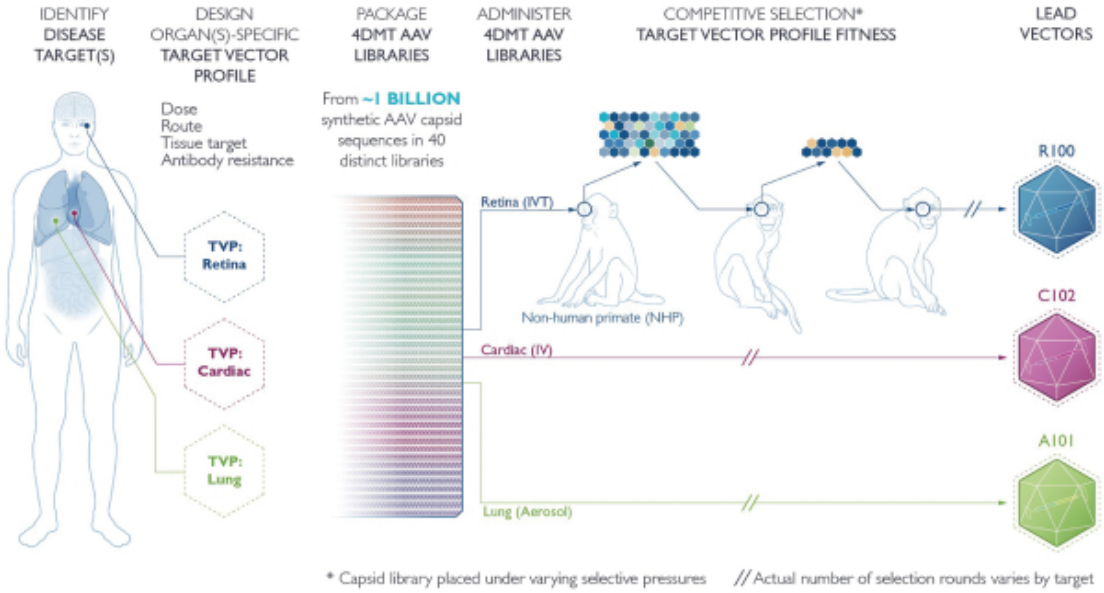
Our Solution: Evolved Vectors for Targeted Gene Therapy

We are pioneering the development of targeted gene therapies based on our targeted and evolved vectors. Using our Therapeutic Vector Evolution platform, we invent targeted and evolved vectors that are designed to address specific diseases and their associated tissue(s). We believe our proprietary vectors will allow us to overcome known limitations of conventional AAV vectors, and to potentially address a broad range of both rare and large patient populations that cannot be addressed with conventional vectors. Based on our Target Vector Profile for a set of diseases, we select vectors in NHPs from our 40 distinct libraries made up of approximately one billion synthetic capsid sequences. Subsequently, we characterize and evaluate a lead targeted and evolved vector for delivery and transgene expression through extensive studies in NHP and human cell and organotypic tissue assays.

The first step in directed evolution is to generate massive genetic diversity. Starting with the genomes of multiple naturally occurring AAV variants, and their ancestral predecessors, we employ numerous molecular biology techniques to create our 40 distinct libraries comprising approximately one billion synthetic capsid sequences.



Starting with our 40 distinct libraries comprising approximately one billion synthetic capsid sequences, we conduct Therapeutic Vector Evolution, including competitive selection, to identify targeted and evolved vectors that fit a Target Vector Profile. The illustration below highlights the Target Vector Profile design and subsequent selection process whereby competitive pressure is applied over a varying number of selection rounds for each program. Capsids with the best fitness for the Target Vector Profile are enriched at each round and are designated lead vectors.



Key Design Features of Our Targeted and Evolved Vectors

Through our proprietary Therapeutic Vector Evolution platform, we invent targeted and evolved vectors that we believe have the potential to display superiority to conventional AAV vectors with respect to four key design features:

- Targeted delivery to specific tissues by routine, well-tolerated and minimally invasive routes of administration
- Improved transduction of target cell types and tissues
- Lower toxicity with reduced inflammation
- Ability to resist neutralization by pre-existing antibodies in humans

As shown below, we have generated animal proof-of-concept data in both NHP and knock-out mouse disease models *in vivo*, and in human cells *in vitro*, that we believe provide evidence regarding the potential for our targeted and evolved vectors to show superiority over conventional AAV vectors. Our goal is to develop products that are safer, more efficacious, administered at lower doses, more efficiently manufactured, and, if approved, more effectively commercialized.

Targeted Delivery to, and Transduction of, Specific Tissues by Routine Clinical Routes of Administration

We select targeted and evolved vectors that are administered through what we believe to be the optimal method of delivery for a particular disease, with the goal of circumventing physical barriers en route to specific tissues or cell types in the body.

In our first example of targeted delivery in NHPs *in vivo*, our targeted and evolved vector for the retina, R100, was invented for intravitreal administration. We believe intravitreal injection is the optimal

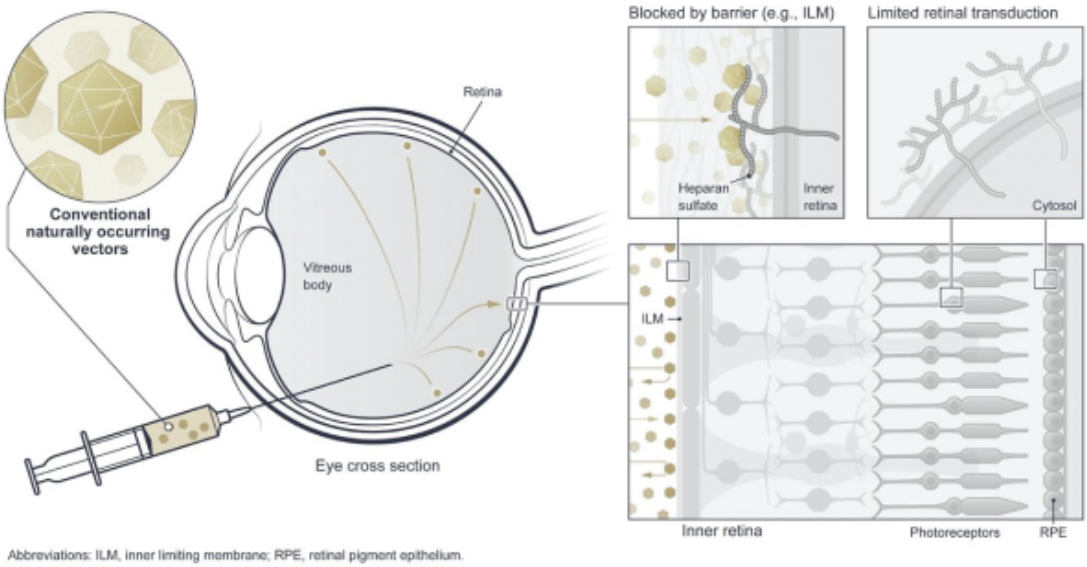
route of gene therapy administration for the retina, as evidenced by widespread use of approved intravitreally administered biologics, that generate over $9.7 billion in annual global sales for the treatment of wet AMD, diabetic retinopathy and related diseases. The R100 vector is leveraged in modular fashion for use in all four of our current ophthalmology product candidates: 4D-110, 4D-125, 4D-135 and 4D-150. Conventional AAV capsid vectors such as AAV2 are not able to reach retinal cells effectively following intravitreal injection due to barriers such as the inner-limiting membrane barrier between the vitreous and target retinal cells. As a result, gene therapies utilizing conventional vectors have relied on delivery by subretinal surgery. This is a complex procedure that requires highly specialized retinal surgeons to perform surgery in an operating room setting, and results in a bleb of fluid within a detached area of retina that comprises less than 1% of the total retina surface, based on published data. Potential complications include retinal tears and retinal detachments.

In contrast, in preclinical studies intravitreal R100 transduced the entire retinal surface area and a high percentage of cells in all layers of the retina, including photoreceptors and retinal pigment epithelial ("RPE") cells in NHP. Of note, the ocular anatomy and physiology in NHPs closely mirrors that of humans. We therefore believe our products designed and engineered with R100 have potential tolerability, biologic activity and commercial advantages compared with product candidates that require subretinal surgical injection.

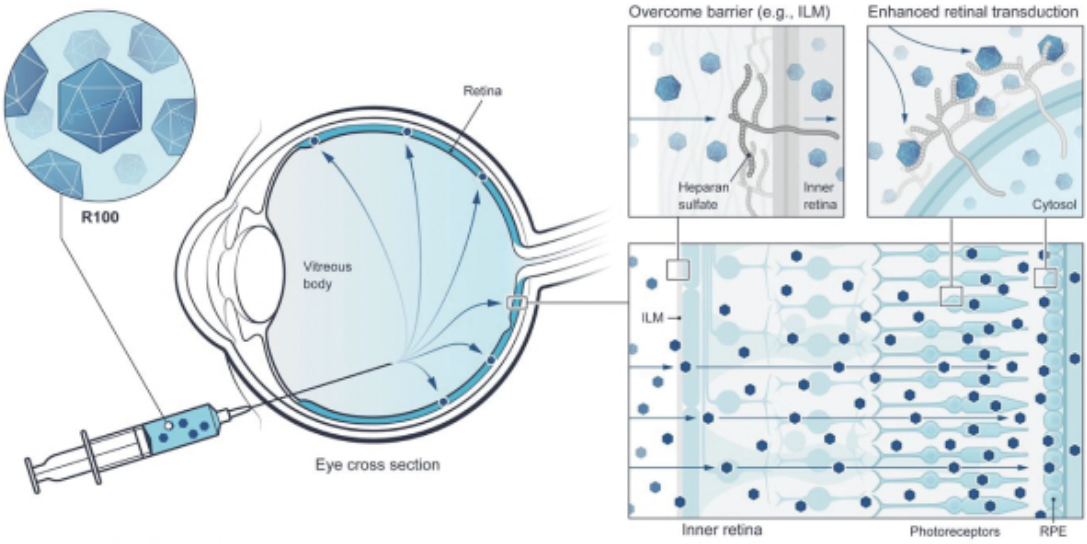
Structure-function studies suggested that the potential of R100 to penetrate through the inner-limiting membrane barrier may be associated with reduced binding to heparan sulfate, which is a major component of the barrier. R100 subsequently binds and transduces target retinal cells at higher efficiency than the conventional AAV2 vector. The improved transduction was associated with enhanced binding to sialic acid on the target cells.

Target Vector Profile for R100 intravitreal delivery to the retina:

Following intravitreal injection, conventional AAV vectors (top panel) such as AAV2 are not able to reach retinal cells effectively due to barriers such as the inner-limiting membrane barrier between the vitreous and target retinal cells. R100 administered by intravitreal injection (bottom panel) was able to penetrate through these barriers to transduce the entire retinal surface area when administered to NHP. A high percentage of cells was subsequently transduced in all layers of the retina, including photoreceptors and retinal pigment epithelial ("RPE") cells. Structure-function studies suggest that the potential of R100 to penetrate through barriers such as the inner-limiting membrane barrier was associated with reduced binding to heparan sulfate. R100 subsequently bound and transduced target retinal cells at higher efficiency than the conventional AAV2 capsid. This improved transduction was associated with enhanced binding to sialic acid on the target cells.

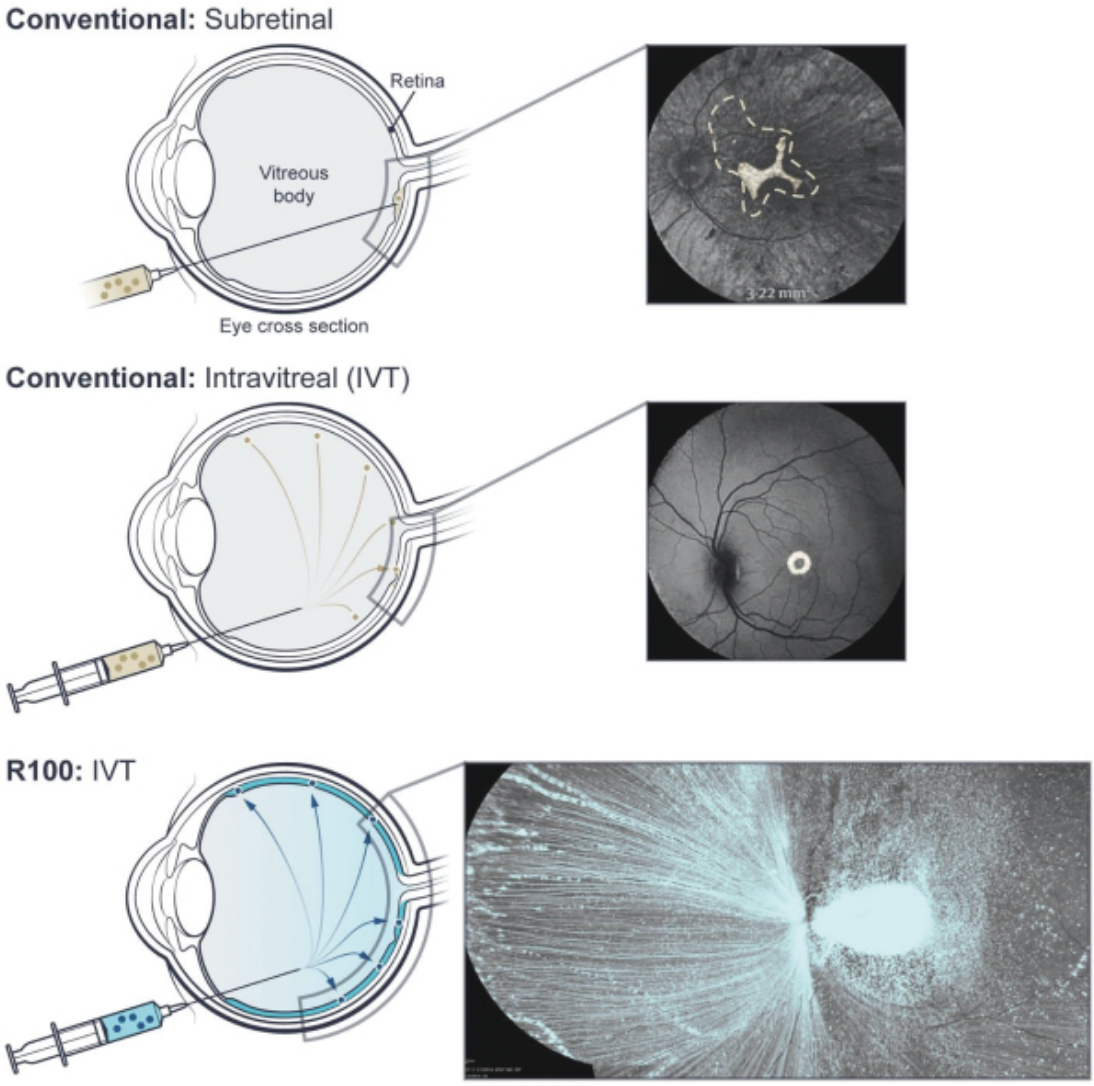


Abbreviations: ILM, inner limiting membrane; RPE, retinal pigment epithelium.

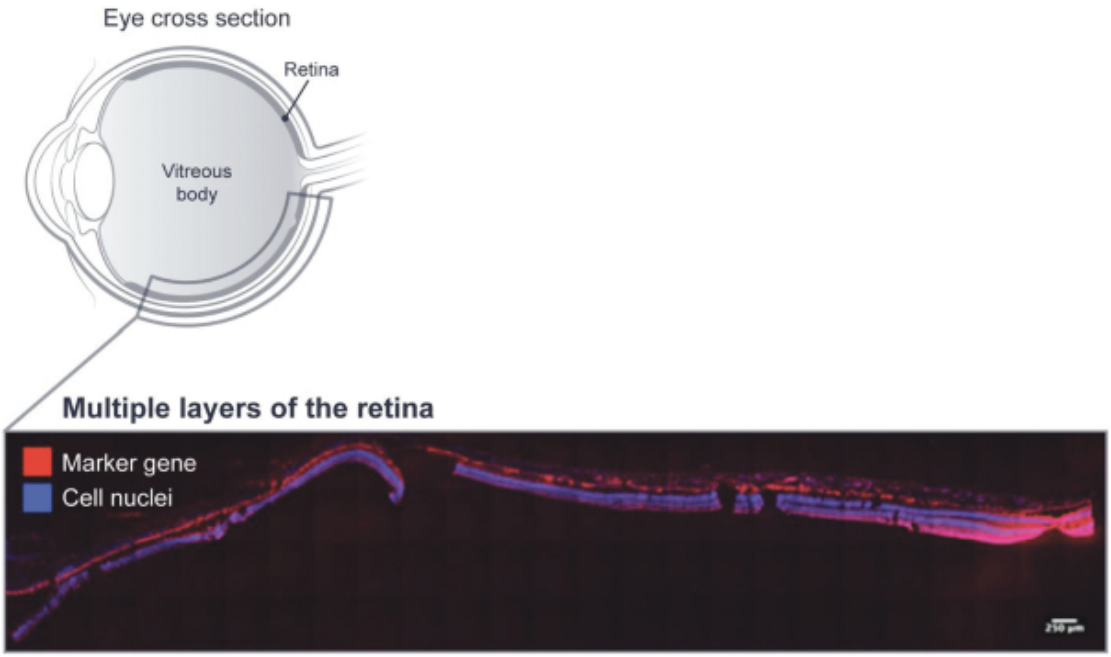


Abbreviations: ILM, inner limiting membrane; RPE, retinal pigment epithelium.

The subretinal surgical injection route of administration with conventional AAV vectors resulted in delivery to a limited bleb area of the retina (top panel, dotted line), leaving the vast majority of the retina untreated; according to published data bleb coverage was <1% of the retina with subretinal injection. Within this bleb, viable retinal cells were transduced (top panel, colorized area). The intravitreal route of administration with conventional vector AAV2 resulted in a small area of transduction around the fovea due to interference across the retina by the inner limiting membrane ("ILM") (center panel, colorized ring). By contrast, intravitreal injection route of administration with our targeted and evolved vector, R100, resulted in transduction across the entire surface area of the retina, including the major cell layers of the retina (bottom panel, colorized area) in NHP.



Intravitreal injection route of administration with our targeted and evolved vector, R100, resulted in transduction across the entire surface area of the retina, including the major cell layers of the retina in NHP.



R100 has been well-tolerated in both NHP and in patients. In our on-going clinical trials, we have administered two product candidates utilizing our R100 vector to patients via intravitreal injection. Treatment has been generally well-tolerated with no dose-limiting toxicities. In addition, we have administered these product candidates in 91 NHP eyes injected in three different GLP toxicology studies with no adverse findings reported.

To date, our two clinical stage ophthalmology product candidates 4D-125 and 4D-110, both of which utilize the R100 vector, have exhibited favorable toxicity and tolerability profiles in GLP toxicology studies as summarized below.

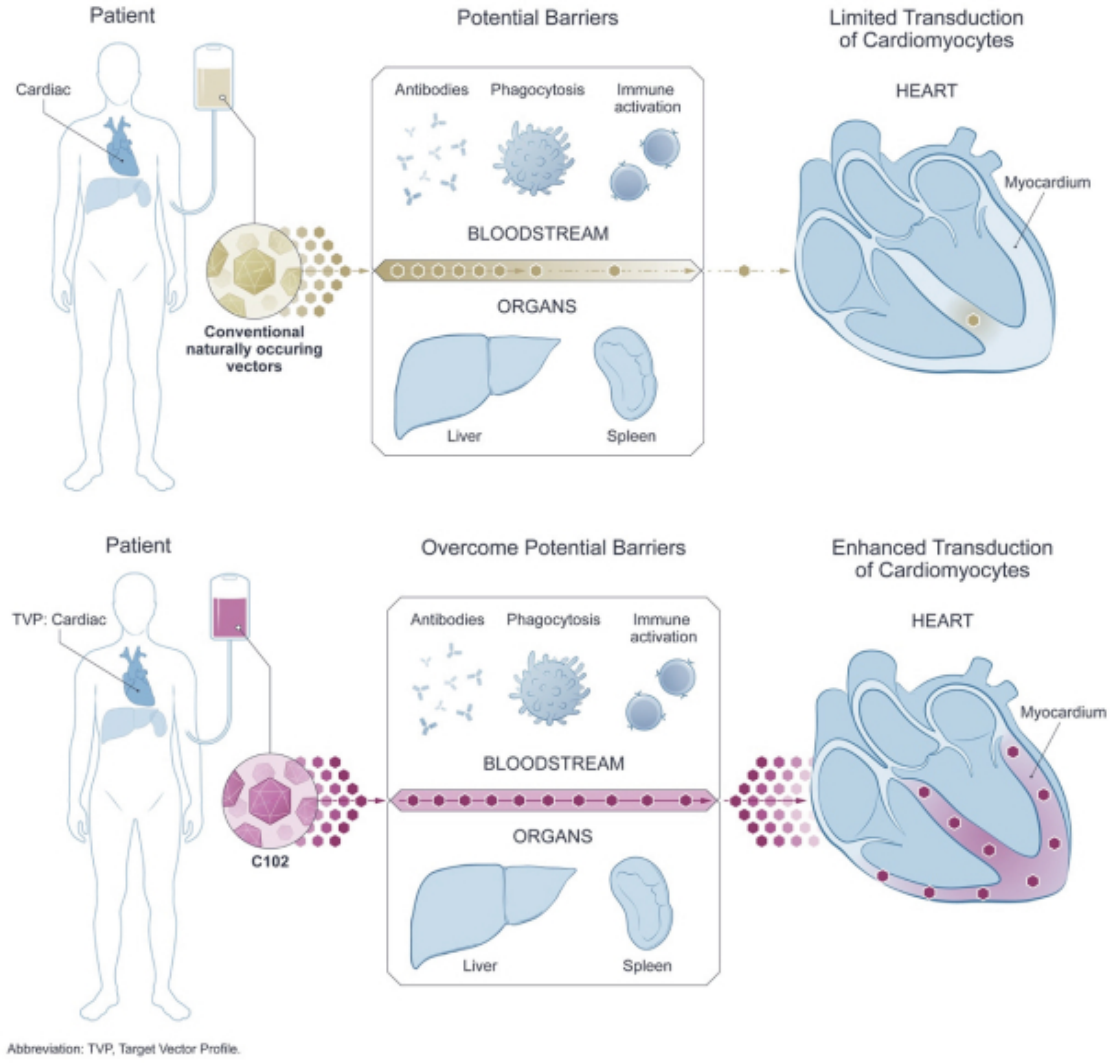
	4D-125	4D-110	
	Unilateral GLP Tox & BD	Unilateral GLP Tox & BD	Bilateral GLP Tox & BD
Species	**NHP**	**NHP**	**NHP**
# of eyes dosed	30	27	34
Route of administration	IVT	IVT	IVT
Highest dose to date	1E12 vg/eye	1E12 vg/eye	1E12 vg/eye
Clinical evaluation	No adverse findings; transient, steroid-responsive uveitis		
Clinical pathology	No adverse findings	No adverse findings	No adverse findings
Hematology	No adverse findings	No adverse findings	No adverse findings
Hematocrit	No adverse findings	No adverse findings	No adverse findings
Clinical chemistry	No adverse findings	No adverse findings	No adverse findings
Liver enzymes (ALT/AST)	No adverse findings	No adverse findings	No adverse findings
Gross pathology	No adverse findings	No adverse findings	No adverse findings
Histopathology	No adverse findings	No adverse findings	No adverse findings
Cellular immune response	ELISpot anti-capsid: Negative; ELISpot transgene: Negative		

Abbreviations: AE, adverse events; ALT, Alanine transaminase; AST; aspartate aminotransferase; BD, biodistribution; GLP, good laboratory practices; IVT, intravitreal; N/A = not yet available, study ongoing.

In our second example of targeted delivery in NHPs *in vivo*, our targeted and evolved vector, C102, was invented for improved delivery to and transduction of cardiac muscle tissues (cardiomyocytes), when administered by IV at low doses, with minimal inflammation. Barriers to IV delivery to heart muscle may include organs such as the liver and blood components including complement, immune cells and antibodies.

Target Vector Profile for C102 intravenous delivery to the heart:

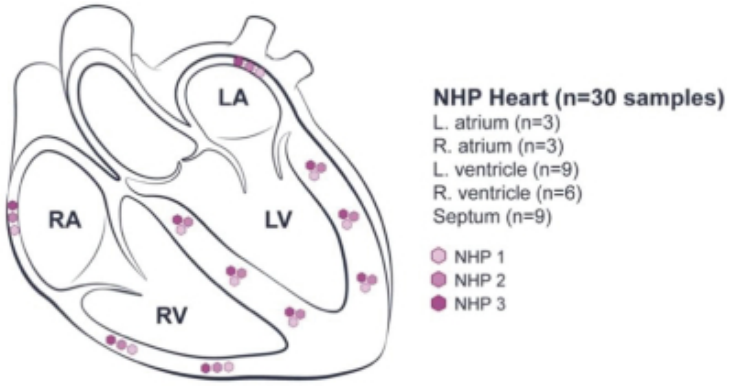
Conventional AAV capsid vectors (top panel) such as AAV8 do not effectively deliver to heart muscle tissue following low dose IV administration. Potential barriers include clearance by organs such as the liver, and blood components including complement, immune cells and antibodies. Conversely, IV administered C102 (bottom panel) has exhibited robust delivery and broad transduction of cardiac tissues, including cardiomyocytes.



In NHPs, we observed that intravenous delivery of C102 at relatively low doses for delivery to muscles (1E13 – 5E13 vg/kg) resulted in genome delivery to 100% of the 30 heart tissue samples evaluated through all regions of the heart in NHP. Transgene protein expression was detected in 29 of the 30 samples, providing evidence of intracellular protein production in cardiomyocytes.

C102 delivery to, and transduction of, NHP cardiomyocytes:

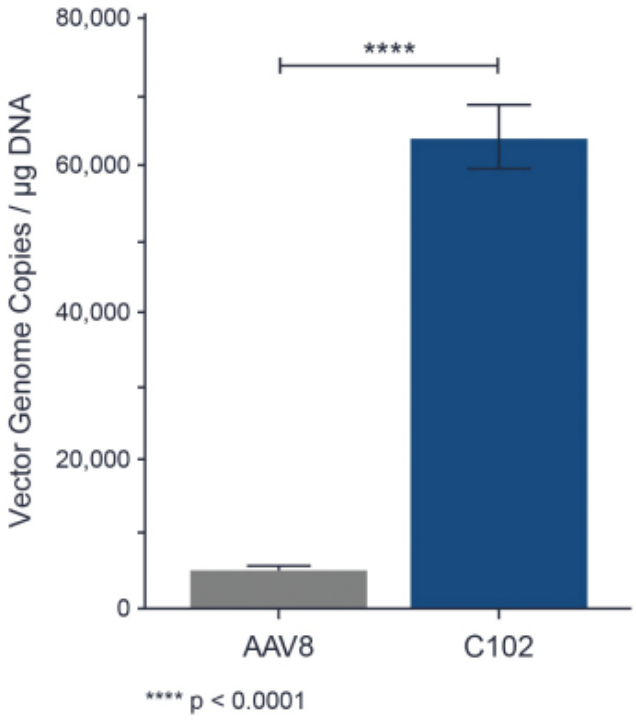
The figure below illustrates the broad distribution of samples collected in our C102 biodistribution study. Samples were collected from 10 locations across the four regions of the heart in 3 NHPs. Intravenous delivery of C102 at relatively low doses (1E13 vg/kg) resulted in genome delivery to 100%, and protein expression in 97%, of the 30 heart tissues evaluated.



Immunohistochemistry for marker transgene protein expression showed widespread gene expression in cardiomyocytes in a preclinical study. In addition, in a preclinical study we observed that C102 was more efficiently delivered to cardiac tissues than conventional vectors such as AAV8 (shown below) and AAV9. C102 targeted the heart muscle tissue more efficiently than AAV8, and showed a 12-fold improvement in genome delivery to the heart muscle tissue. We have not compared C102 to AAV8 or AAV9 in patients in clinical studies.

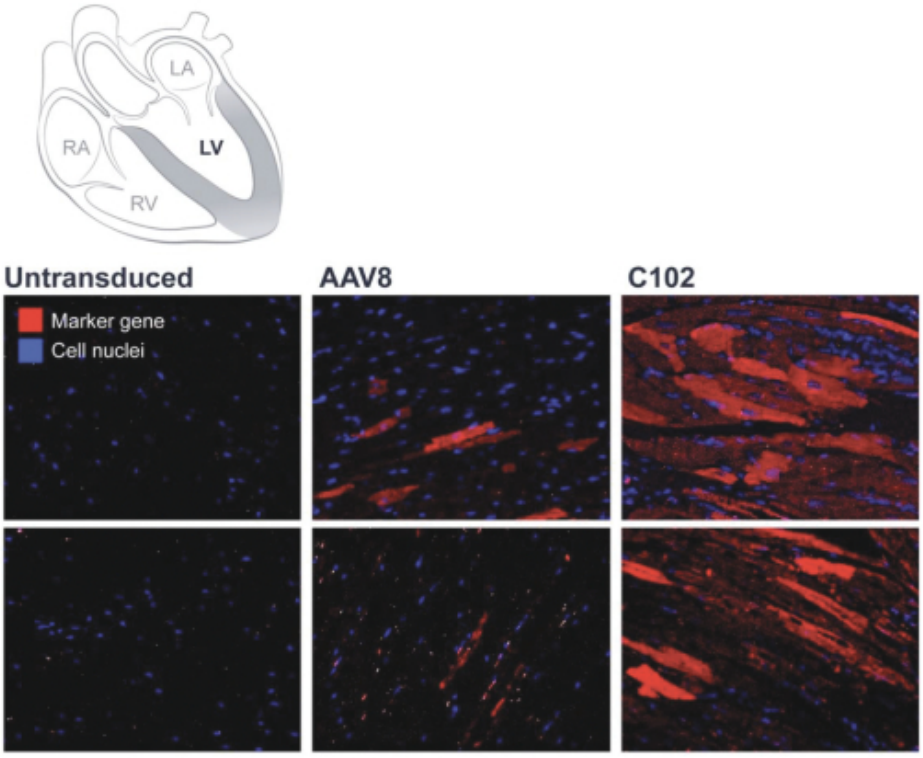
C102 delivered genetic payloads to cardiac tissue more efficiently than conventional AAV vectors in NHP:

In vector characterization studies in NHP, C102 delivered 12-fold more EGFP marker gene to cardiac tissue on average than did AAV8



Cardiac muscle tissue transduction and protein expression in NHP heart:

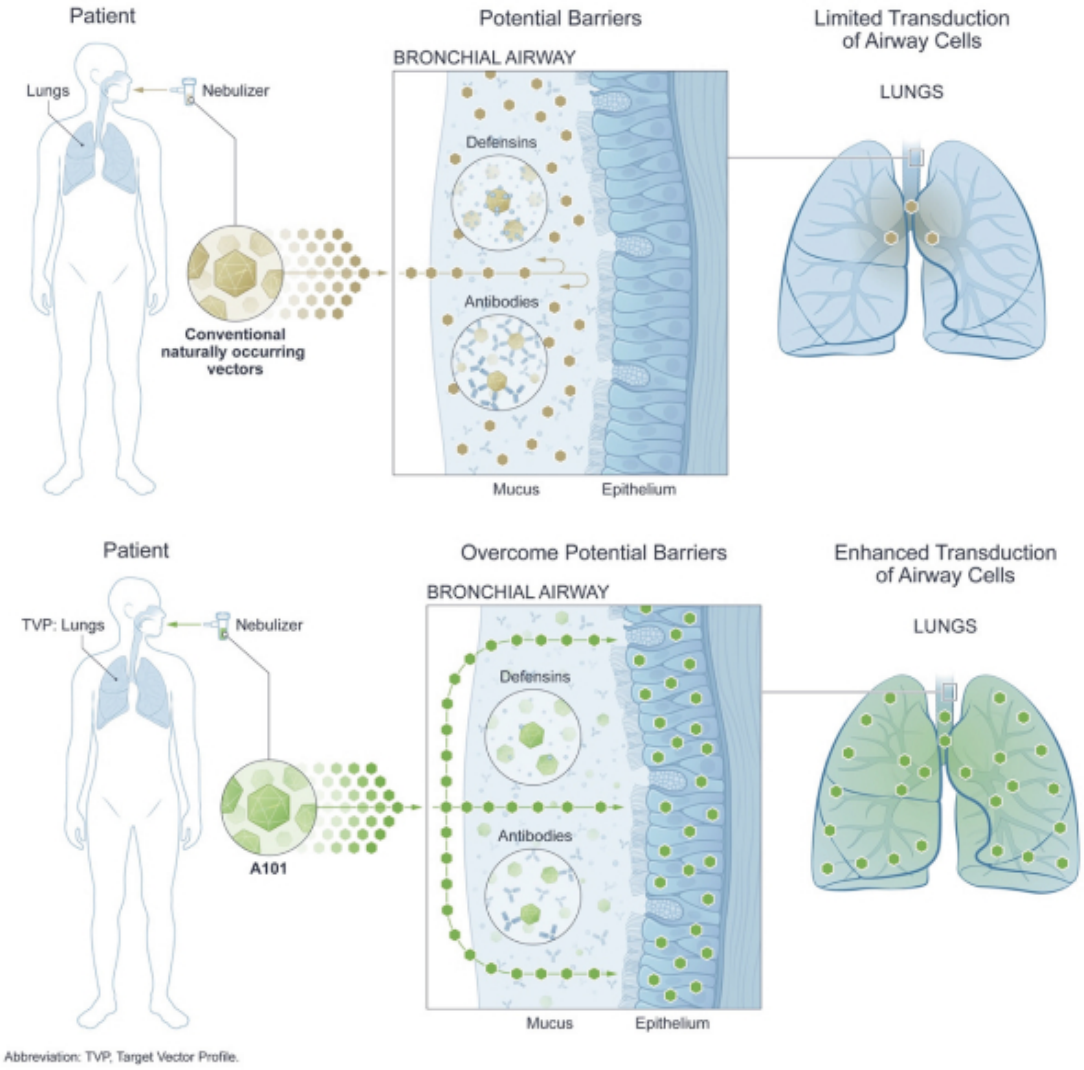
NHP cardiomyocyte transduction and marker transgene expression ("EGFP") was detected by immunofluorescence 8 weeks after intravenous injection of C102 (right panel), whereas conventional vector AAV8 transduced cardiomyocytes to a lesser extent than did C102 (center panel). Non-transduced control NHP heart did not exhibit visible EGFP staining (left panel) (L, left; R, right, V, ventricle; A, atrium)



In our third example of targeted delivery in NHPs *in vivo*, our targeted and evolved AAV vector for lung tissues, A101, was invented for aerosol delivery to lung airway and alveolar cells. This vector was selected for penetration through the mucus and other potential barriers, and for resistance to pre-existing antibodies in humans. A101 is used as the targeted and evolved vector in 4D-710, our product candidate for patients with cystic fibrosis lung disease.

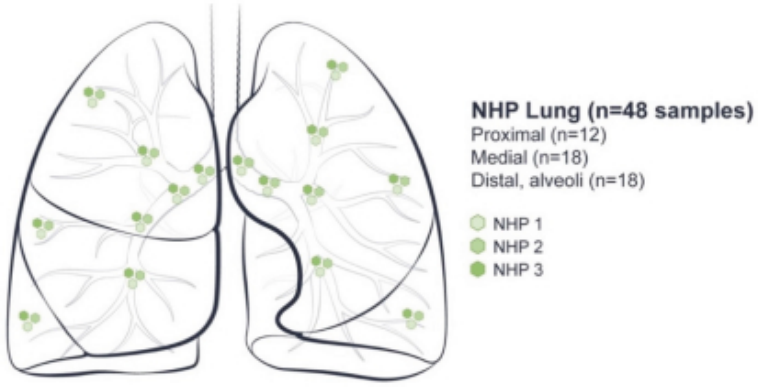
Target Vector Profile for A101 aerosol delivery to lung airway and alveoli:

Conventional AAV capsid vectors such as AAV2 (top panel) are not able to reach lung tissue effectively following aerosol administration, due to mucus and other potential barriers including antibodies and components of innate immunity. Conversely, aerosol administered A101 (bottom panel) is designed for robust and broad transduction of lung cells, including trachea, bronchi and alveoli.

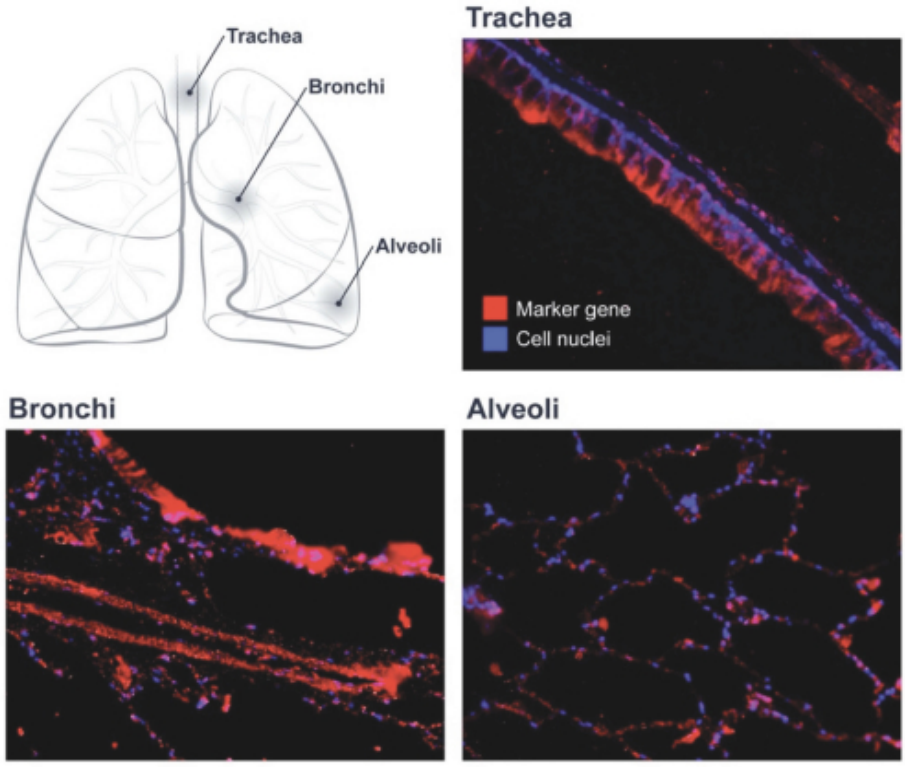


In NHPs, we observed that aerosol delivery of A101 via a standard nebulization device, approved for use in humans, resulted in genome delivery to, and GFP marker gene expression and transduction of, 100% of the 48 lung sites evaluated. We evaluated proximal and medial airways and alveoli in the lung. In addition to efficient lung tissue transduction, we also observed distribution to organs outside the lung was minimal. Genomes in tissues outside the lung were either undetectable or in extremely low concentrations (less than 0.1% of the average genomes per microgram of DNA in the lung tissues) as shown below. This data confirms the efficient protein production throughout all major regions of the lung with minimal biodistribution to the rest of the body.

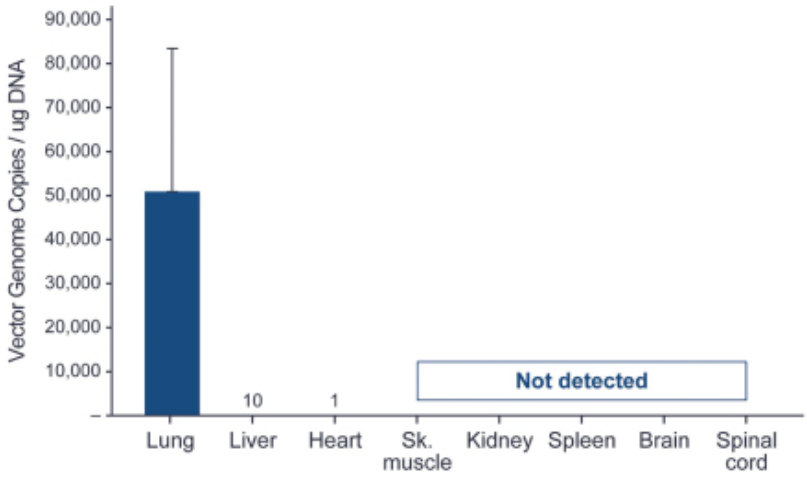
The figure below illustrates the broad distribution of samples in NHPs collected in our A101 biodistribution study. Samples were collected from 16 locations in the three regions of the lung in 3 NHPs. Aerosol delivery of A101 at a dose of 1E13 vg resulted in genome delivery to, and protein expression in, 100% of the 48 lung tissues evaluated.



Aerosol delivery of A101 carrying the EGFP transgene in NHPs was associated with EGFP protein detection (red) by immunofluorescence in proximal (trachea) and medial (bronchi) airway and alveoli.



Aerosol delivery of A101 in NHPs resulted in high levels of genome localization as exhibited in the chart below. A101 genome localization was limited in liver and heart, and not present in other tissues outside the lung. EGFP marker protein expression was also detected in all lung samples.

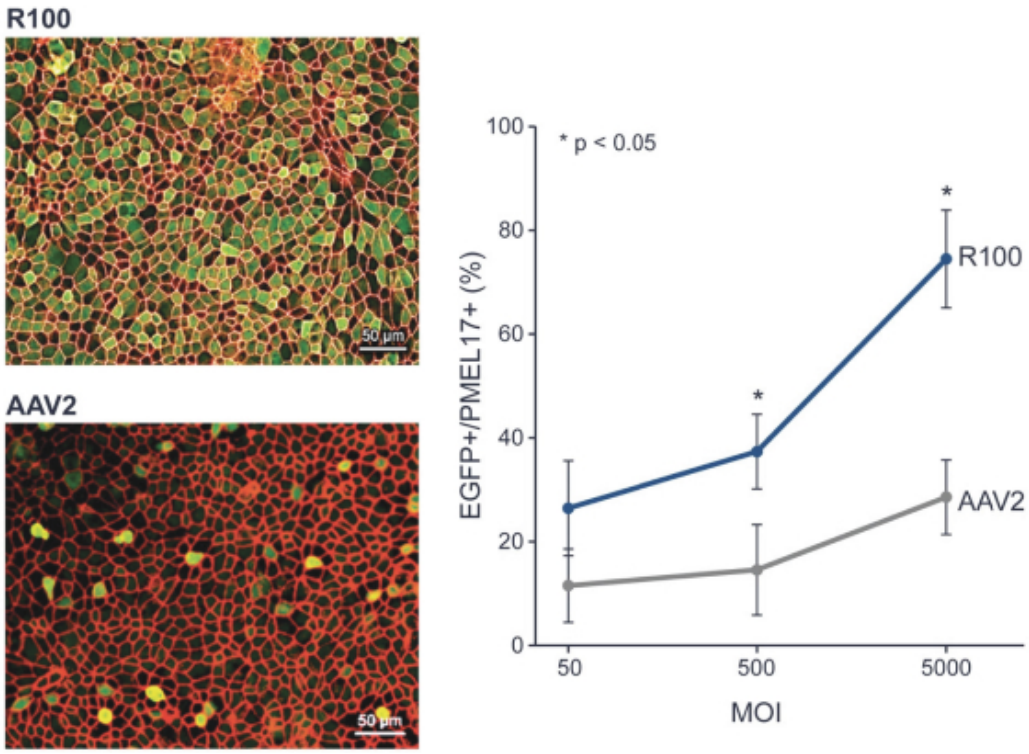


Potential for Improved Transduction and Transgene Expression in Target Human Cell Types and Tissues

We invent targeted and evolved vectors for a specific set of diseases to fit a defined Target Vector Profile, in an effort to generate higher levels of transgene expression than conventional AAV vectors.

In our first example of improved target tissue transduction leading to higher levels of expression and more cells transduced, we observed superior transduction with R100, our intravitreally administered targeted and evolved vector. R100 was significantly more efficient than AAV2 at transducing human retina cells *in vitro*, such as RPE cells below. These in vitro studies comparing R100 to AAV2 helped to inform our decision to move the vector forward and to develop R100-based product candidates. We have not conducted any clinical studies in patients comparing AAV2 to R100. AAV2 is the conventional vector most commonly used for retina treatment in humans. R100 is leveraged in modular fashion for use in all of our ophthalmology product candidates, including 4D-110, 4D-125, 4D-135 and 4D-150.

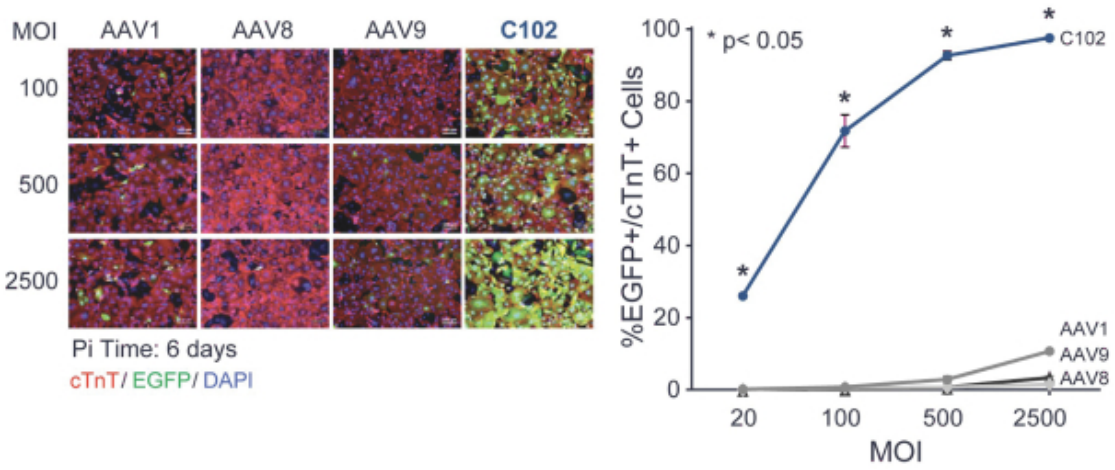
R100 exhibited significantly higher transduction of stem cell derived human retinal pigment epithelial cells in vitro compared to conventional AAV2 across a broad range of concentrations. R100 transduced a higher percentage of cells than AAV2, and marker transgene expression was superior to AAV2



PMEL17 = premelanosome protein, a marker of retinal pigmented epithelial cell identity %EGFP+/PMEL17+ Cells = the percentage of EGFP-expressing cells within the PMEL17-expressing retinal pigmented epithelia population, a quantification of the transduction efficiency of the capsid for the target cell type MOI = multiplicity of infection, a description of dose (vg per cell) for in vitro experiments

In our second example of improved transduction versus conventional AAV vectors, our targeted and evolved vector C102 was invented to efficiently target human heart muscle cells (cardiomyocytes); C102 is used in 4D-310 for Fabry disease. Conventional AAV vectors AAV1, AAV8 and AAV9 have been used by competitors to target heart muscle cells; however, we believe limited transduction with these conventional AAV vectors may limit efficacy and lead to high dose requirements that may present safety challenges. In preclinical studies, C102 exhibited significantly improved transduction of human cardiomyocytes (ventricular phenotype) compared to conventional AAV vectors across a wide range of concentrations, as shown below. These in vitro studies comparing C102 to AAV1, AAV8 and AAV9 helped to inform our decision to move the vector forward and to develop C102-based product candidates. We have not conducted any clinical studies in patients comparing conventional vectors to C102.

C102 exhibited significantly higher transduction in vitro relative to conventional AAV1, AAV8 and AAV9, in human cardiomyocytes of ventricular phenotype. C102 transduced a higher percentage of cells than conventional AAV, and marker transgene expression was superior to conventional AAV



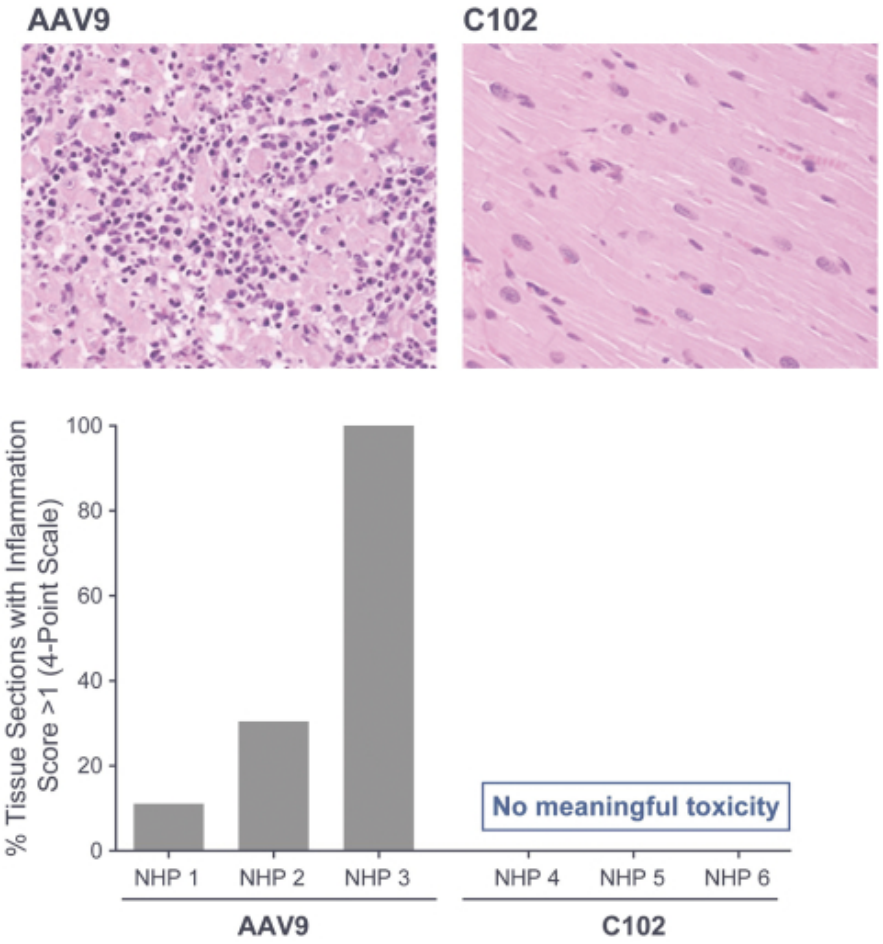
cTnT = cardiac troponin T, a marker of cardiomyocyte cell identity
DAPI = a marker of cell nuclei
MOI = multiplicity of infection, a description of dose (vg per cell) for in vitro experiments
%EGFP+/cTnT+ Cells = the percentage of EGFP-expressing cells within the cTnT-expressing cardiomyocyte population, a quantification of the transduction efficiency of the capsid for the target cell type

Potential for Low Toxicity with Reduced Inflammation Profile

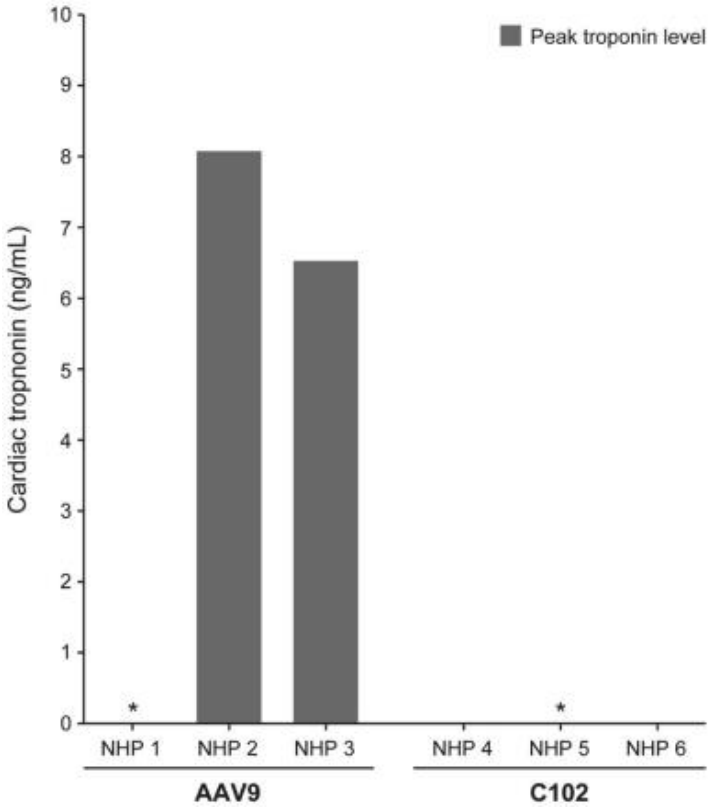
We believe that targeted and evolved vectors invented via Therapeutic Vector Evolution have the potential to cause less inflammation, require lower doses and lead to a lower overall toxicity profile versus conventional AAV vectors such as AAV8 and AAV9. As others have reported, high IV doses with AAV9-based gene therapies in humans and NHPs have been associated with toxicity and inflammation in heart, kidney, liver and neural tissues. Others have also reported that high dose IV treatments with a product candidate incorporating AAV8 have, tragically, resulted in three patient deaths in a clinical trial for X-linked myotubular myopathy.

As illustrated below, in contrast to AAV9, our targeted and evolved vector C102 (used in 4D-310 for Fabry disease) was not associated with significant inflammation or toxicities in NHP heart tissues after IV administration. AAV9 was associated with inflammation and damage in heart tissue as shown on histology and blood tests shown below. These in vivo studies comparing C102 to AAV9 helped to inform our decision to move the vector forward and to develop C102-based product candidates. We have not conducted any clinical studies in patients comparing AAV9 to C102.

After dosing of NHPs with IV C102, no meaningful heart inflammation or toxicity was observed, in contrast to meaningful heart inflammation and necrosis observed in NHPs receiving AAV9, as illustrated in the H&E staining below. Immune cell infiltrate (dark purple) and cardiomyocyte death (rounded formation of cardiomyocytes in pink) associated with AAV9 are highlighted in the left image below. Lack of similar infiltrate associated with C102 is highlighted in the right image below (no dark purple, elongated cardiomyocytes in pink with magenta cell nuclei). Quantification of the full histological analysis provided by an independent veterinary pathologist is included below these images. Of note, the two vectors carried the same CAG promoter and EGFP transgene payload, were packaged and purified using the same process, were quantified using the same assay, and administered in identical fashion at the same contract research organization ("CRO").



After dosing of NHPs with IV C102, no meaningful cardiac troponin release into the blood was observed, in contrast to meaningful elevations in cardiac troponin observed in NHPs receiving AAV9. Of note, the two vectors carried the same CAG promoter and EGFP transgene payload, were packaged and purified using the same process, were quantified using the same assay, and administered in identical fashion at the same CRO.



* *Peak cardiac troponin levels for both NHP 1 and NHP 5 were detectable within the normal range (0.04 ng/mL)*

Overall, our three lead targeted and evolved vectors, R100, C102 and A101, have exhibited favorable tolerability results in NHPs and mice in toxicology studies across our lead product candidate development programs, as summarized below.

	4D-310 GLP Tox	4D-310 Tox & BD	4D-710 Tox & BD	4D-125 Unilateral GLP Tox & BD	4D-110 Unilateral GLP Tox & BD	4D-110 Bilateral GLP Tox & BD
Species	Mouse	NHP	NHP	NHP	NHP	NHP
# dosed	132	9	6	30 eyes	27 eyes	34 eyes
Route of administration	IV	IV	Aerosol	IVT	IVT	IVT
NOAEL	1.5E14 vg/kg	5E13 vg/kg	3E13 vg	1E12 vg/eye	1E12 vg/eye	1E12 vg/eye
Clinical evaluation	No adverse findings	No adverse findings	No adverse findings	No adverse findings; Transient, steroid-responsive uveitis		
Clinical pathology	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Hematology	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Hematocrit	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Clinical chemistry	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Liver enzymes (ALT/AST)	No adverse findings	No adverse findings*	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Gross pathology	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Histopathology	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings	No adverse findings
Cellular immune response	N/A	N/A	BAL: No immune infiltration	ELISpot anti-capsid: Negative; ELISpot transgene: Negative		

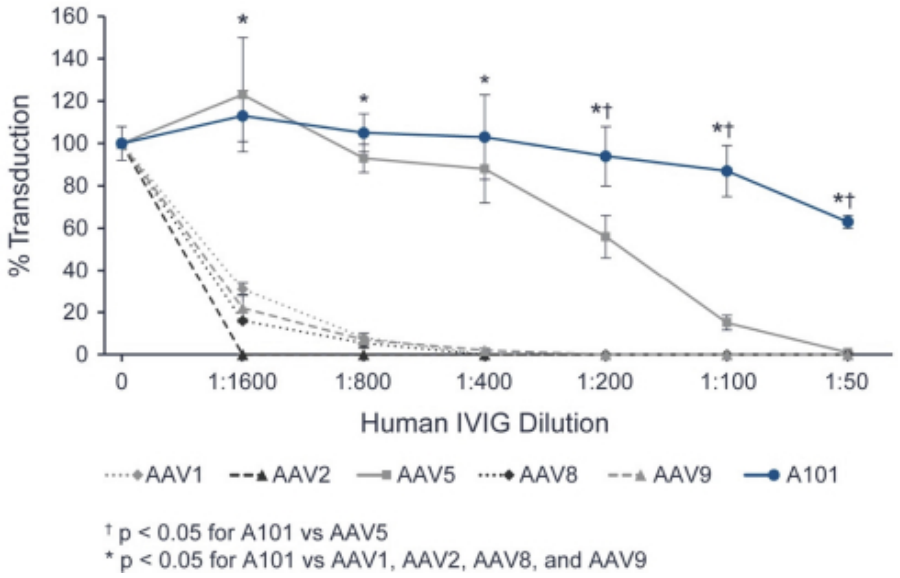
Abbreviations: AE, adverse events; ALT, Alanine transaminase; AST; aspartate aminotransferase; BD, biodistribution; GLP, good laboratory practices; IV, intravenous; IVT, intravitreal; N/A = not yet available, study ongoing; NOAEL, no-observed-adverse-effect-level.

Potential to Resist Inhibition by Pre-Existing Neutralizing Antibodies from Humans: Potential for Re-Dosing and Treating Larger Patient Populations

We have invented targeted and evolved vectors for resistance to inhibition by pre-existing neutralizing antibodies in the human population. We believe that vectors invented in this fashion may broaden our potential addressable patient population compared to conventional AAV vectors. We believe that enhanced resistance to antibodies may result in less neutralization, and therefore potentially better efficacy, after patient treatment. Finally, we believe we have the potential to re-dose patients after receiving other AAV gene therapies, and when desirable by developing product candidates with different targeted and evolved vectors that target the same tissues. This approach would utilize a vector whose antibodies do not cross-react with the vector used in the preceding AAV gene therapy treatment.

For example, the Target Vector Profile for our targeted and evolved vector A101 included aerosol delivery and resistance to antibodies in humans; A101 is used in 4D-710 for cystic fibrosis. As shown below, we observed that A101 had significantly greater antibody resistance than conventional AAV1, AAV2, AAV5, AAV8 and AAV9. These in vitro studies comparing A101 to conventional vectors helped to inform our decision to move the vector forward and to develop A101-based product candidates. We have not performed any clinical studies in patients comparing conventional vectors to A101.

A101 exhibited superior resistance to human antibodies (present in human IVIG) in vitro compared to conventional AAV vectors AAV1, AAV2, AAV5, AAV8 and AAV9 as measured by transduction percentage.



Our Proprietary Therapeutic Vector Evolution Platform

Our proprietary Therapeutic Vector Evolution platform is based on the principles of directed evolution. Directed evolution is a high-throughput platform approach that harnesses the power of evolution in order to create biologics with new and desirable characteristics.

The first step of directed evolution involves the generation of massively diverse libraries of biological variants. In the second step, a target profile is designed with desired biological characteristics. In the final step, selective pressures are applied to these libraries forcing competition to select for improved variants with the desired biological characteristics. This method has been successfully utilized by other researchers to generate protein therapeutics with enhanced biological activities, antibodies with enhanced binding affinity and enzymes with new specificities. The importance of this biotechnology was demonstrated when the Nobel Prize for Chemistry was awarded in 2018 for work on directed evolution of proteins, antibodies and enzymes performed by academic investigators including Dr. Frances H. Arnold at Caltech; these investigators have no relationship to 4DMT.

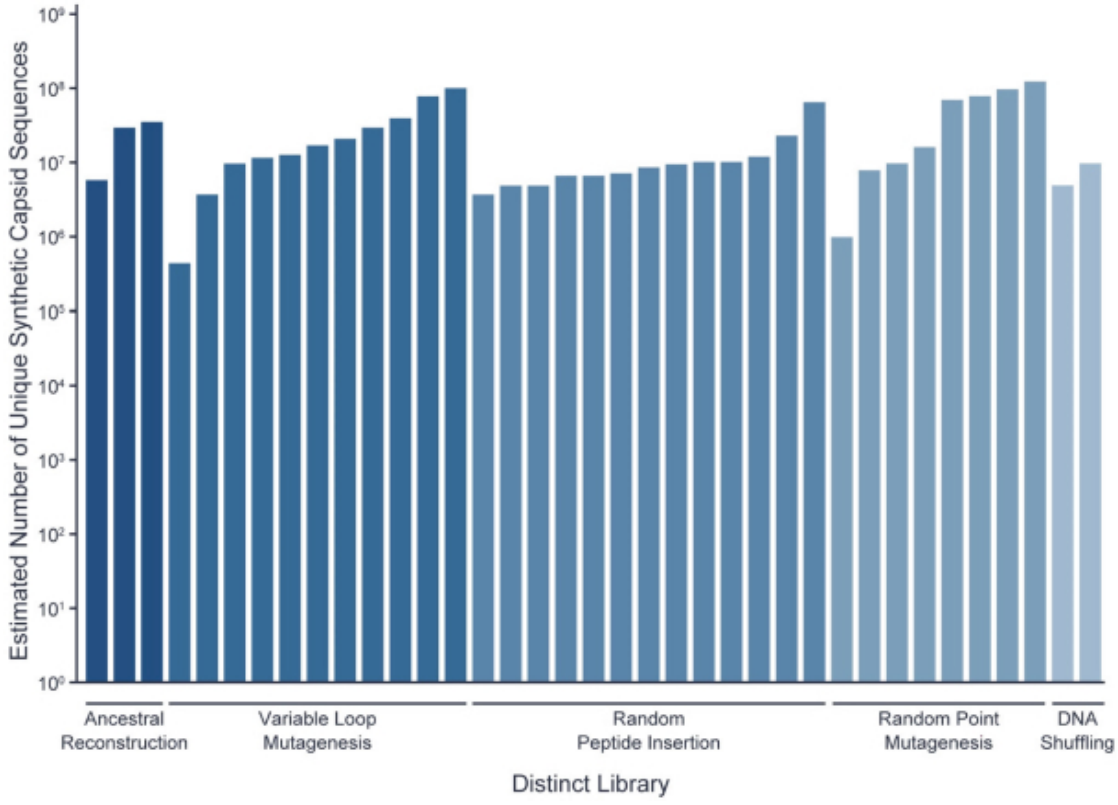
Our co-founder and Chief Scientific Advisor, Dr. David Schaffer, pioneered the use of directed evolution to create improved AAV capsids for use as gene therapy vectors at U.C. Berkeley over 20 years ago. Over the past seven years, we have developed and industrialized our Therapeutic Vector Evolution platform to invent targeted and evolved vectors for use in human therapeutic products. Since in-licensing several libraries from the U.C. Berkeley and creating over 30 newer libraries at our company, we have a total of 40 diverse libraries comprising approximately one billion proprietary synthetic capsid sequences. In addition, we have developed significant experience in performing Therapeutic Vector Evolution programs in NHPs, with 14 capsid selections completed to date. We believe this will help us to develop product candidates to address a broad swath of diseases in rare and large patient populations, including those other gene therapies cannot.

Diverse Libraries of Synthetic Capsid Sequences

Each library results from the application of a different genetic diversification methodology, such as variable loop mutagenesis, random peptide insertion, random point mutagenesis, DNA shuffling and ancestral reconstruction, and is also defined by its starting material (AAV capsid gene sequences). Furthermore, we apply bioinformatics, emerging technologies, and experience and know-how resulting from previous discovery programs to continually improve and expand our libraries and improve our ability to select customized targeted and evolved vectors.

We believe the size and diversity of our proprietary synthetic capsid libraries represent a differentiating competitive advantage for us in the field of gene therapy.

Our 40 distinct libraries comprise approximately one billion synthetic capsid sequences. Each library results from the application of a different genetic diversification methodology, such as variable loop mutagenesis, random peptide insertion, random point mutagenesis, DNA shuffling and ancestral reconstruction, and is also defined by its starting material (AAV capsid gene sequences). We have estimated the number of capsid sequences for 37 of these libraries as illustrated below.



The Target Vector Profile Followed by Competitive Vector Selection

We employ a rigorous approach to inventing targeted and evolved vectors based on what we consider an optimal vector and product profile, which we term the Target Vector Profile. For any set of target diseases that affect the same tissue(s), this profile includes any combination of the following: the optimal route of administration for targeting the specific tissue(s) in humans, the optimal dose range, the desired distribution of vector transduction within the target organs, overall biodistribution and/or antibody resistance.

We use our Therapeutic Vector Evolution platform to select the "fittest" targeted and evolved capsid that best matches our Target Vector Profile. We achieve this through serial rounds of "selection", or discovery, with each round of selection filtering down to fewer and fewer synthetic capsids from the original library. This funneling process is achieved by applying selective pressures—forcing competition—among all synthetic capsid variants in the library to achieve delivery to the target cells as defined in the Target Vector Profile. Each round is performed in a primate *in vivo*, sometimes in the presence of human antibodies.

By the end of a typical Therapeutic Vector Evolution process, we will have identified approximately two to four targeted and evolved vectors, or hits, based on their frequency in the final pool of synthetic capsid sequences, in addition to numerous sequences present at lower frequencies. We then file patent applications disclosing select identified gene sequences from the discovery program. We believe this deliberate approach to selection *in vivo* in NHPs and in human tissues should lead to identification of targeted and evolved vectors with a higher likelihood of therapeutic benefit in humans.

Vector Invention Results to Date

We have completed 14 unique vector selection programs or "selection processes" for specific proprietary synthetic capsids with specific Target Vector Profiles. Across our clinical development and discovery portfolio, we have utilized four different routes of administration, including intravenous, intravitreal, aerosol, and intrathecal administrations. We have completed discovery programs targeting a diverse array of tissue types including various retinal cell types, heart and skeletal muscle tissues, different lung cell types, liver, brain, dorsal root ganglia, and synovial joints. We have identified and filed patent applications on over 300 unique targeted and evolved vectors.

Characterization of Novel Vector Variant "Hits" and "Leads"

Vector hits are typically characterized by three major criteria: manufacturing, human cell and human organotypic model transduction, and delivery to tissues in NHPs by the designated route of administration. Vector hits may also be evaluated for transduction in the presence of human antibodies. In order to perform characterization studies, vectors are armed with marker gene payloads such as enhanced green fluorescent protein ("EGFP"). After these hits have been evaluated, a lead vector is selected.

Directed Evolution-Based Promoter and Transgene Discovery Platforms

To complement our Therapeutic Vector Evolution platform and modular development approach, we are generating next-generation optimized promoter elements and transgenes using a combination of directed evolution and proprietary algorithms.

Currently available promoters may lack sufficient strength of expression and selectivity for clinical benefit of AAV gene therapies. In addition, for some AAV gene therapy products a smaller promoter region may be essential for the gene payload to fit in the AAV. Therefore, we believe there is a need for better promoters for many AAV products to enable or enhance their therapeutic benefit. We generate Target Promoter Profiles for any given product and disease target. This promoter profile includes target

cell specificity and strength in order to maximize tolerability and/or biologic activity, as well as any necessary size constraints. Under one of our sponsored research agreements with U.C. Berkeley, we are working with our co-founder Dr. Schaffer to create customized and proprietary promoters for use in our pipeline products. Our libraries of novel and diverse synthetic promoters have been engineered and currently comprise approximately ten million unique sequences. Our discovery platform identifies the best promoters within the libraries for a specific Target Promoter Profile.

In addition to our synthetic promoters, we are developing next-generation optimized transgene discovery platform. Our discovery platform uses a high-throughput approach, harnessing both directed evolution and rational design algorithms, to identify novel transgenes that express therapeutics proteins. For example, we have developed transgenes to express RNAi in target cells of interest for treatment of disease. These transgene-expressed RNAi molecules, or ddRNAi, are anchored by a microRNA backbone that not only enhances stability and limits off-target effects, but also facilitates high expression within target cells and thereby increases efficacy. Our technology allows us to powerfully knock down disease-causing transcripts, combining a design for a high degree of selectivity with the goal of long-term expression afforded by AAV-based gene therapy.

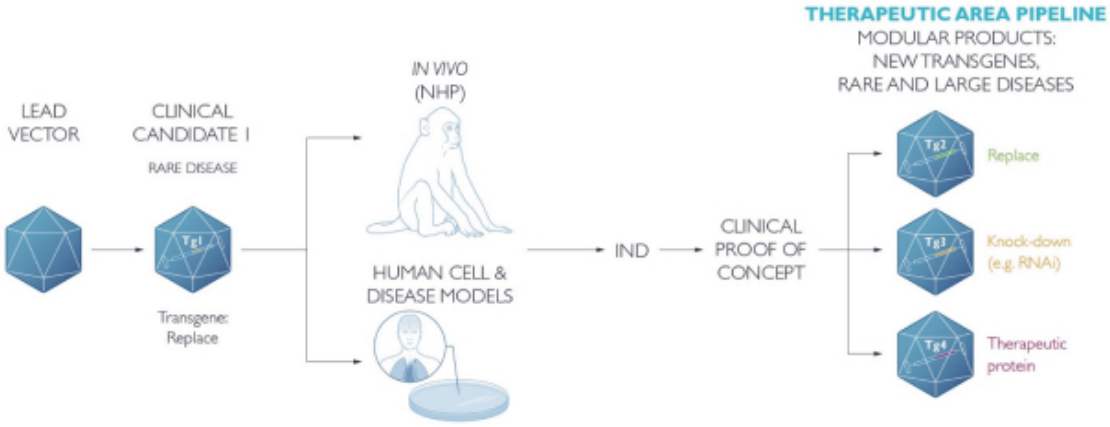
Product Pipeline

Overview

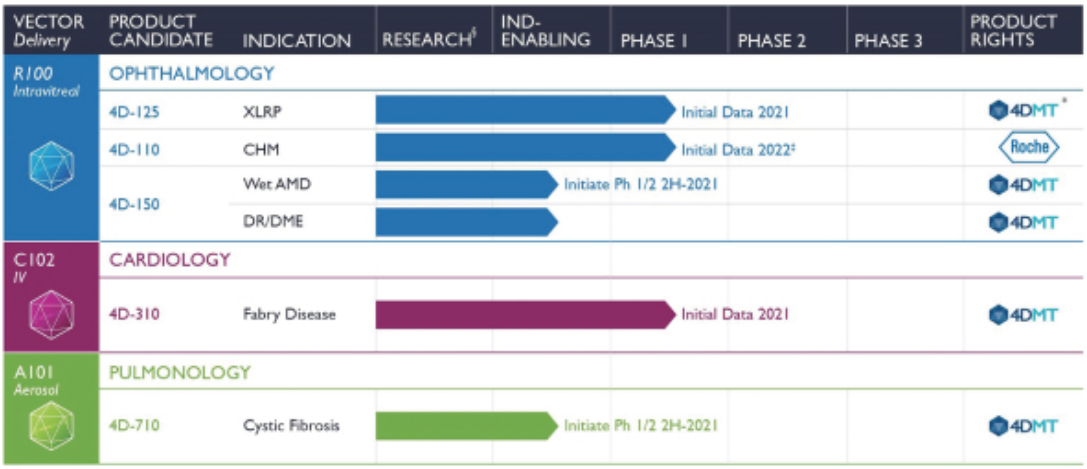
Our platform enables a broad and diverse pipeline of transformative targeted gene therapies that we are advancing through clinical trials. We currently have a product pipeline that includes targeted gene therapies in three therapeutic areas: ophthalmology, cardiology (primary or secondary to systemic diseases) and pulmonology.

For each of these therapeutic areas, we invented a targeted and evolved lead vector employing Therapeutic Vector Evolution. These lead vectors were designed for delivery by optimal and routine clinical routes to the target tissue(s). As illustrated below, our platform is designed to be modular in that an evolved vector invented for a given therapeutic area can be equipped with different transgene payloads to produce unique product candidates to treat other diseases affecting the same tissue type(s). We believe this modularity will help inform the clinical development of subsequent product candidates using the same vector.

Lead vectors that have been invented through Therapeutic Vector Evolution are used to design and engineer product candidates for specific diseases. These product candidates are tested in NHP and in human cell & disease models prior to IND filing and entry into clinical trials. While a first product candidate utilizing one of our targeted and evolved vectors is advancing through development, we build additional product candidates to follow closely and rapidly by using the same lead vector in modular fashion.



Our pipeline includes product candidates for both rare disease and large patient populations and is represented in the chart below.



* *4DMT is responsible for the development of this product candidate; Roche has an exclusive option to assume development and commercialization at its sole cost and expense. Such an option may be exercised prior to pivotal trial initiation.*

‡ Reporting in coordination with our partner Roche.

§ The Research stage involves (1) defining the Target Vector Profile then deploying Therapeutic Vector Evolution with our capsid libraries in non-human primates (NHPs) and using competitive selection to identify targeted and evolved vectors from our libraries that demonstrate the strongest match to the Target Vector Profile; then (2) optimizing our product candidates using the lead vector by conducting in vivo and in vitro evaluation of various transgene and promoter construct candidates in cell and animal models, and the selection of at least one product candidate to move forward into IND-enabling studies.

Ophthalmology Therapeutic Area

Introduction

We are developing product candidates to treat severe ophthalmology diseases. Our targeted and evolved vector, R100, is used in all four of our ophthalmology product candidates and was invented for routine intravitreal injection, leading to transgene expression across the entire surface area of the retina, and in the major cell layers of the retina. We believe this modularity will help inform the clinical development of subsequent product candidates using the same vector.

Our product candidate 4D-125 is enrolling patients in an ongoing Phase 1/2 clinical trial in patients with XLRP related to mutations in the *RPGR* gene. The primary objectives of this trial are to evaluate the safety and maximum-tolerated dose of 4D-125. Secondary endpoints include assessments of biologic activity, including both visual field function and anatomical endpoints. Enrollment has been completed in the dose escalation phase of this study, with six patients treated. The dose expansion phase of this study will enroll patients at the highest Phase 1 dose of 1E12 vg/eye. 4D-125 has been well tolerated without any dose-limiting toxicities. We expect to report initial clinical data in the second half of 2021. 4DMT currently holds the worldwide commercialization rights for 4D-125 and Roche holds an exclusive option to in-license the product prior to pivotal trial initiation.

Our product candidate, 4D-110, is enrolling patients in an ongoing Phase 1 clinical trial in patients with choroideremia related to mutations in the *CHM* gene. The primary objectives of this trial are to evaluate the safety and maximum-tolerated dose of 4D-110. Secondary endpoints include assessments of biologic activity, including visual acuity, visual field function and anatomical endpoints. Enrolled patients have been followed previously in our natural history study, in which we have enrolled 55 patients, and have followed 47 of these patients for at least two years. Enrollment has been completed in the dose escalation phase of this study, with six patients treated. The dose expansion phase of this study will enroll patients at the highest Phase 1 dose of 1E12 vg/eye. 4D-110 has been well tolerated without any dose-limiting toxicities. In coordination with our partner Roche, we expect to report initial clinical data in 2022.

We also have two wholly owned preclinical product candidates. We are developing 4D-150 for the treatment of wet AMD and diabetic retinopathy, including DME, and we expect to initiate a wet AMD clinical trial for 4D-150 in the second half of 2021. We are also developing 4D-135 for the treatment of adRP. We expect to initiate IND enabling studies for 4D-135 in 2021.

4D-125 for X-Linked Retinitis Pigmentosa ("XLRP")

Disease Background, Unmet Medical Need and Target Patient Population XLRP is a rare inherited X-linked recessive genetic disorder that causes progressive vision loss and blindness in boys and young men. There are currently no approved therapies for XLRP. Seventy percent of cases are caused by mutations in the retinitis pigmentosa GTPase regulator ("*RPGR*") gene. The estimated worldwide prevalence of XLRP due to *RPGR* variants is approximately one in 25,600 people, which represents approximately 24,000 patients in the United States, and France, Germany, Italy, Spain and the United Kingdom (together, EU-5). It is characterized by dysfunction and degeneration of photoreceptors in the retina. Loss of *RPGR* function in retinal cells causes the progressive loss of rod and cone photoreceptors, leading to the progressive loss of vision. Symptoms of XLRP are initially characterized by night blindness, followed by loss of peripheral visual field, decreasing visual acuity and eventually blindness. While males are usually the most affected, approximately 25% of heterozygous females experience loss of vision.

Our Solution

We are developing 4D-125 for the treatment of patients with XLRP with *RPGR* mutations. 4D-125 is designed to benefit patients at all stages of XLRP, including early stage patients whose entire viable retinas are not adequately treated by subretinal surgery. This product candidate is comprised of R100 and carries a codon-optimized *RPGR* transgene engineered for expression within human photoreceptors. In NHP models, we have observed widespread transduction and transgene expression across the entire retinal surface. We believe that 4D-125 has the potential to successfully treat XLRP patients at the earliest stages of their disease progression and ideally, slow or prevent progression and retain vision.

Competition and Differentiation: AAV Gene Therapy for XLRP

Several companies are developing subretinal AAV gene therapies for patients with XLRP. Subretinal administration results in transduction and direct treatment of only a small fraction of the retina. On Phase 1 and 2 trials, investigators have reported improvements in visual field function within the localized retina area receiving the treatment bleb in a subset of patients. These AAV gene therapies require invasive subretinal surgery, which has been associated with subretinal surgery-related adverse events. In addition, subretinal surgery results in transduction of only a small fraction of the retina and is therefore limited to patients with more advanced disease with a small remaining area of viable retinal cells.

We believe 4D-125 has the potential to be differentiated from other AAV gene therapies in clinical development, to our knowledge, on the basis of four design features:

1. Safe and routine intravitreal route of administration: Product candidates that utilize conventional AAV vectors such as AAV2, must be administered by subretinal surgery for XLRP. Unlike those product candidates, R100, which is included in our product candidate 4D-125, was

specifically invented for intravitreal injection. Notwithstanding any potential design features of 4D-125, this easier and widely used route of administration should result in safer and faster clinical trial enrollment, better efficacy and faster market uptake.

2. Treatment of the entire retinal surface: Unlike conventional AAV vectors administered by subretinal surgery, which reportedly treat only a small fraction of the retinal surface, 4D-125 can be used to treat the entire retinal surface following intravitreal injection, potentially broadening its therapeutic applicability.
3. Feasibility of treating early stage patients: We believe it will be feasible to safely treat early stage patients before they start to lose their retina. 4D-125 is designed to treat the entire surface of the retina, including the periphery where degenerative diseases like XLRP start. In addition, intravitreal injection is recognized as a safe, simple and routinely used method of administering therapeutics.
4. Commercial opportunity: Intravitreal injections are widely adopted by many practicing ophthalmologists and used to treat a number of ophthalmological indications. As a result, we believe 4D-125 has the potential for rapid market uptake, if approved.

Preclinical Animal Model Pharmacology and Toxicology Studies

We completed a single dose IND-enabling toxicology and biodistribution study in 30 NHPs with 4D-125. 4D-125 was administered at doses of 1E11 vg/eye or 1E12 vg/eye by intravitreal injection. Animals were sacrificed at three weeks, three months or six months. No meaningful toxicities were reported anywhere in the body, including specifically within the retina. Mild, transient uveitis was observed, but no chronic inflammation was reported; all animals were under systemic immunosuppression during the study. We detected vector genomes and XLRP transgene RNA expression in all treated retinas at both dose levels; the genome and RNA levels were higher in the high dose animals.

In an *in vitro* model of the disease, XLRP patient photoreceptors were derived from XLRP-diseased white blood cells that had been reprogrammed into induced pluripotent stem cells. Diseased photoreceptors were transduced with 4D-125 and protein lysates were harvested 30 days post-transduction. 4D-125 transduced cells expressed significantly more transgene product (hRPGRorf15) than control cells. Moreover, this expressed protein was shown to be active as measured by glutamylation (GT335).

Clinical Development: Phase 1/2 Clinical Trial

We are currently enrolling patients on a Phase 1/2 clinical trial. This is a dose-escalation and dose-expansion trial of intravitreal injection with 4D-125 in patients with clinically significant XLRP due to *RPGR* gene mutation. The primary objectives of this trial are to evaluate the safety and maximum tolerated dose of 4D-125. Secondary endpoints include assessments of biologic activity, including both visual field function and anatomical endpoints. Enrollment has been completed in the dose escalation phase of this study, with six patients treated. The dose expansion phase of this study will enroll patients at the highest Phase 1 dose of 1E12 vg/eye. 4D-125 has been well-tolerated and has not resulted in dose-limiting toxicities. No serious adverse events related to the agent have been reported. We expect to report initial clinical data from this trial in the second half of 2021.

4D-110 for Choroideremia

Disease Background, Unmet Medical Need and Target Patient Population

Choroideremia is a monogenic blinding disease, affecting approximately 13,000 patients in the United States and EU-5. No products are approved currently for the treatment of this disease in the United States or European Union. This X-linked, progressive degenerative disease of the retina and choroid is caused exclusively by mutations in the *CHM* gene that encodes for the REP1 protein. While

choroideremia primarily affects men, some heterozygous females also suffer variable visual loss from the condition.

Choroideremia initially manifests as night-blindness and peripheral visual field defects, usually starting in the first two decades of life. As the disease progresses, the visual field begins to constrict relatively early in the disease's progression, which hinders patients' ability to conduct daily activities, such as driving. Many patients become blind by 30 years of age. A patient with advanced disease will be legally blind by virtue of poor visual acuity and minimal preserved visual field. Almost all mutations in the *CHM* gene result in production of a non-functional REP1 protein. REP1 is essential for the activation (prenylation) of Ras-associated binding ("Rab") proteins involved in intracellular vesicle trafficking.

Our Solution

We are developing 4D-110 for the treatment of choroideremia. 4D-110 is designed for a single intravitreal injection and to benefit patients at all stages of disease, including early stage patients whose entire viable retinas are not adequately treated by subretinal injection. 4D-110 is comprised of R100 and is engineered to deliver the *CHM* transgene, the dysfunctional gene in choroideremia, to human RPE cells safely. We believe that 4D-110 has the potential, if approved, to successfully treat choroideremia patients at the earliest stages of their disease progression and ideally, slow or prevent progression and retain vision.

Competition and Differentiation: AAV Gene Therapy for Choroideremia

Conventional subretinal AAV gene therapy approaches are being developed to treat choroideremia. Subretinal administration results in transduction and direct treatment of only a small fraction of the retina. Biogen is developing a subretinally administered product candidate for choroideremia called NSR-REP1. In 2018, data was reported from a Phase 1/2 clinical trial in patients with end-stage choroideremia, who have only a small remaining area of viable retinal cells in the central field of vision and reduced visual acuity. In this trial, investigators concluded that best corrected visual acuity improved in a subset of patients. A pivotal randomized Phase 3 clinical trial was initiated in 2018. This AAV gene therapy approach requires invasive subretinal surgery, which has been associated with subretinal surgery-related adverse events. In addition, subretinal surgery results in transduction of only a small fraction of the retina and is therefore limited to patients with more advanced disease who have a small remaining area of viable retinal cells.

We believe 4D-110 has the potential to be differentiated from AAV gene therapies in development on the basis of four design features:

1. Safe and routine intravitreal route of administration: Unlike conventional AAV vectors such as AAV2, which are utilized in subretinal surgery product candidates for choroideremia, R100 was specifically selected for simple and safe intravitreal injection. Notwithstanding any potential design features of 4D-110, this ease of administration should result in safer and faster clinical trial enrollment, better efficacy and faster market uptake.
2. Treatment of the entire retinal surface: Unlike products candidates utilizing conventional AAV vectors and administered by subretinal surgery, which reportedly treat a small fraction of the retinal surface, 4D-110 can be used to treat the entire retinal surface following intravitreal injection.
3. Feasibility of treating early stage patients: We believe 4D-110 has the potential to safely treat early stage patients before they start to lose their retina. 4D-110 is designed to treat the entire surface of the retina, including the periphery where degenerative diseases like choroideremia start. In addition, intravitreal injection is recognized as a safe, simple and routinely used method of administering therapeutics.
4. Commercial opportunity: Intravitreal injections are widely adopted by many practicing ophthalmologists and used to treat a number of ophthalmological indications. As a result, we believe 4D-110 has the potential for rapid market uptake, if approved.

Preclinical Animal Model Pharmacology and Toxicology Studies

A total of 44 NHPs have been treated with 4D-110 on two GLP toxicology and biodistribution studies. No significant adverse effects or toxicities were reported.

We completed a single dose IND-enabling toxicology and biodistribution study in 27 NHPs dosed with 4D-110. 4D-110 was administered at doses of 1E11 vg/eye or 1E12 vg/eye by intravitreal injection. Animals were sacrificed at three weeks, three months or six months. No meaningful toxicities were reported anywhere in the body, including specifically within the retina. Mild, transient cortico-steroid responsive anterior uveitis was reported in a minority of treated NHP. No chronic inflammation was reported; all animals were under systemic immunosuppression during the study. We detected vector genomes and *CHM/REP1* transgene RNA expression in all treated retinas at both dose levels; the genome and RNA levels were higher in the high dose animals.

We subsequently completed a bilateral intravitreal 4D-110 GLP toxicology and biodistribution study in 17 NHPs dosed with 4D-110. 4D-110 was administered at doses of 3E11 vg/eye or 1E12 vg/eye by intravitreal injection. Animals were sacrificed at three weeks, 13 weeks and 26 weeks. No meaningful toxicities were reported anywhere in the body, including specifically within the retina.

Transient cortico-steroid responsive uveitis was reported. No chronic inflammation was reported; all animals were under systemic immunosuppression during the study. We detected vector genomes and *CHM/REP1* transgene RNA expression in treated retinas at both dose levels.

In preclinical pharmacology studies involving human choroideremia patient-derived RPE cells, 4D-110 led to functional REP1 protein expression that corrected RAB27A trafficking from the cytoplasm to the cell membrane. In similar fashion to normal RPE cells, 4D-110-treated diseased RPE cells derived from choroideremia patients had RAB27A protein associated with their cell membranes; this finding confirmed the functionality of the REP1 protein expressed from 4D-110. In contrast, in untreated diseased cells, RAB27A was demonstrated diffusely throughout the cytoplasm.

Clinical Development: Phase 1 Clinical Trial and Natural History Study

We have fully enrolled a natural history study of over 50 patients with choroideremia to document rate of visual and anatomical decline, and to identify candidates who are most likely to benefit from participation in our current Phase 1/2 clinical trial. Fifty-five patients were enrolled and 47 of these patients have been followed for at least two years. Statistically significant declines in fundus autofluorescence area were reported by investigators over the two-year span after enrollment, with progression evident within 12 months. We expect that many of these subjects will enroll in our current Phase 1 clinical trial, or in future trials we may conduct.

We are currently enrolling patients on a Phase 1 clinical trial. This is a dose-escalation and dose-expansion trial of intravitreal injection with 4D-110 in patients with choroideremia due to *CHM* gene mutation. The primary objectives of this trial are to evaluate the safety and maximum-tolerated dose of 4D-110. Secondary endpoints include assessments of biologic activity, including visual acuity, visual field function and anatomical endpoints. Endpoint changes in each individual treated patient over time, before treatment while on the Natural History Study, will be compared to endpoint changes after 4D-110 treatment in the same patient whenever possible. Patients may therefore serve as their own control for assessments of these endpoints. Enrollment has been completed in the dose escalation phase of this study, with six patients treated. The dose expansion phase of this study will enroll patients at the highest Phase 1 dose of 1E12 vg/eye. 4D-110 has been well-tolerated and has not resulted in dose-limiting toxicities. In coordination with our partner Roche, we expect to report initial clinical data from this trial in 2022. We licensed exclusive worldwide rights to 4D-110 to Roche.

We licensed exclusive worldwide rights of 4D-110 to Roche in 2017. We are primarily responsible for initial development, including preclinical development, manufacturing, filing and maintaining the IND and conducting the Phase 1 clinical trial. Upon completion of initial development, Roche will be

responsible for development including conducting any pivotal clinical trials and commercialization, if approved. We are entitled to development costs reimbursement, development milestones and royalties and sales milestones on this product candidate.

4D-150 for Wet AMD and Diabetic Retinopathy

Disease Background, Unmet Medical Need and Target Patient Population

Wet AMD is a type of macular degeneration where abnormal blood vessels (choroidal neovascularization or CNV) grow into the macula, the central area of the retina. As a consequence, CNV causes retina swelling and edema, and bleeding can occur and cause visual distortion and reduced acuity. The proliferation of abnormal blood vessels in the retina is stimulated by VEGF. This process distorts and can potentially destroy central vision and may progress to blindness without treatment. There are on average 200,000 new incidences of wet AMD per year in the United States alone. Wet AMD accounts for approximately 10% of all diagnosed cases of AMD, but it results in an estimated 90% of the legal blindness caused by all types of AMD. High expression levels of VEGF appear to play a causal role in the symptoms of wet AMD.

Diabetes mellitus affects approximately 400 million adults worldwide and the prevalence is expected to increase by approximately 45% in the next decade. Diabetic eye disease, primarily diabetic retinopathy (“DR”), is a leading cause of vision loss and blindness in working-age adults and occurs due to the development of diabetic macular edema (“DME”; swelling, edema and hemorrhage in the central vision) and complications arising from proliferative diabetic retinopathy (PDR; retinal neovascularization causing bleeding and retinal detachment). The prevalence of diabetic retinopathy is high, affecting almost one-third of adults over 40 years of age with diabetes. In the United States approximately 4.2 million adults have DR and 655,000 have vision-threatening DR.

The current treatment paradigm for wet AMD and diabetic retinopathy, including DME, is intravitreal injection of patients with anti-VEGF proteins that inhibit the proliferation of new blood vessels, reducing edema and bleeding and allowing some visual acuity to be recovered. Most anti-VEGF therapies require repeated intravitreal injections in office every few weeks to every few months to obtain full efficacy. When patients miss doses, they may experience accelerated vision decline. Based on current clinical experience, after several years of treatment, the early vision gains are frequently lost, and acuity declines are observed for reasons that may include variable treatment regimens and poor patient compliance.

We believe these major retinal diseases are ideal candidate applications for gene therapy. There are multiple products on the market that validate the anti-VEGF therapeutic approach, and emerging randomized clinical trial data suggests that inhibiting additional molecular targets can extend the efficacy and durability of anti-VEGF alone. Delivering intravitreal therapies to the eye is routine, and there is an advantage for a single dose gene therapy that can provide long-term efficacy in patients for whom compliance, or treatment resistance, is a problem.

Our Solution

We are developing 4D-150, a wholly owned intravitreal AAV gene therapy candidate for wet AMD and diabetic retinopathy, including DME. These angiogenic diseases of the retina, including wet AMD and diabetic retinopathy, represent therapeutic markets of over $9.7 billion in annual global sales. We retain all worldwide rights to 4D-150.

This product candidate is engineered for three distinct mechanisms-of-action. 4D-150 is engineered to inhibit VEGF and PlGF (placental growth factor) via aflibercept expression and secretion, and to inhibit a third angiogenic factor via an additional transgene insert. We believe that targeting three different angiogenic factors has the potential for greater efficacy versus a single anti-VEGF mechanism-of-action in patients with these retinal diseases, including patients with resistance to anti-VEGF therapy alone. Intravitreal delivery of biologics to the eye is routine, and there would be an advantage for a single

dose therapy that could provide long-term efficacy in patients for whom compliance, or treatment resistance, is a problem.

Competition and Differentiation: AAV Gene Therapy for wet AMD and Diabetic Retinopathy

AAV gene therapy approaches are being developed by several companies to treat wet AMD by delivering a functional copy of an anti-angiogenic transgene by either subretinal injection with a conventional AAV vector, or intravitreal administration with a mouse-evolved vector. It remains to be demonstrated whether conventional AAVs or mouse-evolved vectors can deliver significant retinal coverage while limiting off-target effects. In comparison, our targeted and evolved vectors are designed and tested in NHPs which more closely resembles the anatomy of the human eye. We believe this provides comprehensive retinal coverage through less invasive and more commonly used intravitreal injections while delivering an improved tolerability profile with limited inflammation. To our knowledge, 4D-150 would be the only AAV gene therapy asset in wet AMD and DR to utilize an intravitreal vector (R100) discovered through directed evolution in NHP. In addition, *in vitro* studies of R100 versus AAV2 have shown superior transduction by R100 on human retinal cells. We have not compared R100 to AAV2 in patients in clinical studies. R100 has been associated with a low inflammation profile and lack of adverse findings in 91 NHP eyes injected on GLP toxicology studies.

In addition, to our knowledge, 4D-150 is the first gene therapy product candidate for the eye designed to implement three mechanisms of action by directly inhibiting three different angiogenic growth factor targets, including VEGF and PlGF. We therefore believe there is significant differentiation between our gene therapy product candidate and other AAV gene therapeutics in development in this therapeutic area.

We believe 4D-150 has the potential to be differentiated from approved agents, and those in clinical development to our knowledge, on the basis of five design features:

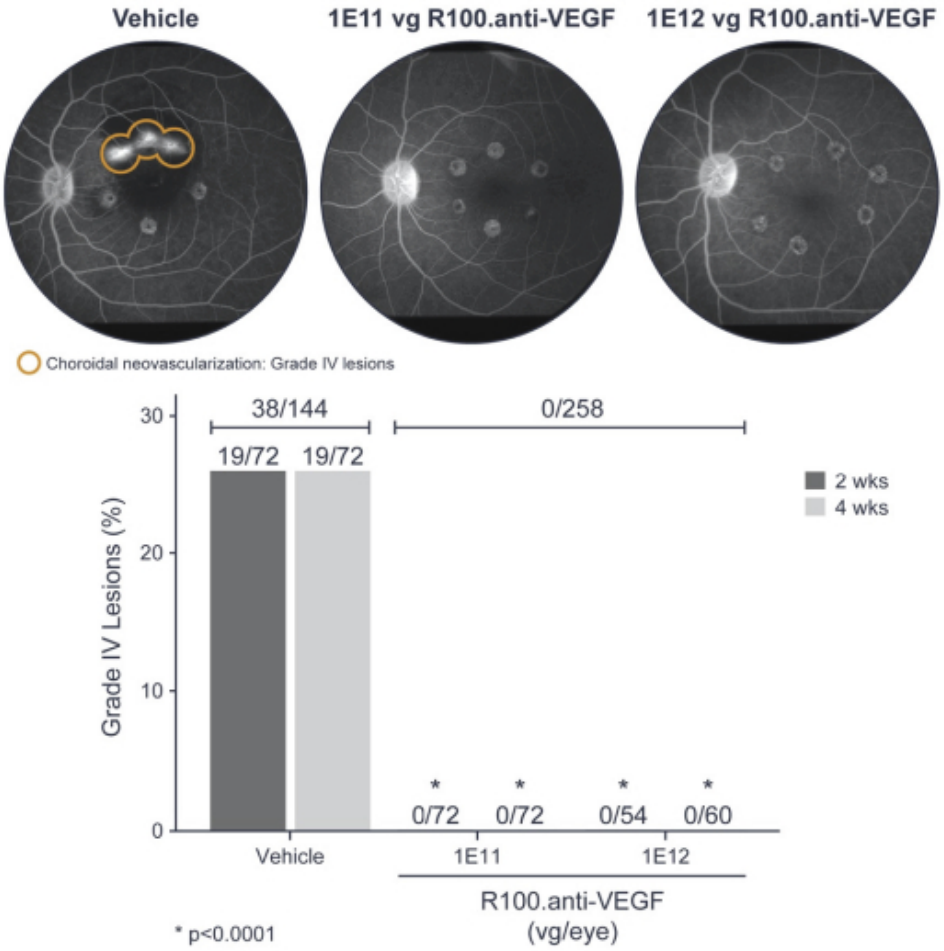
1. Three distinct mechanisms-of-action: An intravitreal dose of 4D-150 should result in sustained anti-angiogenic effects through three distinct mechanisms of action.
2. One-time therapy: Unlike intravitreal protein therapeutics that require repeat dosing every few weeks for a patient's lifetime, 4D-150 is designed as a one-time dose.
3. Novel vector evolved in NHPs for efficient intravitreal delivery: Unlike conventional AAV vectors such as AAV2 or the mouse-evolved AAV vector 7m8, R100 was specifically selected from our collection of over one billion synthetic capsid sequences in NHPs and for use in humans.
4. Low inflammation profile design: Following intravitreal injection, R100 has shown low inflammation profile and no significant adverse findings in three GLP toxicology studies, involving 91 NHP eyes, with two different 4DMT products utilizing the R100 vector (4D-110, 4D-125). In addition, R100 vector-based product candidates 4D-125 and 4D-110 have been administered to twelve patients at doses up to 1E12 vg/eye without dose-limiting toxicities or serious adverse events observed to date.
5. Commercial opportunity: Intravitreal injections are widely adopted by many practicing ophthalmologists and used to treat a number of ophthalmological indications. As a result, we believe 4D-150 has the potential for rapid market uptake, if approved. Additionally, the low inflammation profile we have observed in our R100-based GLP toxicology studies, if reproduced in the clinic with 4D-150, may promote broad product adoption if approved.

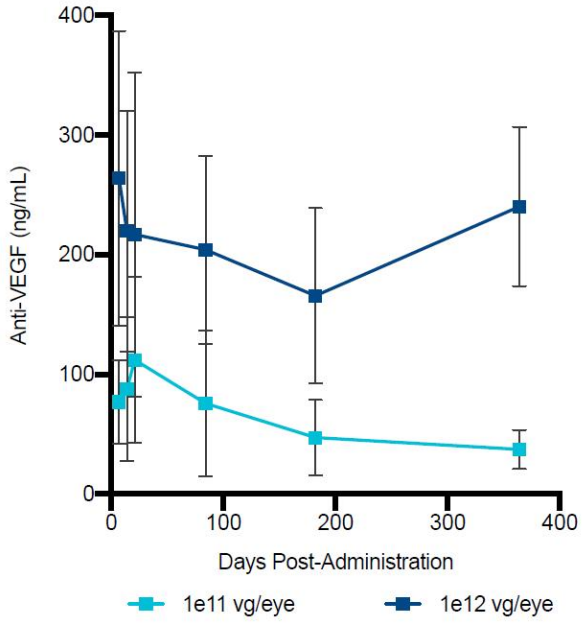
Preclinical Animal Model Pharmacology and Toxicology Studies

We carried out a proof-of-concept efficacy study in NHPs with a research construct using the R100 vector to deliver an anti-VEGF transgene (R100.anti-VEGF). In this study using the retinal laser-induced CNV model, we treated animals with intravitreal R100.anti-VEGF at doses of both 1E11 and 1E12 vg per eye. Animals received steroid treatment for 28 days following IVT administration of R100.anti-VEGF and

remained off steroids for the remainder of the study. No adverse findings were reported in-life through 12 months of follow up. We demonstrated sustained transgene expression through detection of anti-VEGF activity in serial aqueous humor samples. Control animals had the most severe (grade 4) angiogenic and leaky retina lesions in approximately 26% (19 of 72) of laser-targeted sites at two weeks and four weeks. Conversely, none of the sites in treated animals at either dose level at either timepoint had grade 4 lesions (p<0.0001).

Our 4D-150 prototype comprising R100 expressing an anti-VEGF protein prevented development of Grade IV lesions at 2 and 4 weeks after administration in 100% of lasered locations in the NHP retina (at both low and high doses) with evidence of sustained transgene expression through detection of anti-VEGF activity in serial aqueous humor samples.





† In the 1E12 vg treatment group, three NHP eyes (18 lesions) and two NHP eyes (12 lesions) were not assessable at the 2 week and 4 week timepoints, respectively.

A study of 4D-150 is ongoing in the retinal laser-induced CNV model in NHPs to assess efficacy, toxicology and biodistribution.

Development Plan

We expect to initiate a clinical trial in the second half of 2021.

4D-135 for Autosomal Dominant Retinitis Pigmentosa ("adRP")

Disease Background, Unmet Medical Need and Target Patient Population

adRP is a rare inherited autosomal dominant genetic disorder that occurs in both sexes and causes progressive vision loss and blindness. There are currently no approved therapies for adRP. adRP is characterized by dysfunction and degeneration of photoreceptors in the retina. Approximately 35% of adRP cases are caused by mutations in the *rhodopsin* ("RHO") gene. The estimated worldwide prevalence of adRP due to RHO variants is approximately one in 52,000 people, which represents approximately 11,600 patients in the United States and EU-5. Loss of RHO function in retinal cells causes the progressive loss of rod photoreceptors, leading to the loss of vision experienced by patients. Symptoms of adRP are initially characterized by night blindness, followed by loss of peripheral visual field, decreasing visual acuity and eventually blindness.

Our Solution

We are developing 4D-135, a wholly owned intravitreal AAV gene therapy product candidate for the treatment of patients with adRP caused by mutations of the *RHO* gene. 4D-135 is designed to benefit patients at all stages of adRP, including early stage patients whose entire viable retina are not adequately treated by subretinal surgery. This product candidate is comprised of R100, an intravitreally administered targeted and evolved vector. 4D-135 is engineered to carry an RNAi targeting mutation-independent

adRP and a *RHO* transgene resistant to the RNAi in a broad suppress and replace approach. We retain all worldwide rights to 4D-135.

Competition and Differentiation: AAV Gene Therapy for adRP

A few companies are developing therapies for patients with adRP, including a subretinal AAV gene therapy product candidate. We believe 4D-135 has the potential to be differentiated from other AAV gene therapies in development to our knowledge, on the basis of five design features:

1. Long term durable RNAi activity: In contrast to relatively short-acting ASO technology, 4D-135 is designed for DNA-based delivery of long-term RNAi activity against the mutant *RHO* gene product.
2. Safe and routine intravitreal route of administration: Unlike conventional AAV such as AAV2, which are utilized in subretinal surgery product candidates for other retinal diseases like XLRP, R100 was specifically selected for safe and routine intravitreal injection. This ease of administration should result in faster clinical trial enrollment.
3. Treatment of the entire retinal surface: Unlike product candidates utilizing conventional AAV vectors and administered by subretinal surgery, which reportedly treats a small fraction of the retinal surface, 4D-135 is designed to be used to treat the entire retinal surface following intravitreal injection.
4. Feasibility of treating early stage patients: Given the potential of 4D-135 to treat the entire surface of the retina, including the periphery where degenerative disease like adRP start, we believe it will be feasible to safely treat early stage patients before onset of retinal degeneration. In addition, intravitreal injection is recognized as a safe, simple and routinely used method of administering therapeutics.
5. Commercial opportunity: Intravitreal injections are widely adopted by many practicing ophthalmologists and used to treat a number of ophthalmological indications. As a result, we believe 4D-135 has the potential for rapid market uptake, if approved.

Preclinical Animal Model Pharmacology and Toxicology Studies

We plan to complete a single dose IND-enabling toxicology and biodistribution study in NHP. We are also developing an *in vitro* model of diseased photoreceptors derived from adRP patients. These diseased photoreceptors will be treated with 4D-135.

Development Plan

We expect to initiate IND-enabling studies for 4D-135 in 2021.

Cardiology Therapeutic Area

Introduction

We are developing product candidates to treat cardiomyopathies. These target indications may include both primary cardiomyopathies that involve the heart exclusively, as with hypertrophic cardiomyopathies, or secondary cardiomyopathies that occur in the context of a systemic disease syndrome, as with lysosomal storage diseases. In the context of secondary cardiomyopathies, such as Fabry disease, we design and engineer the product to treat all diseased organs including the high unmet medical need in the heart. Our targeted and evolved vector C102, used in all of our cardiology product candidates, was invented for low dose intravenous infusion, leading to transgene expression throughout the myocardium in all regions of the heart. We believe that this modular product approach, utilizing C102 for all of our cardiology product candidates, and by switching the therapeutic transgene inserts, will help inform the clinical development of subsequent product candidates using the same vector.

Our lead product candidate, 4D-310, is currently in an ongoing Phase 1/2 clinical trial in adult patients with Fabry disease. The primary objectives of this trial are to evaluate the safety and maximum-tolerated dose of 4D-310. Secondary endpoints include biomarker assessments of plasma AGA activity and markers of biologic activity in the heart, including cardiac MRI. We expect to treat early onset classic Fabry disease patients as well as severely affected late-onset patients, including those with cardiomyopathy. We expect to report initial clinical data in the second half of 2021. 4D-310 received Fast Track Designation from the FDA in the third quarter of 2020 for the treatment of Fabry disease to improve pain, disability and organ dysfunction.

4D-310 for Fabry Disease

Disease Background, Unmet Medical Need and Target Patient Population

Fabry disease is a monogenic disease caused by mutations in the *GLA* gene which encodes for the alpha-galactosidase A ("AGA") enzyme that results in the body's inability to produce sufficient AGA enzyme activity, causing the accumulation of toxic levels of sphingolipids, such as the substrate globotriaosylceramide-3 ("Gb3"), in critical organs, including the heart, kidney and blood vessels. The cardiomyopathy in Fabry disease is the leading cause of death, accounting for 54% of deaths, and is secondary to the systemic lysosomal storage disease syndrome. Such substrate accumulation in the heart can lead to life-threatening heart failure, arrhythmias, vascular blockages. Fabry disease is progressive and fatal, with an average life expectancy of approximately 50 years. Progression of the disease causes significant reduction in the quality of life and significant economic burden associated with greater patient needs for supportive care.

Annual worldwide sales of Fabry medicines were approximately $1.5 billion in 2019. We estimate the potential initial addressable male Fabry patient population in the United States and EU-5 to be up to 19,000 individuals, 57% of which suffer from Classic Fabry disease. Of note, we estimate the prevalence of individuals with Fabry disease-associated *GLA* mutations in the United States and EU-5 falls between 50,000 and 70,000 in the United States and the EU-5 based on recent newborn screening. Pre-treatment antibody titers to gene therapy, including 4D-310, may result in a reduction in the addressable patient population, if antibody titers at baseline are shown to be predictive of treatment response and/or tolerability.

The current treatment paradigm for Fabry disease is an infusion of replacement AGA enzyme every two weeks, a class of therapies broadly referred to as enzyme replacement therapies ("ERT"). For example, Fabrazyme received accelerated regulatory approval in the United States based on improvements in kidney interstitial capillary substrate biopsy endpoint, but it failed the primary endpoint in registrational trials and lacks full approval in the United States.

In addition to high burdens of therapy, due to the short-half life in the blood, patients on ERTs lack therapeutic concentrations of AGA in their blood for the majority of time between infusions, potentially limiting clinical benefit. Furthermore, since AGA is normally produced within target cells themselves, ERTs reportedly lack efficient uptake by parenchymal cells including cardiomyocytes; hence, patients remain at risk of cardiac complications including death. Finally, antibodies develop to AGA in the majority of classic Fabry disease patients after ERT and can further worsen clinical outcomes.

Therefore, we believe cardiac-targeted treatment of Fabry disease is still an unmet medical need.

Our Solution

We are developing 4D-310 for the comprehensive systemic treatment of Fabry disease. 4D-310 is designed for an efficient, single low dose IV administration to benefit classic and late onset patients, including those who have previously received ERT. 4D-310 is comprised of C102 and is engineered with a codon-optimized *GLA* transgene under control of a ubiquitous promoter. 4D-310 is designed to generate both high, stable plasma AGA activity, potentially resulting in cross correction of a broad range of critical organs, and to generate AGA activity via intracellular production within disease cells including cardiomyocytes.

We believe 4D-310 has the potential for “mutation independent” treatment of both “classic” (early onset, severe) as well as late onset Fabry disease, both of which are often associated with cardiomyopathy. We believe reducing substrate in cardiomyocytes would represent a strategic advantage and significant opportunity in the treatment of Fabry-associated cardiomyopathy, which we believe remains a significant unmet medical need and leading cause of death in Fabry disease patients.

In addition, AGA produced by 4D-310 within target cells themselves will not be exposed to serum antibodies against AGA. These antibodies develop following ERT in approximately 80% of classic Fabry disease patients. We therefore have the potential to treat this patient population via intracellular production of AGA, in contrast to approaches that rely exclusively on delivery of AGA through the bloodstream.

Finally, single dose gene therapy treatment with 4D-310 may obviate the need for biweekly ERT infusions in these patients, and/or for every other day small molecule medicines for patients amenable to AGA chaperone therapy.

Competition and Differentiation: AAV and Lentivirus-Engineered Stem Cell Gene Therapy for Fabry Disease

Several companies are developing liver-expressing AAV gene therapy for Fabry disease through the use of non-targeted AAV designed for expression from the liver only using liver-specific promoters to restrict transgene expression to the liver. These product candidates are designed to produce and secrete AGA enzyme for activity in the blood, as with ERT, but with more stable blood levels than achieved with intermittent ERT infusions. When administered as ERT in patients, the AGA protein has not been shown definitively to enter cardiomyocytes or other affected parenchymal cells. It is therefore unclear whether gene therapy production of AGA from the liver or stem cells alone, with secretion into the bloodstream, would result in effective correction in cardiac muscle cells or other affected parenchymal cells such as in the kidney.

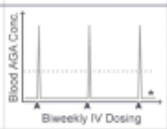
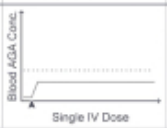
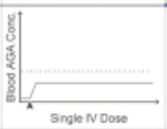
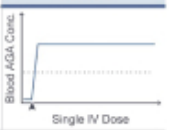
We believe 4D-310 is the only gene therapy candidate designed specifically to express the AGA enzyme in cardiac tissues, as well as in other affected tissues in these patients, potentially addressing a major unmet medical need.

We believe 4D-310 has the potential to be differentiated from approved agents, and those in clinical development to our knowledge, on the basis of four design features:

1. Dual mechanisms-of-action: An IV dose of 4D-310 is designed to generate both stable sustained levels of AGA enzyme activity in blood and endothelial cells following secretion from the liver, plus high AGA levels directly within muscle cells throughout the heart. Cells within the kidney, blood vessels and small intestine also produce intracellular AGA after 4D-310 treatment, albeit at significantly lower levels than in the heart.
2. One-time therapy: Unlike AGA chaperones that require dosing every other day for a patient’s life, or IV ERT every two weeks for life, 4D-310 is designed as a single dose potentially curative therapy.
3. AGA mutation-independent biologic activity: Unlike AGA chaperones that are only effective against specific AGA mutations present in a minority of Fabry patients, 4D-310 is designed to treat in Fabry patients with any AGA mutation.

4. Resistance to AGA antibodies: We believe that 4D-310 may be able to treat patients that have anti-AGA antibodies. Those antibodies develop in approximately 80% of classic Fabry disease patients (early onset, severe disease) treated with ERT. This is in contrast to competing approaches that rely exclusively on AGA delivery through the bloodstream, that may be inhibited by these antibodies since AGA comes into contact with anti-AGA antibodies that may inhibit delivery to target organs. Unlike ERT and gene therapies that are designed to rely exclusively on AGA production and secretion from the liver into the blood, 4D-310 is designed to include intracellular AGA production in target tissues themselves, thus avoiding antibody contact and inhibition. We therefore plan to evaluate the treatment of patients with pre-existing AGA antibodies, potentially resulting in a larger addressable patient population.

The target product profile for 4D-310 is compared to competing technologies below. Many aspects of this profile have been supported by data generated to date with either the C102 vector or with 4D-310 itself.

		ERT		Gene Therapy	
MOA	**Product Design**	AGA enzyme infusions	Patient-derived Stem Cells	AAV-mediated Liver-directed	4D-310
AGA Delivery Through the Bloodstream	Pharmacokinetics ··· Normal ▲ Time of dose ★ Lifelong				
	Cross-correction endothelial cells	+	+	+	+
	Single dose administration	–	+	+	+
	Stable sustained concentration of AGA enzyme activity in blood	–	+	+	+
	AGA production & secretion from the liver	–	–	+	+
	No required chemotherapy—bone marrow ablation	n.a.	–	+	+
AGA Production in Target Cells	Heart	–	–	–	+
	Kidney	–	–	–	+
	Blood vessels	–	–	–	+
Avoid AGA Neutralization	Intracellular production	–	–	–	+

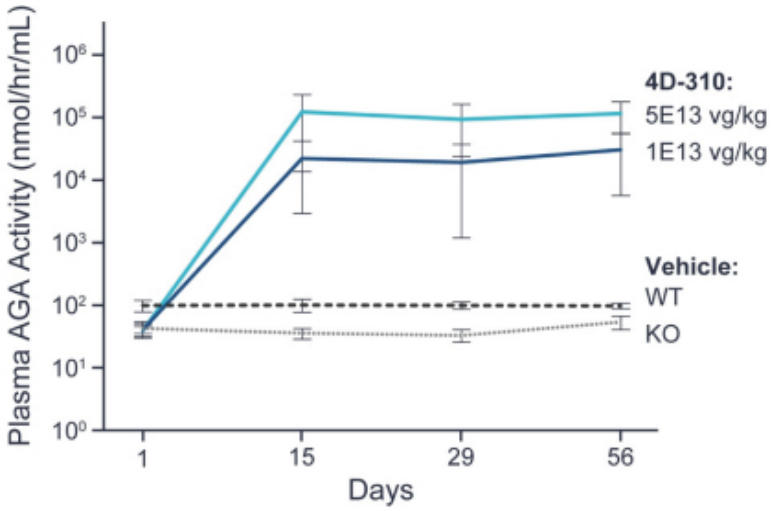
Abbreviations: Ab, antibodies; AGA, aspartylglucosaminidase; AAV, adeno-associated virus; ERT, enzyme replacement therapy; IV, intravenous; n.a., not applicable.

Preclinical Animal Model Pharmacology and Toxicology Studies

We completed an IND-enabling GLP toxicology and biodistribution study of 4D-310 in normal mice. No meaningful toxicity was reported at doses up to 1.5E14 vg/kg, based both on in-life and histopathology assessments. This dose is 300% of the highest planned dose in our Phase 1/2 clinical trial. 4D-310-mediated AGA expression and/or AGA enzyme activity was observed in all target tissues tested, including heart, kidney, blood vessels, small intestine and blood.

Pharmacology studies have been completed in Fabry disease knock-out mice. We observed that a single IV treatment with 4D-310 resulted in high stable blood concentrations and durable AGA production in target tissues, including the heart and kidney, and that toxic Gb3 metabolites were reduced significantly in all evaluated target tissues versus vehicle control. Efficacy was demonstrated with doses as low as 1E12 vg/kg. No adverse findings were observed in these knock-out animals at doses as high as 5E13 vg/kg.

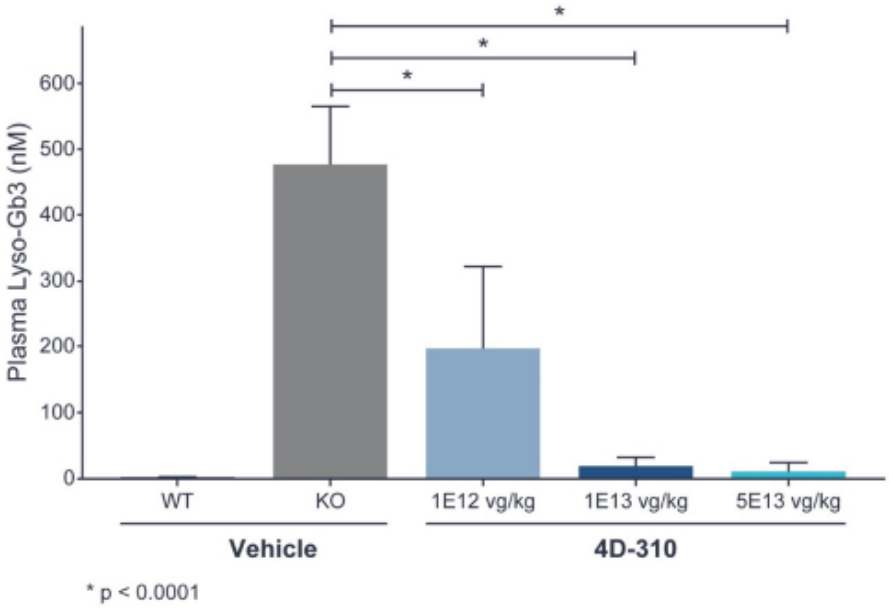
Plasma AGA activity in Fabry mice after treatment with 4D-310 was measured to be approximately 1,200-fold higher than in control vehicle-treated Fabry mice at all measured timepoints after treatment with 4D-310 at 5E13 vg/kg.



WT = wild type

KO = Fabry knock out mouse model

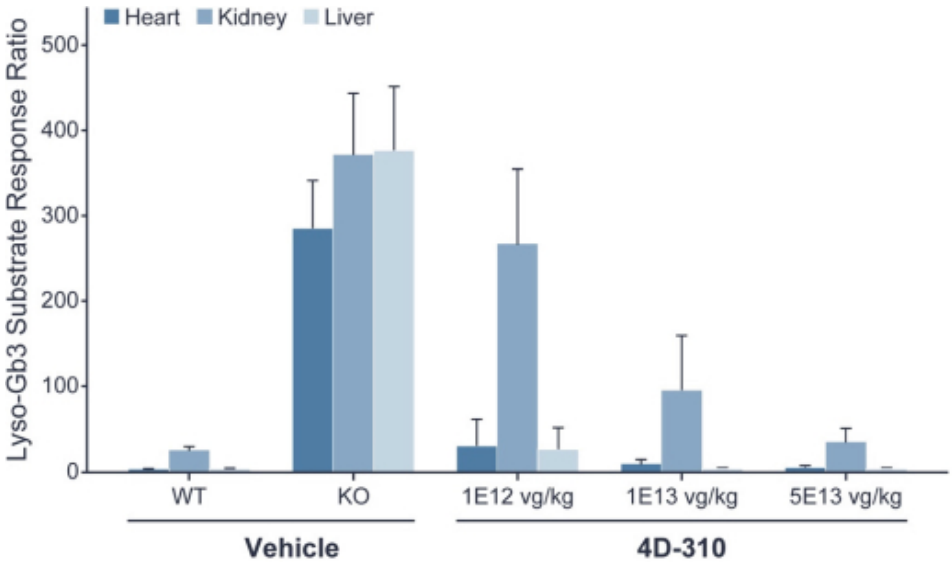
Dose-dependent decrease in plasma lyso-Gb3 was measured at Week 8 in Fabry mice after treatment with 4D-310. 1E13 and 5E13 dose levels achieved reduction of plasma lyso-Gb3 by greater than 95%.



WT = wild type

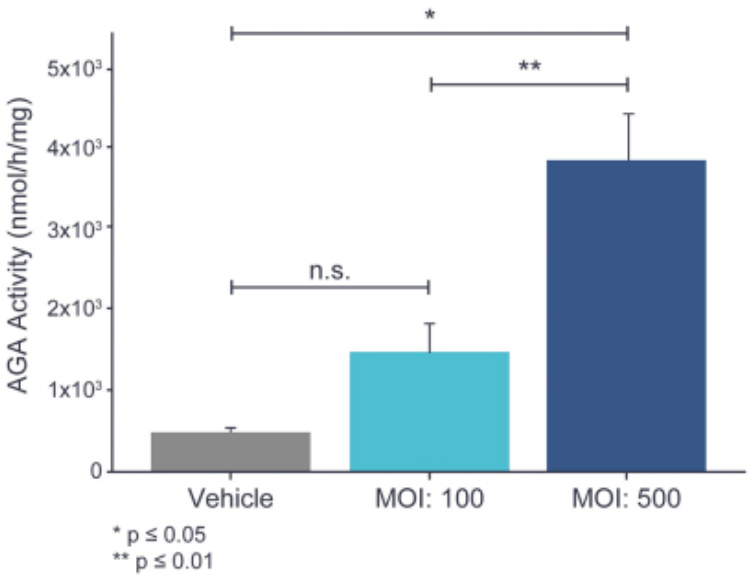
KO = Fabry knock out mouse model

Dose-dependent decrease in tissue Gb3 was measured at Week 8 in Fabry mice after treatment with 4D-310). Tissue Gb3 levels in Fabry mice approached that of normal mice in both heart and liver at 1E13 vg/kg and 5E13 vg/kg dose levels. Kidney Gb3 levels were reduced by approximately 75% in the 1E13 vg/kg group and levels approached normal in the 5E13 vg/kg dose group.



In studies with 4D-310 *in vitro* in human Fabry patient-derived cardiomyocytes, we observed dose-related AGA expression and function. Data in Fabry patient-derived cardiomyocytes demonstrated that treatment with 4D-310 results in efficient transduction and functional AGA protein production; AGA activity was observed both within Fabry cardiomyocytes and secreted into the media.

Cardiomyocytes that were differentiated from Fabry patient-derived fibroblasts expressed functional secreted AGA enzyme after treatment with 4D-310.



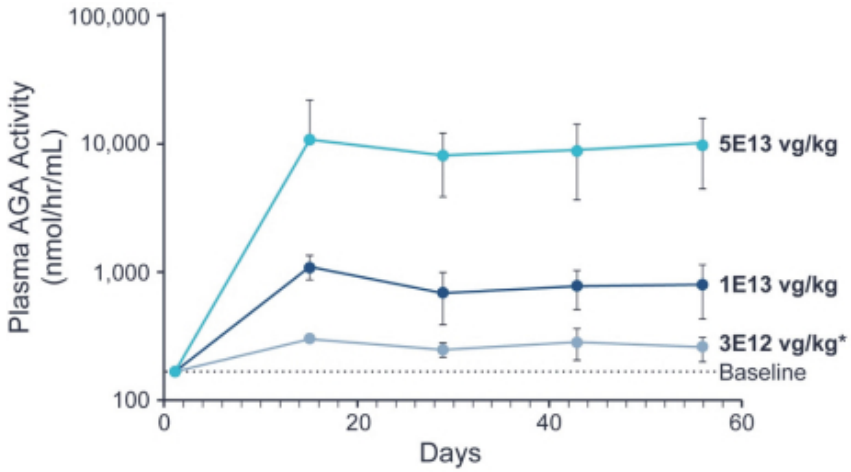
MOI = multiplicity of infection
n.s. = not significant
NT = not treated

We performed a dose-ranging toxicity and biodistribution study in NHPs. Doses of 3E12, 1E13 and 5E13 vg/kg were well-tolerated and resulted in AGA activity concentrations in blood equal to *1.9-fold, 3.4-fold and 70-fold* higher than pretreatment blood levels, respectively, within 14 days after treatment. NHPs used in this study were healthy and had normal baseline levels of AGA activity. No meaningful toxicity was noted clinically or with blood testing. Histopathology assessments were normal. Tissue analyses demonstrated dose-related 4D-310 genome delivery, RNA expression and AGA activity throughout the heart, especially within the left ventricle which is the key target tissue; AGA expression and enzymatic activity were also demonstrated within the kidney.

Delivery (genomes) and transduction (mRNA) were consistently measured throughout organs important to the management of Fabry disease in all NHPs treated with 4D-310. The number of positive tissue samples within NHPs across all three dose levels are indicated below.

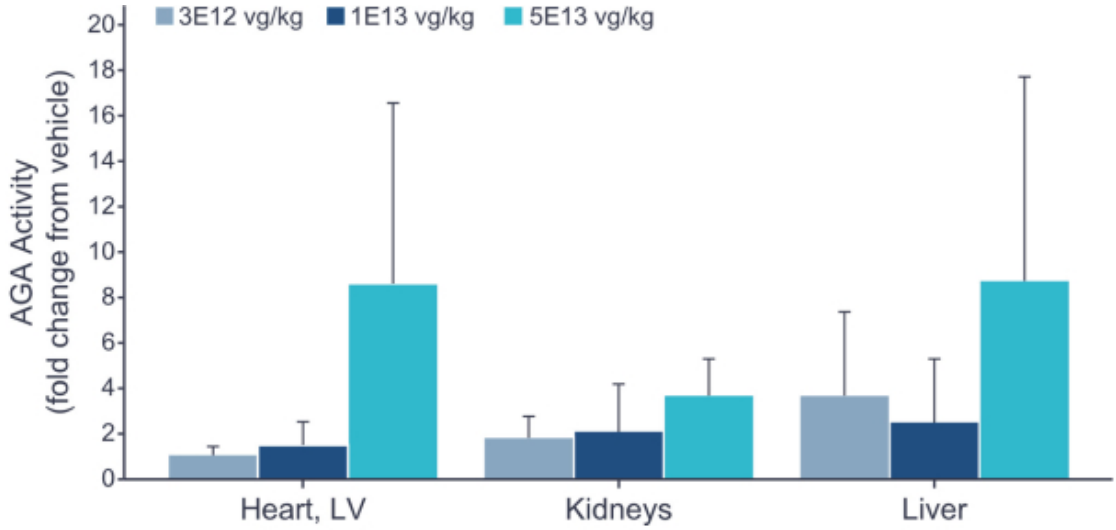
4D-310	Heart (LV)	Kidneys	Liver
Genome (qPCR)	18/18 (100%)	18/18 (100%)	18/18 (100%)
mRNA (RT-qPCR)	18/18 (100%)	18/18 (100%)	18/18 (100%)

Median plasma AGA activity in NHPs after treatment with 4D-310 was measured to be approximately 70-fold, 3.4-fold and 1.9-fold higher than baseline at 8 weeks after treatment with 4D-310 at 5E13, 1E13 and 3E12 vg/kg doses, respectively. Average plasma AGA activity levels for these time points are presented below.

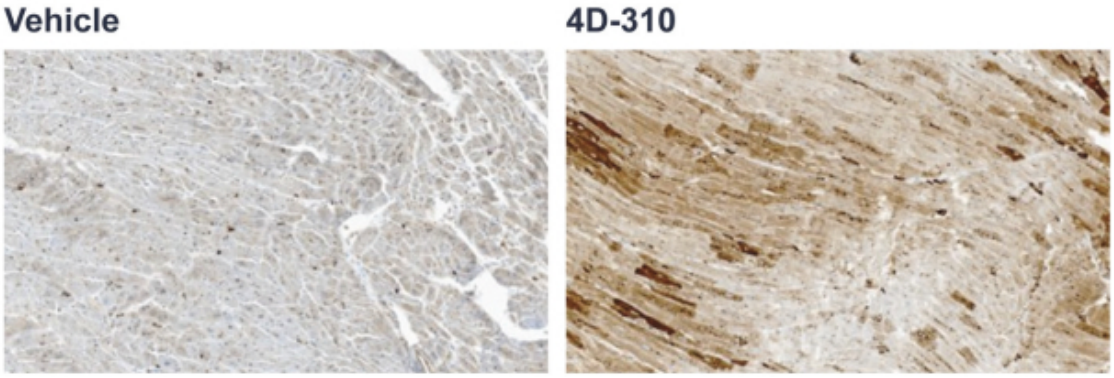


* *One NHP in the low dose cohort has been excluded from the dataset as a positive statistical outlier as it exhibited AGA activity that was 66 to 124 standard deviations higher than the average of other NHPs treated with low dose 4D-310.*

Tissue AGA activity was measured in key organs in healthy NHPs, with normal baseline AGA activity levels, after treatment with 4D-310 at low, medium and high doses. Below are data for tissues which are most important to the management of Fabry disease.



IV delivery of 4D-310 in NHPs was associated with AGA enzyme detection (brown) by immunohistochemistry in the heart, kidneys and liver at low and high dose. Illustrative images below highlight transduction of cardiomyocytes at 5E13 vg/kg dose.



Clinical Development: Phase 1/2 Clinical Trial

We are currently enrolling patients on a Phase 1/2 clinical trial. The first patient dosed in the first quarter of 2021. This is a dose-escalation and dose-expansion trial expected to enroll early onset classic Fabry disease patients and severely affected late-onset patients with cardiomyopathy. The primary objectives of this trial are to evaluate the safety and maximum-tolerated dose of 4D-310. Secondary objectives include biomarker assessments of plasma AGA activity and markers of biologic activity in the heart, including cardiac MRI. We expect to report initial clinical data from this trial in the second half of 2021.

Pulmonology Therapeutic Area

Introduction

We are developing product candidates to treat lung diseases. Our targeted and evolved vector, A101, is used in all of our pulmonology disease product candidates and was invented for aerosol delivery, leading to transgene expression throughout all regions of the lung airways and alveoli, as well as resistance to pre-existing antibodies in the human population. We believe that this modular product approach, utilizing A101 for multiple product candidates by switching the therapeutic transgene insert, will help inform the clinical development of subsequent product candidates using the same vector.

Our first pulmonology product candidate is 4D-710 for cystic fibrosis lung disease. This IND candidate has completed a non-GLP dose-ranging toxicology and biodistribution testing study in NHPs by aerosol delivery. No notable adverse effects were reported, and widespread biodistribution and transgene expression were observed throughout all lung segments tested in all NHPs. We have initiated an IND-enabling GLP toxicology and biodistribution study in NHPs. We expect to initiate a Phase 1/2 clinical trial for 4D-710 in the second half of 2021.

4D-710 for Cystic Fibrosis Lung Disease

Disease Background, Unmet Medical Need and Target Patient Population

Cystic fibrosis is the most common fatal inherited disease in the United States and results from mutations in the cystic fibrosis transmembrane conductance regulator (“CFTR”) gene. Cystic fibrosis causes impaired lung function, inflammation and bronchiectasis and is commonly associated with repeat and persistent lung infections due to the inability to clear thickened mucus from the lung, often resulting in frequent exacerbations and hospitalizations and eventual end-stage respiratory failure. There is no cure for cystic fibrosis, and the median age of death for patients is approximately 40 years in developed

countries. Cystic fibrosis is considered a rare, or orphan, disease by both the FDA and the EMA. According to the Cystic Fibrosis Foundation, more than 30,000 people in the United States and more than 70,000 people worldwide are living with cystic fibrosis, and approximately 1,000 new cases of cystic fibrosis are diagnosed in the United States each year. Patients with cystic fibrosis require lifelong treatment with multiple daily medications, frequent hospitalizations and, ultimately, lung transplants in some end-stage patients. The quality of life for cystic fibrosis patients is compromised as a result of spending significant time on self-care every day and frequent outpatient doctor visits and hospitalizations.

Until recently, approved therapies to treat cystic fibrosis patients were only designed to treat the symptoms of cystic fibrosis, for example by preventing and controlling infections that occur in the lungs, rather than addressing the underlying cause of the disease. Accordingly, antibiotics are frequently used along with mucus-thinning drugs.

More recently, a new class of drugs called correctors and modulators target CFTR for patients with certain gene mutations. Several therapies from Vertex Pharmaceuticals Inc. have been approved for marketing in the United States and the European Union based on their ability to improve lung function in genetically defined subsets of cystic fibrosis patients. In 2019, the FDA approved triple drug therapy with Trikafta (elexacaftor/ivacaftor/tezacaftor), which Vertex believes would be applicable for up to 90% of cystic fibrosis patients, leaving at least 10% with no CFTR-targeted options. While these therapies improve lung function, they fall short of restoring it to the normal range in most patients, and these chronic therapies require daily dosing for the patient's lifetime. In addition, the existing cystic fibrosis drugs have been associated with tolerability issues, thus limiting their use.

We believe there is a clinical need and market opportunity for a durable aerosolized therapy, delivered by breath-actuated nebulizer, that can restore normal CFTR function across all cystic fibrosis patient subgroups, including patients who are receiving combination CFTR-modulator therapies and/or do not have appreciable CFTR protein expression and are therefore not amenable to CFTR modulators. We expect to explore single agent therapy with 4D-710 initially in patients who are not amenable to CFTR modulators (estimated to include approximately 10% of all cystic fibrosis patients), and to explore single agent or combination therapy with CFTR modulators for the remaining approximately 90% of cystic fibrosis patients.

Our Solution

We are developing 4D-710 for the treatment of a broad range of cystic fibrosis patients independent of their specific *CFTR* mutation. 4D-710 is designed for efficient single dose aerosol delivery to the proximal and medial airways and alveoli, subsequent mucus barrier penetration, lung epithelial cell transduction, and resistance to pre-existing antibodies in humans. The intended result is to achieve CFTR expression within lung airway epithelial cells for correction of cystic fibrosis lung disease. 4D-710 is comprised of our targeted and evolved vector, A101, and a codon-optimized version of a synthetic truncated *CFTR* transgene *deltaR-CFTR*, which we refer to as *microCFTR*. *microCFTR* is a construct that retains the most critical functional components of the full-size *CFTR* gene and is small enough to fit within AAV vector packaging constraints.

We believe 4D-710 has the potential to treat a broad range of cystic fibrosis patients independent of their specific *CFTR* mutation. Initially we plan to focus on the approximately 10% of all patients who are not amenable to existing medicines targeting the CFTR protein as we believe these patients have the highest unmet medical need. In patients with CFTR mutations that are amenable to modulator medicines, while therapies demonstrate improvements in lung function, these modulators do not restore normal lung function in most patients. Further, these chronic therapies require daily dosing for the patient's lifetime. We therefore expect to eventually develop 4D-710 in this patient population, as a single agent and/or in combination with these CFTR modulator small molecule medicines.

We have funding and an on-going research and development collaboration with the Cystic Fibrosis Foundation for the development of 4D-710.

Competition and Differentiation: AAV Gene Therapy for Target Disease

A number of biotechnology companies have pursued gene therapy solutions to treat cystic fibrosis. We believe these prior attempts to deliver AAV gene therapy to the lungs of cystic fibrosis patients have failed due to an inability of conventional AAV vectors to penetrate through the lung mucus barrier and transduce lung cells efficiently. Further, we believe antibody neutralization of AAV likely also played a role in the lack of significant efficacy, as the mucosal immune system actively transports large quantities of antibodies into all mucus secretions, including the lung mucosa.

While a number of companies are currently pursuing other gene therapy solutions utilizing liposomes, lentivirus or conventional AAV vectors, these product candidates are in early stages of development. Moreover, they are not, to our knowledge, comprised of AAV vectors evolved in NHPs for aerosol delivery diffusely throughout the lung airways and alveoli. In addition, we believe these products were not designed for resistance to pre-existing antibodies to conventional AAVs, which is potentially a key requirement for successful delivery in the lung. As a result, to our knowledge, 4D-710 is the only AAV gene therapy product candidate in development designed specifically with a vector selected for aerosol delivery in NHPs, including humans, and with resistance to antibodies in the human population.

We believe 4D-710 has the potential to be differentiated from approved agents, and those in clinical development to our knowledge, on the basis of four design features:

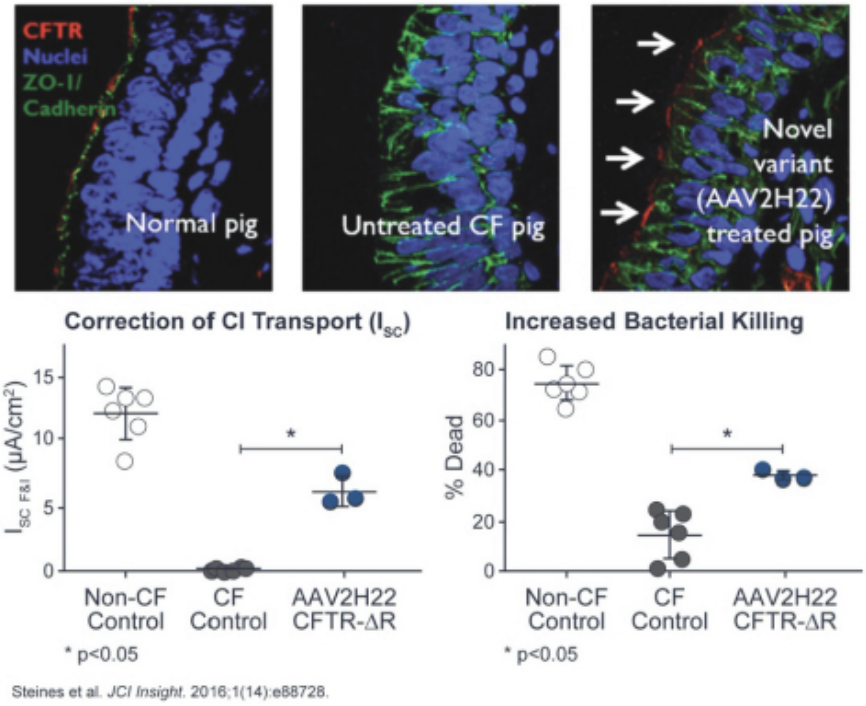
1. Corrective mechanism-of-action: An aerosol dose of 4D-710 is designed to result in high levels of the CFTR protein directly within target cells lining the airway and alveoli. 4D-710 comprises a targeted and evolved vector invented for aerosol delivery, mucus barrier penetration and transduction of epithelial cells within the airways and alveoli of NHPs and humans.
2. One-time therapy: Unlike CFTR-targeted small molecules that require daily dosing for a patient's entire life, 4D-710 is designed for single or significantly less frequent dosing.
3. CFTR mutation-independent efficacy: Unlike CFTR-targeted small molecules that are only effective against specific mutations, 4D-710 is designed to be used in cystic fibrosis patients with any mutation, including in the approximately 10% of patients who are not amenable to standard medical therapy.
4. Resistance to AAV antibodies: Unlike conventional AAV vectors, which are sensitive to anti-AAV antibody inhibition, 4D-710 utilizes A101, a vector invented for resistance to human antibody inhibition.

Preclinical Proof-of-Concept Study with Evolved AAV for Aerosol Delivery in the Cystic Fibrosis Pig Model

Our co-founder Dr. Schaffer and his academic colleagues conducted preclinical proof-of-concept studies for utilizing directed evolution to discover vectors for delivering a corrective *CFTR* gene construct to cystic fibrosis lung tissue in a large animal model of cystic fibrosis, and in a human cystic fibrosis patient lung tissue model. Building on these previous proof-of-concept studies, our product candidate 4D-710 will utilize a vector, A101, that was evolved and selected in NHPs, which we believe is more relevant for human use. The product was designed to package the same *microCFTR* transgene payload in this vector that was customized for use in humans.

Dr. Schaffer and his colleagues first demonstrated the potential to treat cystic fibrosis via aerosolized delivery of a targeted and evolved AAV vector (AAV2H22) in a pig model of cystic fibrosis. AAV2H22 was selected for highly efficient transduction of lung epithelial cells in pigs by conducting multiple rounds of directed evolution using aerosolized dosing in pigs. Aerosol delivery of *micro*CFTR using the *AAV2H22 vector* resulted in CFTR expression in diseased pig lungs with expression patterns that resembled those observed in normal lungs from both pigs and humans. In addition to CFTR protein expression, *AAV2H22-CFTR* gene therapy also resulted in a significant increase in chloride ion transport compared to untreated controls as well as a reduction in bacterial colonies within the lungs of treated animals. Therefore, selection of an aerosol AAV vector *in vivo* in normal pigs led to the discovery of an AAV vector that was subsequently able to penetrate the thickened mucus barrier in the severe pig cystic fibrosis model.

Illustrative images in the top panels below exhibit the pattern of microCFTR expression observed by Steines et al. in normal pigs, untreated cystic fibrosis pigs and cystic fibrosis pigs treated with AAV2H22 carrying the microCFTR transgene payload (also referred to as CFTR-deltaR; same transgene utilized in 4D-710, but different AAV vector). The study involved six healthy pigs, six untreated cystic fibrosis pigs and three AAV2H22.microCFTR-treated cystic fibrosis pigs. These animals are represented by the dots in each of the graphs in the bottom panels which illustrate the range of responses between animals, and the significant difference between treated and untreated cystic fibrosis pigs.



CFTRDR = MicroCFTR, Cystic Fibrosis transmembrane conductance regulator with removal of the R domain, a truncated version of the CFTR transgene engineered to fit within the payload size limitations of AAV
Cl-= chloride ion
I_{SC} = short circuit current, a measurement of Cl- movement through cell membranes
μA = microAmp
cm2 = square centimeter.

In addition, Dr. Schaffer and colleagues used directed evolution in an *in vitro* human organotypic air-liquid interface model of lung epithelium to select AAV2.5T, which we in-licensed with exclusive worldwide rights. In preclinical studies, AAV2.5T carrying *micro*CFTR transduced human lung epithelial tissue and resulted in expression of functional protein as suggested by increased chloride ion transport as compared to untreated control.

We believe that these results demonstrate that a targeted and evolved vector can penetrate the mucus layer of diseased cystic fibrosis lungs and deliver functional CFTR protein in a well-validated large animal model of the disease, as well as in human cystic fibrosis patient-derived organotypic lung models.

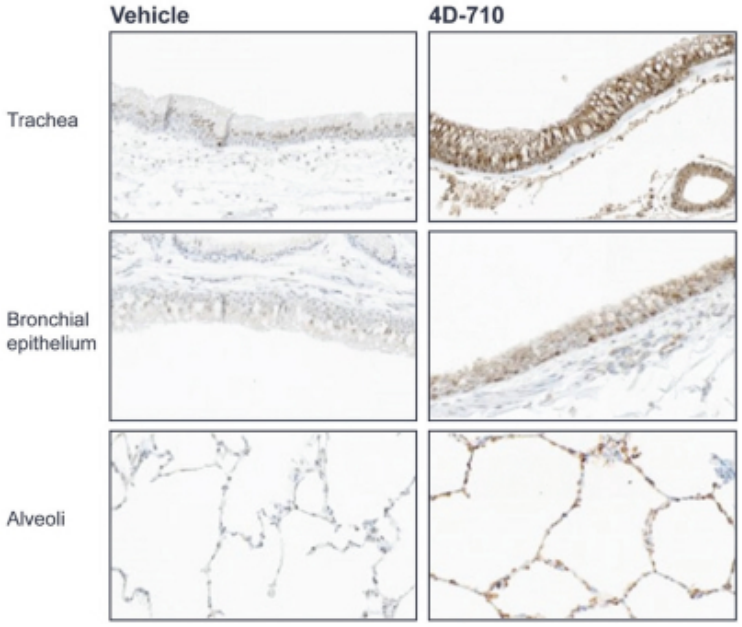
Preclinical Animal Model Pharmacology and Toxicology Studies

In our NHP study of a single aerosol delivered dose of 4D-710 at two different dose levels, treatment resulted in widespread distribution, CFTR transgene expression throughout both proximal and medial airways and alveoli. No meaningful inflammation or adverse findings were reported on in-life examinations, hematology or clinical chemistry analyses, or lung histology analyses. *Ex vivo* studies demonstrated highly significant resistance to neutralization by human pooled antibody preparations, with human IVIG pooled from over 1,000 individuals.

Delivery (genomes) and transduction (mRNA) were consistently measured throughout lung segments and samples in NHPs treated with 3E13 vg of aerosolized 4D-710. Number of positive tissue samples across three NHPs are indicated below.

4D-710	Lung
Genome (qPCR)	46/48 (95.8%)
mRNA (RT-qPCR)	44/48 (91.7%)

Aerosol delivery of 4D-710 in NHPs was associated with microCFTR protein detection by IHC (brown) in the proximal (trachea) and medial (bronchi) airway and in alveoli at low and high dose. Illustrative images below highlight transduction of the NHP lung at the 3E13 dose.



We plan to perform pharmacology studies in human cystic fibrosis lung tissues *ex vivo* in order to evaluate the function of the *microCFTR* transgene product; this protein has previously been shown to have relatively normal functional activity in a similar model *ex vivo*.

Development Plan

We have initiated an IND-enabling GLP toxicology and biodistribution study of 4D-710 in NHP. We expect to initiate a Phase 1/2 clinical trial for 4D-710 in the second half of 2021.

Competition

We are aware of several companies focused on developing gene therapies in various indications as well as companies addressing methods for modifying genes and regulating gene expression. We may also face competition from large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions with genetic medicine and other therapeutic approaches.

With respect to 4D-125 for the treatment of XLRP, we consider our most direct AAV gene therapy competitors to be as follows: Biogen Inc. (candidate administered by subretinal surgery in a Phase 2 clinical trial), Applied Genetic Technologies Corporation (candidate administered by subretinal surgery in a Phase 1/2 clinical trial), Janssen Pharmaceuticals Inc. / MeiraGTx Holdings Plc (candidate administered by subretinal surgery in a Phase 1/2 clinical trial).

With respect to 4D-110 for the treatment of choroideremia, we consider our most direct competitors to be as follows: Biogen Inc. (candidate administered by subretinal surgery in a Phase 3 clinical trial) and Spark Therapeutics, Inc., a wholly owned subsidiary of Roche Holdings AG (candidate administered by subretinal surgery in a Phase 1/2 clinical trial).

We consider our most direct competitors with respect to 4D-150 for the treatment of diabetic retinopathy and wet AMD to be Eylea (aflibercept) from Regeneron Pharmaceuticals Inc., which is the

current wet AMD standard of care, and a combination of antibody-based programs including Lucentis and faricimab from Roche, KSI-301 from Kodiak Sciences Inc., and OPT-302 from Opthea Limited, and gene-therapy based programs including ADVM-022 from Adverum Biotechnologies and RGX-314 from RegenxBio Inc., which are both AAV-based programs in Phase 1 studies. In addition, Roche is developing the Port Delivery System with Lucentis for use in patients with wet AMD.

We consider our most direct competitors with respect to 4D-310 for the treatment of Fabry disease to be Amicus Therapeutics, which has Galafold (migalastat) approved as a small molecule chaperone for specific mutations, and several gene therapy companies including AvroBio Inc., which is in Phase 3 development of an *ex-vivo* lenti-AGA based program, Freeline Therapeutics Holdings Plc, which is in Phase 1 development of AAVS2-based FLT-190, and Sangamo, which is in Phase 1 development of AAV2/6-based ST-920. Other competitors include Sanofi Genzyme, Takeda Pharmaceutical Company Limited and Protalix BioTherapeutics, all of which either commercialize or develop enzyme replacement therapy for the treatment of Fabry disease.

We consider our most direct competitors with respect to 4D-710 for the treatment of cystic fibrosis to be Vertex, which has several approved CFTR modulators, as well as other gene therapy companies in preclinical development of cystic fibrosis programs, including Krystal Biotech Inc., Abeona Therapeutics Inc., Spirovant Sciences Inc. and Editas Medicine Inc.

Manufacturing

CMC Strategy

In order to fulfill our strategy to maximize the robustness and internal control of our manufacturing processes from discovery and process development through to clinical-grade cGMP manufacturing, we have designed and are continually developing and scaling a robust in-house manufacturing platform for both GMP and non-GMP manufacturing. While many companies in the AAV gene therapy field in-license clinical trial material or manufacturing technologies from other companies or academic manufacturing centers, in contrast, our manufacturing processes were developed internally using internal technology transfers from our own process development labs. Our current in-house manufacturing capabilities include GMP manufacturing (upstream, downstream and fill/finish), production capabilities for IND-enabling GLP toxicology studies and research candidate production. We intend to further scale these capabilities to support later stage clinical programs and indications requiring more patients and/or higher intravenous doses. In addition to our internal activities, we also collaborate with CMOs (Contract Manufacturing Organizations) such as Catalent.

Current Good Manufacturing Practices ("cGMP") Capabilities

Our team has extensive experience with the manufacturing and analytical testing of numerous unique AAV capsids. Our team has internally manufactured approximately 90 unique AAV vectors, including both proprietary evolved 4DMT capsid variants and naturally occurring capsids. Our team has manufactured over 160 total lots of AAV vectors for research or clinical use. We have in-house cGMP manufacturing capabilities for clinical trial material production. Our manufacturing team has completed and released multiple lots of clinical trial material for our three product candidates in clinical development. This total also includes 13 lots of product candidate material for GLP toxicology and biodistribution studies. Leveraging internal testing capabilities in addition to qualified contract testing laboratories, we fully test and release our GLP and GMP lots for use in toxicology and clinical trials, respectively. We have developed and qualified assays for characterization, in-process testing and release and stability testing of our internally and externally manufactured proprietary AAV vectors.

Process Development Capabilities

We use robust, scalable and transferable manufacturing unit operations throughout both the vector characterization process and product development, which are both platform-specific and product-specific. The upstream manufacturing step involves triple plasmid transfections in an adherent HEK293 mammalian production cell line. Downstream manufacturing steps for purification and concentration

include multiple orthogonal column chromatography steps and tangential flow filtration. The downstream purification columns used in our process are from stable sources including General Electric. Using internally developed manufacturing processes and testing, we characterize our novel capsids and payloads. In addition, leveraging internal expertise and capabilities, we package and test our novel vectors with payloads using internally developed manufacturing processes.

Manufacturing Facilities

Our manufacturing facilities are on site at company headquarters in Emeryville, California and include process development labs, an analytical development lab, and a cGMP manufacturing facility. These manufacturing facilities are also designed for production of material for GLP toxicology and biodistribution studies. Our manufacturing facility is approximately 3,200 square feet, of which approximately 1,500 square feet is dedicated to product manufacturing. For larger scale production for Phase 1 to Phase 3 clinical trials as well as potentially commercial launch materials, we intend to build a second cGMP facility. In this new facility, we expect to utilize large-scale bioreactors that are designed to enable higher titer clinical trial material lots as well as commercial launch materials. These manufacturing facilities are also designed for production of material for GLP toxicology and biodistribution studies.

Manufacturing Team

Our team of approximately 30 highly trained individuals is led by our Chief Technical Officer and Chief Operating Officer, Dr. Kamal, and includes eight Ph.D. scientists. Collectively, they have significant experience in viral vector manufacturing, chemistry-manufacturing-controls ("CMC"), regulatory affairs, analytical and process development, and quality assurance and controls. Our team also has experience prior to 4DMT with manufacturing multiple viral vectors from preclinical studies through to multiple Phase 3 trials. For example, Dr. Kamal helped to write and compile the AAV gene therapy BLA for Zolgensma (Novartis), the first AAV gene therapy approved for intravenous administration in infants and babies.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, manufacturing and process discoveries, and other know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position.

Our product and lead optimization candidates were discovered by us utilizing our proprietary technology. We have filed several non-provisional and provisional patent applications, all owned by us, relating to our product and lead optimization candidates in the United States, certain foreign countries, and the World Intellectual Property Organization that are directed to compositions-of-matter, dosage unit forms, methods-of-treatment and medical use. We have also licensed several non-provisional patent applications, granted patents and international patent applications relating to our product and lead optimization candidates from U.C. Berkeley.

As of March 15, 2021, our solely owned patent portfolio includes seven pending U.S. non-provisional applications, seventy-one pending foreign applications, ten allowed foreign applications and six granted foreign patents. We expect that United States and European patents and the patent applications, if issued, would expire between May 2037 and November 2038, excluding any additional term from patent term adjustment or patent term extension if appropriate maintenance and other governmental fees are paid. Additional patent term for the presently issued or later issued U.S. patents may be awarded as a result of the patent term extension provision of the Hatch-Waxman Amendments of 1984. In the European Union member countries, a supplementary protection certificate, if obtained, provides a maximum five years of market exclusivity. Our solely owned patent portfolio also includes five pending U.S. provisional patent applications.

In other jurisdictions (currently, Australia, Bahrain, Brazil, Canada, Chile, China, Colombia, Costa Rica, Egypt, India, Indonesia, Iran, Israel, Japan, Korea, Kuwait, Malaysia, Mexico, New Zealand, Oman, Peru, Philippines, Qatar, Russia, Saudi Arabia, Singapore, South Africa, Thailand, United Arab Emirates, Ukraine and Vietnam), granted patents, and any patents issued on pending applications, where applicable, relating to our product and lead optimization candidates, including composition of matter, dosage unit form, method-of-treatment and medical use, are expected to expire between May 2037 and November 2038, if the appropriate maintenance, renewal, annuity, and other government fees are paid. These patents and patent applications (if applicable), depending on the national laws, may benefit from extension of patent term in individual countries if regulatory approval of any of our product or lead optimization candidates is obtained in those countries. For example, in Japan, the term of a patent may be extended by a maximum of five years in certain circumstances.

As of March 15, 2021, our in-licensed patent portfolio includes five granted U.S. patents and nine granted foreign patents or allowed foreign applications; each of these patents is expected to expire between June 2024 and June 2029. Our in-licensed patent portfolio also includes seven pending U.S. non-provisional patent applications and thirty-eight pending foreign patent applications. We expect that United States and European patents, if issued from applications in our in-licensed portfolio would expire between June 2024 and June 2038.

In other jurisdictions (currently, Australia, Brazil, Canada, China, France, Germany, Great Britain, Hong Kong, India, Italy, Japan, Korea and Mexico), granted patents issued on pending applications, where applicable, relating to our product and lead optimization candidates, including composition of matter and various other patents, including dosage unit form, method-of-treatment and medical use patents are expected to expire between June 2024 and June 2038, if the appropriate maintenance, renewal, annuity, and other government fees are paid. These patents and patent applications (if applicable), depending on the national laws, may benefit from extension of patent term in individual countries if regulatory approval of any of our product or lead optimization candidates is obtained in those countries. For example, in Japan, the term of a patent may be extended by a maximum of five years in certain circumstances.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are effective for 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office (“USPTO”) delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. The actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

We also protect our proprietary technology and processes, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and other contractors. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our drugs or processes, obtain licenses or cease certain

activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have a material adverse impact on us.

Strategic Collaborations

Collaboration and License Agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

In November 2017, we entered into a Collaboration and License Agreement (the "Roche Agreement"), with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., collectively referred to as Roche. Under the Roche Agreement, we granted Roche an exclusive, sublicensable, worldwide license under certain intellectual property rights to research, develop, make, use, import, export, and sell products and constructs using our proprietary AAV vectors to treat ophthalmological diseases and disorders, excluding treatment and prevention of cancer and central nervous system conditions (but not retinal nerves) and delivery of DNA-directed RNA interference (the "Roche Field").

Under the terms of the Roche Agreement, we and Roche will engage in collaboration programs to develop one or more products, and choroideremia has been designated as the first collaboration program. We are primarily responsible for the initial development of such collaboration programs and Roche agreed to reimburse us for our development costs and expenses in accordance with the terms of the agreement. Upon completion of such initial development, we will transfer data, know-how and regulatory filings to the applicable collaboration program to Roche and Roche will be responsible for the development and commercialization of such program at its own cost and expense.

Subject to the terms of the Roche Agreement, either party may also develop one or more programs in the Roche Field independent of the other party at such party's own cost and expense. Roche has an option to elect one or more of the programs that we may independently develop under the agreement, including XLRP, which we have designated as our initial independent program. If Roche exercises its option, and subject to its payment of the applicable option exercise fee, we will transfer our data, know-how and regulatory filings related to such programs. If Roche does not exercise its option within the applicable option period, we will have the sole right to commercialization of such product. Each party agreed to various diligence obligations under the agreement.

Pursuant to the Roche Agreement, we received an upfront payment from Roche of $21.0 million. In addition, we are entitled to contingent payments including (i) $1.0 million for each Roche nominated product beyond the first three, (ii) up to $30.0 million upon exercise of the option to convert a product we nominated and developed prior to pivotal clinical studies, (iii) up to $223.0 million in specified development milestones in connection with the licensed products, $86.0 million of which relate to choroideremia; and (iv) sales-based milestones of up to $123.0 million based on worldwide calendar year net sales in connection with licensed products. On a product-by-product basis, Roche will also be required to pay us tiered royalties for worldwide calendar year net sales of products at percentages ranging from the mid-to high-single digit to mid-teens, in each case subject to reductions in accordance with the terms of the agreement. The royalties are payable on a product-by-product and country-by-country basis until the later of ten years after the date of first commercial sale of such product in such country and the expiration of the last-to-expire licensed patent right covering such product, which will expire on May 12, 2037.

The Roche Agreement will expire on the later of expiration of all payment obligations and the date when no products are actively developed by either party or both parties in accordance with the terms of the agreement. Either party may terminate the agreement in its entirety or on a country-by-country basis if the other party fails to cure its material breach within 90 days of receiving notice. Roche may terminate the agreement in its entirety, on a product-by-product basis or on a country-by-country basis upon 90 days' prior written notice. If we terminate the agreement for Roche's material breach or if Roche terminates the agreement without cause, the rights to the products generally revert back to us. If we commercialize reverted products after such termination, we may be required to pay Roche tiered royalties for worldwide calendar year net sales of such products at percentages ranging from zero to the low-teens,

in each case subject to reductions in accordance with the terms of the agreement. If Roche terminates the agreement for our material breach, Roche may retain its rights under the license that we grant to Roche under our intellectual property rights and Roche's payment obligations will survive.

Collaboration and License Agreements with uniQure biopharma B.V.

In August 2019, we entered into an Amended and Restated Collaboration and License Agreement (the "Amended and Restated uniQure Agreement") with uniQure biopharma B.V., now uniQure N.V. ("uniQure"), which amended and restated the Collaboration and License Agreement that we entered into with uniQure in January 2014.

Under the Amended and Restated uniQure Agreement, we granted uniQure an exclusive, sublicensable, worldwide license under certain of our intellectual property rights, and other rights, to research, develop, make, use, and commercialize pre-selected AAV capsid variants ("Selected Variants"), and compounds and products containing such Selected Variants, using our proprietary AAV technology for delivery of gene therapy constructs to cells in the central nervous system and the liver (the "uniQure Field"). uniQure is solely responsible, at its cost and expense, to develop and commercialize the compounds and products containing the Selected Variants in accordance with the terms of the Amended and Restated uniQure Agreement. We retain all rights to all other AAV capsid variants, and compounds and products containing such AAV capsid variants, in the uniQure Field.

Also in August 2019, we entered into a separate Collaboration and License Agreement with uniQure ("Second uniQure Agreement"). Under the Second uniQure Agreement, the parties agreed to research and develop new AAV capsid variants that are not Selected Variants (New Variants) using our proprietary AAV technology for delivery of transgene constructs that affect certain targets ("uniQure Targets") in the uniQure Field. We are responsible for the research of the New Variants, and uniQure is responsible for the development and commercialization of a certain number of compounds and products containing New Variants, that affect the uniQure Targets ("Licensed Products"). We granted uniQure an exclusive, sublicensable, worldwide license under certain of our intellectual property rights, and other rights, to research, develop, make, use, and commercialize the Licensed Products. We retain all rights to New Variants in the uniQure Field that affect targets other than the uniQure Targets. We also retain all rights to any new AAV capsid variants developed under the agreements that are not New Variants, and compounds and products containing such variants.

Under both the Amended and Restated uniQure Agreement and the Second uniQure Agreement, uniQure will be required to pay us royalties on worldwide annual net sales of licensed products at a mid-single digit percentage rate, subject to certain specified reductions. These royalties are payable on a product-by-product and country-by-country basis until the latest of ten years after the date of the first commercial sale of such product in such country, the expiration of the last-to-expire licensed patent right covering such product in such country (of which there are none), and the expiration of any applicable exclusivity granted by a regulatory authority in such country for such product (the "uniQure Royalty Term"). uniQure will also be required to pay us a portion of the amounts it receives for licensing or sublicensing to third parties our intellectual property rights licensed or other rights otherwise granted under the Amended and Restated uniQure Agreement, and a portion of the amounts it receives for licensing to third parties our intellectual property rights granted under the Second uniQure Agreement, each at a rate between mid-single digit to mid-twenties percentages, depending on the stage of development at which such third-party grant occurs.

Under both the Amended and Restated uniQure Agreement and the Second uniQure Agreement, under certain circumstances, we may propose to uniQure, and uniQure may grant to us, a non-exclusive right for us to develop and commercialize certain licensed products based on Selected Variants in the uniQure Field, or the New Variants in the uniQure Field to deliver transgene constructs that affect the uniQure Targets ("4DMT Proposed Products"). Pursuant to the Second uniQure Agreement, under certain circumstances, uniQure may propose to us, and we may grant to uniQure a non-exclusive right for uniQure to develop and commercialize certain licensed products using any new AAV capsid variants developed under the agreement that are not New Variants in the uniQure Field to deliver transgene

constructs that affect targets other than the uniQure Targets ("uniQure Proposed Products"). If either party obtains the rights to develop and commercialize a 4DMT Proposed Product or a uniQure Proposed Product, as applicable, such party will be required to pay the other party royalties on worldwide annual net sales of such products at a mid-single digit percentage rate, subject to specified reductions. These royalties will be payable on a product-by-product basis during the uniQure Royalty Term for such products. The party receiving such license will also be required to pay the other party a portion of the amounts that it may receive for licensing or sublicensing to third parties rights for such 4DMT Proposed Products or uniQure Proposed Products, as applicable, at a rate between mid-single digit to mid-twenties percentages depending on the stage of development at which the sublicense is granted.

Each of the Amended and Restated uniQure Agreement and the Second uniQure Agreement will expire on the expiration of all payment obligations of the parties under such agreement. Each party may terminate either agreement for the other party's insolvency or bankruptcy. Each party may also terminate either agreement in its entirety in some circumstances or on an indication-by-indication basis if the other party fails to cure its material breach under the applicable agreement within 90 days of receiving notice, subject to an additional cure period in accordance with the terms of such agreement. uniQure may terminate either agreement upon 90 days' prior written notice. In addition, uniQure may terminate the Second uniQure Agreement at any point prior to the first anniversary of the effective date if the joint research committee determines that it would be futile to continue the research program under the agreement, including if such committee determines that certain agreed-upon development success criteria will not be able to be met, or if we are not making bona fide efforts to achieve the mutually agreed timelines set forth in the research plan. If we terminate either agreement for uniQure's material breach, insolvency or bankruptcy or if uniQure terminates either agreement for convenience or due to its determination of futility, the rights to the Selected Variants, and compounds and products containing such Selected Variants, or the uniQure New Variants, and compounds and products containing such uniQure New Variants, as applicable, generally revert back to us. If uniQure terminates either agreement for our material breach under the applicable agreement, insolvency or bankruptcy, uniQure may retain its rights to the intellectual property license grant under such agreement and uniQure's payment obligations will survive.

Exclusive License and Bailment Agreements with The Regents of the University of California

In December 2013, we entered into two Exclusive License and Bailment Agreements (the "UC Agreements") with The Regents of the University of California (the "UC Regents") with one of the agreements covering AAV2 capsid mutants with novel properties for enhanced performance in gene therapy and the other covering AAV for enhanced gene delivery in the presence of neutralizing antibodies. Under both UC Agreements, the UC Regents granted us an exclusive, sublicensable license under certain patent rights to make, use, sell, offer to sell, and import products and services, and to practice methods in the United States and foreign countries where the licensed patent rights exist. The license grant under one UC Agreement is in all fields of use and the license grant under the other UC Agreement is in all fields of use, with the exception of the ophthalmic field. We agreed to certain general and specific diligence obligations under both UC Agreements in connection with the development, manufacture and sales of the licensed products, services and methods, in accordance with the terms of the UC Agreements.

Under each UC Agreement, we paid the UC Regents an upfront payment of $5,000. Further, at the closing of our Series A financing that was a qualified financing pursuant to the UC Agreements, we issued 311,812 shares of our common stock in aggregate under both agreements. Under each UC Agreement, we agreed to pay the UC Regents a specified annual license maintenance fee in each year in which we do not owe royalties to the UC Regents. We also agreed to pay the UC Regents a mid-teens to mid-twenties percentage range of any consideration, including royalties ("Sublicense Consideration"), we receive for the grant of a sublicense under the licensed patent rights under each UC Agreement, with the consideration payable to the UC Regents to not exceed such percentage range in the aggregate under both UC Agreements for the same sublicense grant. We may reduce any Sublicense Consideration if we sublicense any of our own or third-party patent rights under the sublicense grant based on the relative value of the sublicensed patents. Upon the achievement of specified development and regulatory

milestones by the first licensed product or method, we will be required to pay the UC Regents up to $3.1 million under each UC Agreement. We will also be required to pay the UC Regents a royalty on net sales of licensed products, services and methods covered by the patents licensed under the UC Agreements at a percentage in the low single-digit percentage rate, subject to certain specified reductions. Under the UC Agreements, a specified minimum annual royalty will also be due to the UC Regents beginning the first calendar year after the year in which any net sales of a licensed product first occur, such minimum royalty amount to increase on an annual basis, but not to exceed $0.1 million in the aggregate under both UC Agreements. Under each UC Agreement, royalties are payable until the expiration of the last-to-expire licensed patent right covering the licensed product, service or method, which will expire on June 28, 2038 (the "UC Royalty Term"). Milestone, royalty and sublicense revenue payments will be due to the UC Regents under only one of the UC Agreements covering any licensed product, regardless of the number of patents covering a given licensed product.

Each UC Agreement will expire at the end of the UC Royalty Term. The UC Regents may terminate each of the UC Agreements if we fail to cure a breach of such UC Agreement within 60 days of notice. If we fail to meet our diligence obligations, the UC Regents has the right to either terminate the UC Agreement or to reduce our exclusive license to a non-exclusive license, after giving us 60 days to cure or request arbitration. We may terminate either UC Agreement at-will in its entirety or with respect to any portion of the licensed patent rights upon 90 days prior written notice. Each UC Agreement will terminate immediately if we or a third party on our behalf files a claim asserting that the licensed patent rights are invalid or unenforceable.

Cystic Fibrosis Foundation

In 2016, we received a grant from Cystic Fibrosis Foundation ("CFF") in the amount of $525,000 to support discovery and development of product candidates to treat cystic fibrosis. The grant was increased to $3.5 million in 2017 and was subsequently amended to allocate the $3.5 million to different milestones. The grant provides for repayment to CFF upon the commercialization of any product developed under the grant. The repayment is capped at nine times multiple of the grant actually paid to us.

In April 2020, CFF made a $10.0 million investment in our Series C redeemable convertible preferred stock financing. In return for the investment, CFF received shares of our Series C redeemable convertible preferred stock, and we and CFF entered into a Funding Agreement (the Funding Agreement). Pursuant to the terms of the Funding Agreement, we agreed to use the proceeds of the CFF investment to support development of 4D-710, our product candidate for the treatment of cystic fibrosis, and to match CFF's support for the product candidate. Upon acceptance by the FDA of an IND for 4D-710 ("Acceptance"), CFF will make an additional $4.0 million investment (the "Subsequent Investment"), except in the event of a change of control transaction occurring prior to Acceptance or Acceptance occurring after April 29, 2026. At the time of Acceptance, CFF will receive shares of common stock priced at the 10-day average reported closing price of our common stock for the date of Acceptance. We have agreed to use the additional $4.0 million from the Subsequent Investment to support development of 4D-710 and to match CFF's support of the product candidate. Under the terms of the Funding Agreement, neither the $10.0 million investment in the Series C redeemable convertible preferred stock nor the $4.0 million of funding upon Acceptance are restricted as to withdrawal or usage.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of biological product candidates such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and

the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biologics Regulation

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and other federal, state, local and foreign statutes and regulations. The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's GLPs;
- submission to the FDA of an IND which must become effective before clinical trials may begin;
- approval by an IRB or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with Good Clinical Practices ("GCPs"); and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical trials. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In addition to the submission of an IND to the FDA, under the National Institutes of Health, or NIH, Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines), supervision of certain human gene transfer trials may also require evaluation and assessment by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to the public health or the environment, and such assessment may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

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

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

BLA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to

the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee to FDA, and the sponsor of an approved BLA is also subject to an annual program fee. A waiver of user fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, or, if the application qualifies for priority review, six months after the filing date. Priority review designation will direct overall attention and resources to the evaluation of applications for products that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may also convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions regarding approval.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy ("REMS"), to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication

plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase IV post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product 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 a BLA is submitted, the product candidate may be eligible for priority review. For a fast track product, the FDA may consider sections of the BLA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the application. A fast track designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA at six months after the FDA accepts the application for filing.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

In 2017, the FDA established a new regenerative medicine advanced therapy ("RMAT") designation as part of its implementation of the 21st Century Cures Act. The RMAT designation program is intended to fulfill the 21st Century Cures Act requirement that the FDA facilitate an efficient development program for, and expedite review of, any drug or biologic that meets the following criteria: (i) the drug or biologic qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (ii) the drug or biologic is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the drug or biologic has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides all the benefits of breakthrough therapy designation, including more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of clinical trial sites, including through expansion of trials to additional sites.

Any marketing application for a drug or biologic submitted to the FDA for approval, including a product candidate with a fast track designation, RMAT designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product candidate is eligible for

priority review if it is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review). Under the accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the 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. FDA may withdraw approval of a drug or indication approved under accelerated approval on an expedited basis if, for example, the sponsor fails to conduct required post-marketing trials in a timely manner or if such trials fail to verify the predicted clinical benefit of the product.

Fast Track designation, priority review, accelerated approval, RMAT designation 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.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. We have obtained orphan drug designation for 4D-110 for the treatment of Choroideremia and for 4D-310 for the treatment of Fabry disease, and we plan to seek additional orphan drug designations for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products.

Post-Approval Requirements

Biologics are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or 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 license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product’s labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer’s communications on the subject of off-label use of their products.

Biosimilars and Exclusivity

The Affordable Care Act, signed into law in 2010, includes a subtitle called the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing 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 study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal and state anti-kickback, fraud and abuse, false claims, pricing reporting, data privacy and security, and transparency laws and regulations as well as similar foreign laws in the jurisdictions outside the U.S. For example, the federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act and the civil monetary penalties statute. The federal civil and criminal false claims laws, including the civil False Claims Act, prohibit, among other things, any individual

or entity from knowingly presenting, or causing to be presented, a false claim for payment to 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. The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), created additional federal civil and criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or other transfers of value made to physicians, certain other health care professionals beginning in 2022, and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the 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 or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives. Violation of any of such laws or any other governmental regulations that apply may result in significant penalties, including, without limitation, administrative civil and criminal penalties, damages, disgorgement fines, additional reporting requirements and oversight obligations, contractual damages, the curtailment or restructuring of operations, exclusion from participation in government healthcare programs and imprisonment.

Data Privacy and Security Laws

Pharmaceutical companies may be subject to domestic and foreign privacy, security and data breach notification laws, which are rapidly evolving in many jurisdictions worldwide. In the United States, federal and state health information laws may govern the collection, use, disclosure and protection of health-related and other personal information. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations implemented thereunder, which impose obligations on "covered entities," including certain healthcare providers, health plans, and healthcare clearinghouses, as well as their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. State laws may be more stringent, broader in scope or offer greater individual rights with respect to protected health information ("PHI") than HIPAA and state laws may differ from each other, which may complicate compliance efforts. For example, California enacted the California Consumer Privacy Act (the "CCPA") on June 28, 2018, which went into effect on January 1, 2020. The CCPA gives California residents expanded rights regarding their personal information. Although CCPA contains certain exemptions for health-related information, including PHI, uncertainties over how it applies and how our treatment of non-PHI personal information may be interpreted mean that the CCPA may ultimately increase our compliance costs and potential liability. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured PHI, a complaint about privacy practices or an audit by the 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.

European Union member states, the United Kingdom, Switzerland and other jurisdictions have also adopted data protection laws and regulations, which impose significant compliance obligations. In the European Economic Area ("EEA") and the United Kingdom, the collection and use of personal data, including clinical trial data, is governed by the provisions of the General Data Protection Regulation ("GDPR"). The GDPR became effective on May 25, 2018, and imposes strict requirements for processing the personal data of individuals within the EEA and the United Kingdom. The GDPR, together with national legislation, regulations and guidelines of the European Union and EEA member states and the United Kingdom governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA or the United Kingdom, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for breaches of the data protection obligations. The law is also developing rapidly and, in July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EU to the U.S. European data protection authorities may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in or from the EEA or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product, particularly for gene therapy products where the Centers for Medicare & Medicaid Services ("CMS") and other third-party payors in the United States have not yet established a uniform policy of coverage and reimbursement. Therefore, decisions. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufacturers to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the

medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of us placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively the "ACA") was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and fraud and abuse changes. Additionally, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; 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 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 & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, in 2017, Congress enacted the Tax Cuts and Jobs Act, which eliminated the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas (the "Texas District Court Judge"), ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case, although it is unclear when a decision will be made or how the Supreme Court will rule. It is also unclear how other efforts to challenge, repeal or replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2020, absent additional congressional action.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on

pharmaceutical price increases. Additionally, the Trump administration's budget proposal for the fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, on July 24, 2020, the Trump administration announced four executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. While some existing measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

Employees and Human Capital

As of December 31, 2020, we had 83 full-time employees. Of these employees, 61 are engaged in research and development. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and 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 and cash-based performance bonus awards.

Facilities

We lease approximately 51,000 square feet of office and laboratory space in Emeryville, California under leases that expire in September 2026 and December 2029. We believe that our facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

Corporate Information

We were formed on September 12, 2013 as a Delaware limited liability corporation under the name 4D Molecular Therapeutics, LLC. On March 11, 2015, 4D Molecular Therapeutics, Inc. was incorporated as a Delaware corporation. On March 20, 2015, 4D Molecular Therapeutics, LLC merged with 4D Molecular Therapeutics, Inc., with 4D Molecular Therapeutics, Inc. being the surviving entity. Our principal executive offices are located at 5858 Horton Street #455, Emeryville, California 94608, and our telephone number is (510) 505-2680.

Available Information

Our website address is www.4dmoleculartherapeutics.com. The information on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K. The U.S. Securities and Exchange Commission ("SEC") maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at www.sec.gov. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") are also available free of charge on our investor relations website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes and the section of this Annual Report on Form 10-K "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. If any of the following risks actually occurs, our business, reputation, financial condition, results of operations, revenue and future prospects could be seriously harmed. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that adversely affect our business. Unless otherwise indicated, references to our business being seriously harmed in these risk factors and elsewhere will include harm to our business, reputation, financial condition, results of operations, future prospects and stock price. In that event, the market price of our common stock could decline, and you could lose part or all of your investment.

Risk Factor Summary

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. The following is a summary of the principal risks that could materially adversely affect our business, results of operations, and financial condition, all of which are more fully described in the section titled "Risk Factors." This summary should be read in conjunction with the "Risk Factors" section and should not be relied upon as an exhaustive summary of the material risks facing our business.

- We are in the early stages of drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.
- We have had recurring net losses, and we expect to continue to incur significant net losses for the foreseeable future.
- We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.
- All of our product candidates are based on a novel AAV gene therapy technology with which there is limited regulatory and clinical experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. Further, 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 therapeutic modalities.
- Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products or otherwise seriously harm our business.
- Adverse public perception or regulatory scrutiny of gene therapy technology may negatively impact the developmental progress or commercial success of products that we develop alone or with collaborators.
- Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.
- The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, expensive, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.
- Our employees, independent contractors, consultants, research or commercial partners or collaborators and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

- Our success depends on our ability to protect our intellectual property and our proprietary technologies.
- Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors.

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

We are in the early stages of drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are a clinical-stage gene therapy company pioneering the development of product candidates using our targeted and evolved AAV vectors. We commenced operations in September 2013, have no products approved for commercial sale and have not generated any product revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. If our product candidates are not successfully developed and approved, we may never generate any revenue. To date, we have not completed any clinical trials (including any pivotal clinical trial), obtained marketing approval for any product candidates, manufactured commercial scale quantities of any of our product candidates or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our limited operating history as a company and early stage of drug development make any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will be seriously harmed.

We have had recurring net losses, and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred recurring net losses, including net losses of $56.7 million and $49.3 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $135.7 million.

We have devoted substantially all of our financial resources and efforts on research and development activities, including for our product candidates and our Therapeutic Vector Evolution platform. We do not expect to generate revenue from product sales for several years, if at all. We continue to incur significant research and development and other expenses related to our ongoing operations. The amount of our future net losses will depend, in part, on the level of our future expenditures and our ability to generate revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We expect to continue to incur significant and increasingly higher expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- progress our current and any future product candidates through preclinical and clinical development;
- experience delays in our preclinical studies and clinical trials, whether current or planned, due to the novel coronavirus (“COVID-19”) pandemic, or other factors;
- expand our manufacturing facilities and work with our contract manufacturers to scale up the manufacturing processes for our product candidates;
- continue our research and discovery activities;
- continue the development of our Therapeutic Vector Evolution platform;

- initiate and conduct additional preclinical, clinical or other studies for our product candidates;
- change or add additional contract manufacturers or suppliers;
- seek regulatory approvals and marketing authorizations for our product candidates;
- establish sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval;
- acquire or in-license product candidates, intellectual property and technologies;
- make milestone, royalty or other payments due under any current or future collaboration or license agreements;
- obtain, maintain, expand, protect and enforce our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- experience any delays or encounter other issues related to our operations;
- meet the requirements and demands of being a public company;
- defend against any product liability claims or other lawsuits related to our products; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' deficit and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time consuming, expensive and uncertain process that takes years to complete. Our operations have required substantial amounts of cash since inception. To date, we have financed our operations primarily through the sale of equity securities and to a lesser extent from cash received pursuant to our collaboration and license agreements. We have initiated clinical trials, which are ongoing, and have several other product candidates in preclinical development that may enter clinical development shortly thereafter. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early stage research projects, continue preclinical and clinical development of our product candidates and, in particular, advance our product candidates through clinical trials. Even if we are successful in developing our product candidates, obtaining regulatory approvals and launching and commercializing any product candidate will require substantial funding.

As of December 31, 2020, we had $276.7 million in cash and cash equivalents. Based on our current operating plan, we believe that our existing cash and cash equivalents will allow us to fund our planned operations for at least one year from the date of the issuance of the financial statements included in this Form 10-K.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the

United States and worldwide resulting from the ongoing COVID-19 pandemic. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities or eliminate one or more of our development programs altogether; or
- delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, or reduce our flexibility in developing or maintaining our sales and marketing strategy.

We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to, or jointly own some aspects of, our product candidates or technologies that we would otherwise pursue on our own. We do not expect to realize revenue from sales of products or royalties from licensed products in the foreseeable future, if at all, and unless and until a product candidate is clinically tested, approved for commercialization and successfully marketed.

We will be required to seek additional funding in the future and currently intend to do so through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives. Any of the above events could seriously harm our business and cause the price of our common stock to decline.

Due to the significant resources required for the development of our product candidates, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on product candidates that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Due to the significant resources required for the development of our product candidates, in particular our product candidates in IND-enabling studies and those in clinical trials, we must decide which product candidates and indications to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain product candidates may subsequently also prove to be less than optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the biopharmaceutical industry, in particular for ophthalmology, cardiology and pulmonology diseases, our business could be seriously harmed. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

The amount of our future losses is uncertain and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control and may be difficult to predict, including:

- the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or collaboration partners;
- the timing and cost of, and level of investment in research, development and commercialization activities, which may change from time to time;
- the timing of receipt of approvals from regulatory authorities in the United States and internationally;
- the timing and status of enrollment and safety and efficacy readouts for our clinical trials;
- the cost of manufacturing, as well as building out our supply chain, which may vary depending on the quantity of production, the cost of continuing to establish and scale up our internal manufacturing capabilities, and the terms of any agreements we enter into with third-party suppliers;
- timing and amount of any option, milestone, royalty or other payments due under any current or future collaboration or license agreement;
- coverage and reimbursement policies with respect to our gene therapy product candidates and potential future drugs that compete with our products, if approved;
- expenditures that we may incur to acquire, develop or commercialize additional products and technologies;
- the level of demand for our gene therapy products, if approved, which may vary significantly over time; and
- future accounting pronouncements or changes in our accounting policies.

For example, most of our collaboration and license revenue for the year ended December 31, 2020 was from Roche. The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Risks Related to the Research, Discovery, Development and Commercialization of Our Product Candidates

All of our product candidates are based on a novel AAV gene therapy technology with which there is limited regulatory and clinical experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. Further, 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 therapeutic modalities.

All of our product candidates are based on gene therapy technology and our future success depends on the successful development of this novel therapeutic approach. We cannot assure you that any development problems we or other gene therapy companies experience in the future related to gene therapy technology will not cause significant delays or unanticipated costs in the development of our product candidates, or that such development problems can be solved. In addition, the clinical study requirements of the U.S. Food and Drug Administration ("FDA") and other 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 therapeutic modalities. Further, as we are developing novel treatments for diseases in which there is limited clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, European Medicines Agency ("EMA") or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, few gene therapy products have been approved by the FDA or comparable foreign regulatory authorities, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union or other jurisdictions. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

Regulatory requirements governing gene therapy products have evolved and may continue to change in the future. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research ("CBER") to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

Under the National Institutes of Health ("NIH") Guidelines for Research Involving Recombinant DNA Molecules ("NIH Guidelines"), supervision of human gene transfer trials, including evaluation and assessment by an Institutional Biosafety Committee ("IBC") a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution, is required. The IBC assesses the safety of the research and identifies any potential risk to the public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

We are subject to significant regulatory oversight by the FDA, and in addition to the government regulators, the applicable IBC and Institutional Review Board ("IRB"), of each institution at which we or our collaborators conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review and approve the proposed clinical trial.

Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines.

Changes in applicable regulatory guidelines may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions.

As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Adverse public perception or regulatory scrutiny of gene therapy technology may negatively impact the developmental progress or commercial success of product candidates that we develop alone or with collaborators.

The developmental and commercial success of our current product candidates, or any that we develop alone or with collaborators in the future, will depend in part on public acceptance of the use of gene therapy technology, including the use of AAVs, for the prevention or treatment of human diseases. Adverse public perception of gene therapies may negatively impact our ability to raise capital or enter into strategic agreements for the development of product candidates.

Gene therapy remains a novel technology. The commercial success of our gene therapy products, if successfully developed and approved, may be adversely affected by claims that gene therapy is unsafe, unethical or immoral. This may lead to unfavorable public perception and the inability of any of our product candidates to gain the acceptance of the public or the medical community. Unfavorable public perceptions may also adversely impact our or our collaborators' ability to enroll clinical trials for our product candidates. Moreover, success in commercializing any product candidates that receive regulatory approval will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of such product candidates in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Publicity of any adverse events in, or unfavorable results of, preclinical studies or clinical trials for any current or future product candidates, or with respect to the studies or trials of our competitors or of academic researchers utilizing similar technologies, even if not ultimately attributable to our technology or product candidates, could negatively influence public opinion. Negative public perception about the use of AAV technology in human therapeutics, whether related to our technology or a competitor's technology, could result in increased governmental regulation, delays in the development and commercialization of product candidates or decreased demand for the resulting products, any of which may seriously harm our business.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval.

If any serious adverse events occur, clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business could be seriously harmed. Treatment-related side effects could also affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us or our collaborators to cease further development of, deny approval of, or require us to cease selling any product candidates or products for any or all targeted indications. If we or our collaborators elect, or are required, to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated. Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label including “boxed” warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a Risk Evaluation and Mitigation Strategy (“REMS”), which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers and/or other elements to assure safe use;
- the product may become less competitive;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have no products approved for commercial sale, and we have never generated any revenue from product sales, and we may never generate revenue or be profitable.

We have no products approved for commercial sale and have not generated any revenue from product sales. We do not anticipate generating any revenue from product sales until after we have successfully completed clinical development and received regulatory approval for the commercial sale of a product candidate, which will not occur for several years if ever.

Our ability to generate revenue and achieve profitability depends significantly on many factors, including:

- successfully completing research and preclinical and clinical development of our product candidates;
- the COVID-19 pandemic, which has and in the future may continue to result in delays to patient enrollment, patients discontinuing their treatment or follow up visits or changes to trial protocols;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;

- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and any commercial demand for our product candidates;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future approved products, if any;
- patients' willingness to enroll or continue to participate in a clinical trial during the COVID-19 pandemic;
- launching and successfully commercializing product candidates for which we obtain marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- obtaining adequate reimbursement for our product candidates or procedures using our product candidates from payors;
- the convenience and durability of our treatment or dosing regimen;
- acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidate, or any future product candidates, if approved, including relative to alternative and competing treatments;
- patient demand for any of our product candidates that may be approved;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable, and we will need to obtain additional funding through one or more equity or debt financings in order to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines or the price and available third-party reimbursement are lower than anticipated, we may not generate significant revenue from sales of such products, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock, all or any of which may seriously harm our business.

Public health crises such as pandemics or similar outbreaks have affected and could continue to seriously and adversely affect our preclinical and clinical trials, business, financial condition and results of operations.

In March 2020, the World Health Organization declared COVID-19 a global pandemic, and the United States declared a national emergency with respect to COVID-19. In response to the COVID-19 pandemic, "shelter in place" orders and other public health guidance measures have been implemented across much of the United States and Europe, including in the locations of our offices, clinical trial sites, key vendors and partners. We expect that our clinical development program timelines will be negatively affected by COVID-19, which could harm our business. Further, due to "shelter in place" orders and other public health guidance measures, we have implemented a work-from-home policy for all staff members excluding those necessary to maintain minimum basic operations. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay or otherwise seriously harm our business. For example, with our personnel working from home, some of our research activities that require our personnel to be in our laboratories will be delayed.

As a result of the COVID-19 pandemic, or similar pandemics, and related "shelter in place" orders and other public health guidance measures, we have, and may in the future, experience disruptions that could seriously harm our business. Disruptions due to the COVID-19 pandemic that have and may in the future impact our business include, but are not limited to:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in initiating or expanding clinical trials, including delays or difficulties with clinical site initiation and recruiting clinical site investigators and clinical site staff;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19 or other health conditions or being forced to quarantine;
- interruption of key clinical trial activities, such as clinical trial site data monitoring and efficacy, safety and translational data collection, processing and analyses, due to limitations on travel imposed;
- recommendations by federal, state or local governments, employers and others or interruptions of clinical trial subject visits, which may impact the collection and integrity of subject data and clinical trial endpoints;
- 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;
- delays or disruptions in preclinical experiments and IND-enabling studies due to restrictions of on-site staff and unforeseen circumstances at CROs and vendors;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, raw materials shortages, production slowdowns or stoppages and disruptions in delivery systems;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- limitations on employee or other resources that would otherwise be focused on the conduct of our clinical trials and preclinical work, including because of sickness of employees or their families, the desire of employees to avoid travel or contact with large groups of people, an increased reliance on working from home, school closures or mass transit disruptions;

- changes in regulations as part of a response to the COVID-19 pandemic 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;
- 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; and
- refusal of the FDA to accept data from clinical trials in affected geographies outside the United States.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19, could continue to spread to additional countries or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct clinical trials and our business generally, and could seriously harm our business.

The COVID-19 pandemic continues to rapidly evolve, including the spread of new variants that have proven to be more contagious and deadly. The extent to which the COVID-19 pandemic may affect our clinical trials, business, financial condition and results of operations will depend on future developments (such as the prevalence of new variants), which are highly uncertain and cannot be predicted at this time, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Future developments in these and other areas present material uncertainty and risk with respect to our clinical trials, business, financial condition and results of operations.

We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be initiated or conducted as planned or completed on schedule, if at all. For example, in the first half of 2019 a manufacturing batch of our product candidate 4D-110 produced at a CMO failed to meet the specifications required for use in our planned clinical trial due to an issue identified with one of the plasmids used in the manufacturing process. As a result, we delayed the initiation of our planned first-in-human trial of 4D-110 until July 2020, so that we could produce the clinical-grade material required for the trial using our in-house manufacturing facility. We also cannot be sure that submission of an IND or a clinical trial application ("CTA") will result in the FDA or other regulatory authority, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in reaching a consensus with regulatory agencies on study design or implementation of the clinical trials;
- adverse impacts from the COVID-19 pandemic as further described elsewhere in these risk factors;
- delays or failure in obtaining regulatory authorization to commence a trial;
- delays in 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 clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;

- delays in obtaining required IRB approval at each clinical trial site;
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, CTA or amendment, or equivalent foreign application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites;
- developments on trials conducted by competitors for related technology that raise FDA or foreign regulatory authority concerns about risk to patients of the technology broadly; or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical trial protocols;
- failure to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements ("GCPs") or applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization ("CMO") or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the severity and difficulty of diagnosing the disease under investigation, size of the patient population and process for identifying subjects, eligibility and exclusion criteria for the trial in question, design of the trial protocol, availability and efficacy of approved therapies or other clinical trials for the disease or condition under investigation, perceived risks and benefits of the product candidate under trial or testing, availability of genetic testing for potential patients, efforts to facilitate timely enrollment in clinical trials, patient referral practices of physicians, ability to obtain and maintain subject consent, the

risk that enrolled subjects will drop out before completion of the trial, the ability to monitor patients adequately during and after treatment, and the proximity and availability of clinical trial sites for prospective patients. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to, or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may seriously harm our business.

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

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. 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.

The limited number of patients who have the diseases for which our product candidates are being studied may make it more difficult for us to enroll or complete clinical trials or may result in findings in our clinical trials that do not reach levels of statistical significance sufficient for marketing approval.

Most of the conditions for which we plan to evaluate our current product candidates in clinical trials are rare genetic diseases. Accordingly, there are limited patient pools from which to draw for clinical trials. In addition to the rarity of these diseases, the eligibility criteria of our clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their disease is either severe enough or not too advanced to include them in a trial. We or our collaborators may not be able to initiate or continue clinical trials on a timely basis or at all for any of our product candidates if we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Similarly, because most of the conditions we intend to treat are rare in nature, we plan to design and conduct clinical trials utilizing a small number of patients in order to evaluate the safety and therapeutic activity of our product candidates. Conducting trials in smaller subject populations increases the risk that any safety or efficacy issues observed in only a few patients could prevent such trials from reaching statistical significance or otherwise meeting their specified endpoints, which could require us to conduct additional clinical trials, or delay or prevent our product candidates from receiving regulatory approval, which would seriously harm our business.

Research and development of biopharmaceutical products is inherently risky. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized or if they will ever be successfully commercialized.

We are at an early stage of development of our product candidates. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;
- delays in our clinical development plans due to the COVID-19 pandemic;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- our competitors may develop platform technologies that render our Therapeutic Vector Evolution platform technology obsolete or less attractive;
- the product candidates and Therapeutic Vector Evolution platform technology that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights or may be covered by third-party patents or other intellectual property or exclusive rights;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If any of these events occur, we or our collaborators may be forced to abandon our development efforts for a product candidate or candidates, which would seriously harm our business. Failure of a product candidate may occur at any stage of preclinical or clinical development, and, because our product candidates and our Therapeutic Vector Evolution platform technology are in an early stage of development, there is a relatively higher risk of failure and we may never succeed in developing marketable products or generating product revenue.

We may not be successful in our efforts to further develop our Therapeutic Vector Evolution platform technology and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all. Any clinical trials that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future clinical trials are inconclusive with respect to the efficacy of our product candidates or if we do not meet the clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for our product candidates.

If any of our product candidates successfully completes clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would seriously harm our business. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, purity, potency, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing and distribution of our product candidates. We may also rely on our collaborators or collaboration partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or collaboration partners will conduct these activities successfully or do so within the timeframe we desire. Even if we (or our collaborators or collaboration partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. Failure to obtain approval for our product candidates in multiple jurisdictions, will seriously harm our business.

Even if we receive regulatory approval to market any of our product candidates, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Any approval we may obtain could be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a REMS. The failure to obtain timely regulatory approval of product candidates, any product marketing limitations or a product withdrawal would seriously harm our business.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could seriously harm our business.

The ability of the FDA to review and/or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most foreign inspections of manufacturing facilities, and subsequently, on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could seriously harm our business.

Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we or our collaborators must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Further, because our product candidates are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our planned clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could seriously harm our business.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential.

Interim "top-line" and preliminary data from studies or trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim "top-line" or preliminary data from preclinical studies or clinical trials. Interim data are subject to the risk that one or more of the outcomes may materially change as more data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary or "top-line" 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, interim and preliminary data should be viewed with caution until the final data are available. Additionally, interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could seriously harm our business.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the top-line data that we report differ from final results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could seriously harm our business.

We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.

One of our strategies is to identify and pursue preclinical and clinical development and commercialization of additional product candidates through our Therapeutic Vector Evolution platform technology. Our Therapeutic Vector Evolution platform technology may not produce a pipeline of viable product candidates, or our competitors may develop platform technologies that render our Therapeutic Vector Evolution platform technology obsolete or less attractive. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be

shown to have harmful side effects or may have other characteristics that may make them unmarketable or unlikely to receive marketing approval. Identifying, developing and obtaining regulatory approval and commercializing additional product candidates will require substantial funding and is prone to the risks of failure inherent in drug development. If we are unable to successfully identify, acquire, develop and commercialize additional product candidates, our commercial opportunity may be limited.

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

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of the indications for which we have product candidates, including XLRP, choroideremia, Fabry disease, wet AMD, and cystic fibrosis lung disease. Certain of our competitors have commercially approved products for the treatment of the diseases that we are pursuing or may pursue in the future, including Biogen, Roche, Sanofi, Takeda and Vertex. These drugs are well established therapies and are widely accepted by physicians, patients and third-party payors, which may make it difficult to convince these parties to switch to our product candidates. Companies that we are aware are developing therapeutics in the ophthalmology, cardiology and pulmonology disease areas include large companies with significant financial resources, such as Allergan, Biogen, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda and Vertex, and biopharmaceutical companies such as Abeona, Adverum, AGTC, Amicus, Avrobio, Freeline, Kodiak Sciences, Krystal, MeiraGTx, RegenxBio, Sangamo, and Spirovant. In addition to competition from other companies targeting ophthalmology, cardiology and pulmonology, any products we may develop may also face competition from other types of therapies, such as gene-editing therapies and drug delivery devices.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our product candidates. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of ophthalmology, cardiology and pulmonology indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists 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 and other commercialization 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 commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, compliance, customer service, medical affairs and other support personnel;
- our inability to recruit and build a commercial infrastructure due to the impacts of COVID-19;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

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

Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- sufficient third-party coverage or reimbursement;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, EMA or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

Risks Related to Manufacturing

Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products or otherwise seriously harm our business.

We currently have a development, manufacturing and testing agreement and cooperation agreement with Catalent to manufacture supplies of our product candidates in the future. Our product candidates require processing steps that are more complex than those required for most chemical and protein pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory, which could delay or prevent the initiation of clinical trials or receipt of regulatory approvals. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, or other comparable applicable foreign standards or specifications with

consistent and acceptable production yields and costs. For example, in the first half of 2019, a manufacturing batch of our product candidate 4D-110 produced at a CMO failed to meet the specifications required for use in our planned clinical trial due to an issue identified with one of the plasmids used in the manufacturing process. As a result, we delayed the initiation of our planned first-in-human trial of 4D-110 until July 2020, so that we could produce the clinical-grade material required for the trial using our in-house manufacturing facility.

In addition, FDA and other comparable foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other comparable foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches which could be costly to us and otherwise seriously harm our business.

We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing process which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to meet market demand for our products. Additionally, should our agreement with Catalent or agreements with other parties with whom we have manufacturing agreements be terminated for any reason, there are a limited number of manufacturers who would be suitable replacements, and it would take a significant amount of time to transition the manufacturing to a replacement.

Delays in obtaining regulatory approval of our manufacturing process or disruptions in our manufacturing process may delay or disrupt our commercialization efforts.

Before we can begin to commercially manufacture our product candidates in third-party or our own facilities, we must obtain regulatory approval from the FDA to market our product using the manufacturing process and facility we proposed in our marketing application. In addition, we must pass a pre-approval inspection of our manufacturing facility by the FDA before any of our product candidates can obtain marketing approval, if ever. In order to obtain approval of a BLA for our product candidates, we will need to ensure that all of our manufacturing processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

Delays in developing our manufacturing capabilities or failure to achieve operating efficiencies from it may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines.

We have a small operational manufacturing facility that we are using to manufacture clinical trial material. In addition, we have leased approximately 17,000 square feet of space primarily for our second manufacturing facility in Emeryville, California, most of which we plan to devote to manufacturing activities for our clinical trials. We may face delays in the production of clinical supply at our manufacturing facility

and cannot guarantee when our facility will be able to produce sufficient quantities of product candidates needed to support our planned clinical trials. Any delays in developing our internal manufacturing capabilities may disrupt or delay the supply of our product candidates if we have not maintained a sufficient back-up supply of such product candidates through third-party manufacturers. Moreover, changing manufacturing facilities during the clinical development process may also require that we or our collaborators conduct additional studies, make notifications to regulatory authorities, make additional filings to regulatory authorities, and obtain regulatory authority approval for the new facilities, which may be delayed or which we may never receive. We will further need to comply with the FDA's and applicable foreign regulatory authorities' cGMP requirements for the production of product candidates for clinical trials and, if approved, commercial supply, and will be subject to FDA and comparable foreign regulatory authority inspection. These requirements include the qualification and validation of our manufacturing equipment and processes. We may not be able to develop or acquire the internal expertise and resources necessary for compliance with these requirements.

In order to develop internal manufacturing expertise, we may be forced to devote greater resources and management time than anticipated, particularly in areas relating to operations, quality, regulatory, facilities and information technology. We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing processes. If we experience unanticipated employee shortage or turnover in any of these areas, we may not be able to effectively manage our ongoing manufacturing operations and we may not achieve the operating efficiencies that we anticipate from developing these capabilities, which may negatively affect our product development timeline or result in difficulties in maintaining compliance with applicable regulatory requirements. Any such problems could result in the delay, prevention or impairment of clinical development and commercialization of our product candidates and would seriously harm our business.

We currently rely and expect to continue to rely on third parties to conduct product manufacturing for certain of our product candidates, and these third parties may not perform satisfactorily.

Although we are in process of expanding internal manufacturing capabilities, we currently rely, and expect to continue to rely, on third parties for the production of some of our preclinical study and planned clinical trial materials and, therefore, we can control only certain aspects of their activities. The facilities used by us and our contract manufacturers to manufacture certain of our product candidates must be reviewed by the FDA pursuant to inspections that will be conducted after we submit our BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMPs for manufacture of our products. If we or our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to obtain and/or maintain regulatory approval for our products as manufactured at their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

In addition, we rely on additional third parties to manufacture plasmids used in the manufacture of our product candidates and to perform quality testing, and reliance on these third parties entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- reduced control for certain aspects of manufacturing activities;
- termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future product candidates. Some of these events could be the basis for FDA or European Union Member State regulatory authority action, including injunction, recall, seizure or total or partial suspension of product manufacture.

Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our research studies, preclinical, clinical development or marketing schedules.

Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage.

Some of the raw materials required in our manufacturing process, such as plasmids, are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could seriously harm our business.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could seriously harm our business.

We rely on third-party suppliers for the raw materials required for the production of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors who are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any interruption in supply of raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supplier in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would seriously harm our business.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, expensive, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be seriously harmed.

We and any collaborators are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. We have not submitted for or obtained regulatory approval for any product candidate. We and any collaborators must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in

humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, implementation or results of our or our collaborators' clinical trials;
- the FDA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use of our products;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we or our collaborators may be unable to demonstrate to the FDA, or comparable foreign regulatory authorities that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would seriously harm our business.

In addition, even if we or our collaborators were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a REMS. Regulatory authorities may not approve the price we or our collaborators intend to charge for products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could seriously harm our business.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We may in the future seek an accelerated approval for one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post- approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit a BLA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or receive an expedited regulatory designation (e.g., breakthrough therapy designation) for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we or our collaborators obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

If one of our product candidates is approved, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we

work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs and biologics are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products "off-label" for indications or uses for which they do not have approval, though we may share truthful and not misleading information that is otherwise consistent with our product's FDA approved labeling. The holder of an approved application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval or label restrictions.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, our business will be seriously harmed.

Moreover, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We have received Fast Track designation for 4D-310 for the treatment of Fabry disease to improve pain, disability and organ dysfunction, and we may seek Fast Track designation for certain future product candidates, but we may not be able to obtain such designations, and there is no guarantee that 4D-310 will experience a faster regulatory review or obtain regulatory approval.

If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this disease condition, the product sponsor may apply for Fast Track designation. The sponsor of a Fast Track product has

opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. We have received Fast Track designation for 4D-310 for the treatment of Fabry disease to improve pain, disability and organ dysfunction, and we may receive Fast Track designation for other product candidates in the future; however, we may not experience a faster development, review or approval process, and receipt of the designation does not increase the likelihood that the FDA will approve 4D-310 for any indication. In addition, the FDA may rescind the Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

We have received orphan drug designation for 4D-110 for the treatment of choroideremia and for 4D-310 for the treatment of Fabry disease, and we may seek orphan drug designation for certain future product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced.

We have received orphan drug designation in the United States for 4D-110 for the treatment of choroideremia and for 4D-310 for the treatment of Fabry disease. Although we may seek orphan product designation for some or all of our other product candidates, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a drug or biologic product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation must be requested before submitting a BLA. In the European Union, the EMA's Committee for Orphan Medicinal Products ("COMP"), grants 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 affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

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 application fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA.

In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity for the orphan patient population. Exclusive marketing rights in the United States may also be unavailable if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six

years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Even if we obtain orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process.

If the product candidates that we or our collaborators may develop receive regulatory approval in the United States or another jurisdiction, they may never receive approval in other jurisdictions, which would limit market opportunities for such product candidate and seriously harm our business.

Approval of a product candidate in the United States by the FDA or by the requisite regulatory agencies in any other jurisdiction does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions. The approval process varies among countries and may limit our or our collaborators' ability to develop, manufacture, promote and sell product candidates internationally. Failure to obtain marketing approval in international jurisdictions would prevent the product candidates from being marketed outside of the jurisdictions in which regulatory approvals have been received. In order to market and sell product candidates in the European Union and many other jurisdictions, we and our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional preclinical studies or clinical trials both before and after approval. In many countries, any product candidate for human use must be approved for reimbursement before it can be approved for sale in that country. In some cases, the intended price for such product is also subject to approval. Further, while regulatory approval of a product candidate in one country does not ensure approval in any other country, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we or our collaborators fail to comply with the regulatory requirements in international markets or to obtain all required marketing approvals, the target market for a particular potential product will be reduced, which would limit our ability to realize the full market potential for the product and seriously harm our business.

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

In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively the "ACA") was enacted, which substantially changed the way healthcare is financed by both governmental and private payors. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;

- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting “transfers of value” made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- an increase to the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and an extension the rebate program to individuals enrolled in Medicaid managed care organizations;
- 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;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer’s Medicaid rebate liability;
- a licensure framework for follow-on biologic products;
- 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
- establishment of 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.

Since its enactment, there have been judicial, U.S. Congressional and executive branch challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the Tax Cuts and Jobs Act of 2017 was enacted, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas (“Texas District Court Judge”) ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case, although it is unclear when a decision will be made or how the Supreme Court will rule. It is also unclear how other efforts to challenge, repeal or replace the ACA will impact the ACA or our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2020, unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, seriously harm our business.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. On March 10, 2020, the Trump administration sent “principles” for drug pricing to Congress, calling for

legislation that would among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, on July 24, 2020, the Trump administration announced four executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals, including a policy that would tie Medicare Part B drug prices to international drug prices; one that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and makes other changes allowing for personal importation of drugs from Canada; one that directs HHS to finalize the rulemaking process on modifying the federal Anti-Kickback Statute safe harbors for discounts for plans, pharmacies, and pharmaceutical benefit managers; and one that reduces costs of insulin and epipens to patients of federally qualified health centers. Although a number of these will require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures and could seriously harm our business.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could seriously harm our business. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. Prescription drugs and biological products that are in violation of these requirements will be included on a public list. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing and could seriously harm our business.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or judicial action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to

maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Even if we are able to commercialize any product candidates, due to unfavorable pricing regulations and/or third-party coverage and reimbursement policies, we may not be able to offer such products at competitive prices which would seriously harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. 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 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 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 any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. 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 medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs (“VA”) hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, other third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. 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. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, that the level of reimbursement will be sufficient.

Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, 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 drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into

existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could seriously harm our business.

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

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

We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell any products effectively, if approved, or generate product revenue.

We currently do not have a marketing or sales organization. In order to commercialize any product, if approved, in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In advance of any of our product candidates receiving regulatory approval, we expect to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize each such product candidate, which will be expensive and time-consuming. We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates. If we are not successful in commercializing products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses and our business would be seriously harmed.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties and seriously harm our business.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, 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 any U.S. federal healthcare program, 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 civil and criminal false claims and civil monetary penalties laws, including the civil federal False Claims Act, which can be enforced through civil whistleblower or *qui tam* actions, which prohibit, among other things, individuals or entities from 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. Pharmaceutical manufacturers can cause false claims to be presented to the U.S. federal government by engaging in impermissible marketing practices, such as the off-label promotion of a product for an indication for which it has not received FDA approval. 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 civil False Claims Act;
- the 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 U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to report annually to CMS information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding payments and transfers of value provided during the previous year to certain other healthcare providers, including

physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives;

- analogous U.S. 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
- similar healthcare laws in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

We may also be subject to additional federal laws, such as the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof, and federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

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, including certain of our advisory board arrangements with physicians, some of whom are compensated in the form of stock or stock options, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

We use and generate materials that may expose us to material liability.

Our research programs involve the use of hazardous materials and chemicals. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products such as human tissue samples that may have the potential to transmit diseases. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers' compensation, property and business

interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims.

Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our products.

The Animal Welfare Act ("AWA") is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

Risks Related to Our Reliance on Third Parties

We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, clinical data assessments and analysis organizations, medical institutions and clinical investigators, to conduct some aspects of our research, preclinical testing and clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities, but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We are also required to register ongoing clinical trials and to post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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 any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

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

We have sought, and may in the future seek third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional, national and international pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates that result from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to collaborations;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide not to pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;

- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become party to a business combination transaction and the continued pursuit and emphasis on our development or commercialization program by the resulting entity under our existing collaboration could be delayed, diminished or terminated;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, devices, materials, know-how or intellectual property of the collaborator relating to our products and product candidates;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- 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 or our Therapeutic Vector Evolution platform technology; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate or delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue which could seriously harm our business.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator’s technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this “Risk Factors” section, and any negative impact on our collaborators may adversely affect us.

Risks Related to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. 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. Further, we have one pending patent application (patent no. 14/774,972), that was made with government support, that may be subject, under certain circumstances, to march-in-rights under 35 U.S.C. 203, which is a right that allows the government, in certain limited circumstances, to force a party with a license to intellectual property funded, at least in part, by the government, to grant a license to such property to another entity. This patent was made with the support of U.C. Berkeley and relates to our A101 vector. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our product candidates and proprietary technologies and erode or negate any competitive advantage we may have, which could seriously harm our business.

We and our licensors have applied, and we intend to continue applying, for patents covering aspects of our product candidates, proprietary technologies and their uses that we deem appropriate. However, we may not be able to apply for patents on certain aspects of our current or future product candidates, proprietary technologies and their uses in a timely fashion, at a reasonable cost, in all jurisdictions, or at all, and any potential patent coverage we obtain may not be sufficient to prevent substantial competition.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators or licensors will be successful in protecting our product candidates, proprietary technologies and their uses by obtaining and defending patents. These risks and uncertainties include the following:

- the U.S. Patent and Trademark Office (“USPTO”) and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;

- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same methods or devices or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any products or product candidates that we may develop;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates, proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013;
- 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; and
- 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 patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. Moreover, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents, if issued, patents obtained by our collaborators or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical products or product candidates, or limit the duration of the patent protection of our product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor’s or potential competitor’s product or service. We may not prevail in any

lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering our product candidates are invalidated or found unenforceable, or if a court found that valid, enforceable patents held by third parties covered one or more of our product candidates, our competitive position could be harmed or we could be required to incur significant expenses to enforce or defend our rights. If we initiate lawsuits to protect or enforce our patents, or litigate against third-party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- any of our pending patent applications or those of our licensors may issue as patents;
- others will not or may not be able to make, use, offer to sell, or sell products that are the same as or similar to our own but that are not covered by the claims of the patents that we own or license;
- we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we or our licensors were the first to make the inventions covered by each of the patents and pending patent applications that we own or license;
- we or our licensors were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe the patents we own or license;
- any of the patents we own or license will be found to ultimately be valid and enforceable;
- any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable products or will provide us with any competitive advantages;
- a third party may not challenge the patents we own or license and, if challenged, a court would hold that such patents are valid, enforceable and infringed;
- we may develop or in-license additional proprietary technologies that are patentable;
- the patents of others will not have an adverse effect on our business;
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

Where we obtain licenses from or collaborate with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have

obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could seriously harm our business.

Furthermore, our owned and in-licensed intellectual property rights may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could seriously harm our business.

The lives of our patents may not be sufficient to effectively protect our product candidates and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective non-provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, proprietary technologies and their uses are obtained, once the patent life has expired, we may be open to competition. In addition, although upon issuance in the United States a patent's life can be extended based on certain delays caused by the USPTO and clinical development, this extension can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. 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. If we do not have sufficient patent life to protect our product candidates, proprietary technologies and their uses, our business would be seriously harmed.

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

We rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. We have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees and consultants. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and 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. In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third party with authorized access. Our security measures may not prevent an employee, consultant, collaborator or customer or third party from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our product candidates that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and

time-consuming, and the outcome is unpredictable. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions.

Though our agreements with third parties typically restrict the ability of our employees, collaborators, licensors, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we have relied on, and in future expect to rely on third parties in the development, manufacture, and distribution of our product candidates and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets 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. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors.

We currently are reliant upon licenses of certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology, including technology related to our product candidates. For example, we rely on our exclusive license agreements with U.C. Berkeley for all of our rights with respect to the intellectual property covering certain compositions of matter and methods of use of certain AAV variants related to our research candidates in lead optimization stage. These and other licenses we may enter into in the future may not provide adequate rights to use such intellectual property and technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize our technology and product candidates in the future. As a result, we may not be able to develop and commercialize our technology and product candidates in fields of use and territories for which we are not granted rights pursuant to such licenses.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could seriously harm our business.

In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our product candidates. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance

with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

Our current licenses, and our future licenses likely will, impose various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, we may be required to pay damages and the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights, and could prevent us from developing and commercializing our product candidates and proprietary technologies. Our business would be seriously harmed if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of royalty obligations we would be required to pay on the sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in product candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize any product candidates, we may be unable to achieve or maintain profitability.

If our trademarks and trade names, whether registered in the future or unregistered now, 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.

Any trademarks we may register in the future or any current unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names, to the extent any are registered, to third parties, such as distributors. Though 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. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could seriously harm our business.

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 gene therapy products that are similar to our product candidates or utilize similar gene therapy technology 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 patents or pending patent applications 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 our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be 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; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could seriously harm our business.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products.

Any future collaborations that we enter into may not be successful, such as our collaboration agreements with Pfizer that was terminated in 2018 and with AstraZeneca that concluded in 2020 without AstraZeneca exercising its option. 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 product candidates 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 and product candidates that compete directly or indirectly with our product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products and product candidates 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 current or future product candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may adversely affect the price of our common stock and may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- collaborators may own or co-own intellectual property covering our product candidates 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.

Risks Related to Our Operations

We are highly dependent on our key personnel, and if we are not successful in attracting, motivating 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, motivate and retain highly qualified managerial, scientific and medical personnel. The loss of the services provided by 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 the development of our product candidates and harm our business.

We conduct our operations at our facilities in Emeryville, California, in a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region, and doing so may be costly and difficult.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock option grants. The value to employees of these equity grants 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. In addition, our employees are employed at-will, which means that any of our employees could leave our employment at any time, with or without notice. If we are unable to attract, incentivize and retain quality personnel on acceptable terms, or at all, it could seriously harm our business.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2020, we had 83 full-time employees. As our development plans and strategies develop, and as we transition into operating as a public company, we must add a significant number of additional managerial, operational, financial and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining and motivating additional employees;

- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;
- expanding our operational, financial and management controls, reporting systems and procedures; and
- managing increasing operational and managerial complexity.

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

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

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

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the U.S. dollar would make those clinical trials more costly to operate. Furthermore, a severe or prolonged economic downturn, including a recession or depression resulting from the current COVID-19 pandemic or political disruption could result in a variety of risks to our business, including weakened demand for our product candidates or any future product candidates, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption, including any international trade disputes, could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our potential products. Any of the foregoing could seriously harm our business, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could seriously harm our business.

If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;

- the issuance of our equity securities which would result in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product candidates and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Our information technology systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches and other disruptions.

We have experienced cyberattacks, including a phishing attack in September 2019 in which the email account of a single non-officer employee was compromised. Our security controls detected the compromise, and we were able to block the unauthorized access, but not before the attacker was able to use the account to send out additional phishing emails. We do not believe the phishing attack was a material incursion because, among other reasons, we believe that none of our data was accessed or compromised, and we have not incurred any related material remediation costs. Despite the implementation of security measures like those that detected the phishing attack, our internal information technology systems and those of our collaborators, future CROs and other contractors and consultants may be vulnerable to damage from computer viruses, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, denial or degradation of service attacks, unauthorized access or use, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. The costs to us to investigate and mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service, negative publicity and other harm to our business and our competitive position. Although to our knowledge we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss, corruption or unauthorized disclosure of our trade secrets, personal data or other proprietary or sensitive information or other similar disruptions.

For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of clinical trial data or personal data, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media, and other parties pursuant to privacy and security laws. Likewise, we rely on our third-party research institution

collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their information technology systems could also seriously harm our business. Any security compromise affecting us, our partners or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures, and lead to regulatory scrutiny. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary or personal information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed.

Business disruptions could seriously harm our business.

Our operations, and those of our CROs, CMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our business.

All of our operations including our corporate headquarters are located in multiple facilities in Emeryville, California. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, earthquake and other natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business could be seriously harmed by such delays and interruption.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the United States and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could seriously harm our business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations implemented thereunder, imposes, among other things, certain standards on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by 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. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, California enacted the California Consumer Privacy Act ("CCPA") on June 28, 2018, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. In the event that we are subject to or affected by HIPAA, the CCPA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. In Europe, the GDPR went into effect in May 2018 and introduces strict requirements for processing the personal data of individuals within the European Economic Area ("EEA") and the United Kingdom. The law is also developing rapidly and, in July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EU to the U.S. by invalidating the EU-U.S. Privacy Shield as a basis for transfers of personal data from the EU to the U.S. and raising questions about the continued validity of one of the primary alternatives to the EU-U.S. Privacy Shield, namely the European Commission's Standard Contractual Clauses. At present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the Standard Contractual Clauses. Inability to transfer personal information from the European Union, Switzerland or United Kingdom to the United States or elsewhere, may restrict our activities in those jurisdictions and limit our ability to provide our products and services in those jurisdictions. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Relatedly, following the departure of the United Kingdom from the EU after the expiry of the transition period, the United Kingdom will operate a separate but similar regime to the EU, which allows for fines of up to £17.5 million or 4% of the total worldwide annual turnover of the preceding financial year.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, CROs, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and seriously harm our business.

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

Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards ("NOLs") and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre-change NOLs or other pre-change tax attributes if we undergo a future ownership change. We have experienced ownership changes in the past. We may also experience ownership changes as a result of any future shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our NOLs and other pre-change tax attributes to offset post-change taxable income or taxes may be subject to limitation. We will be unable to use our NOLs or other tax attributes if we do not attain profitability sufficient to offset our available NOLs or other tax attributes prior to their expiration, to the extent subject to expiration.

Changes in tax laws or regulations that are applied adversely to us or our customers may seriously harm our business.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of any of our future domestic and foreign earnings. Any new taxes could adversely affect our domestic and international business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be volatile, which could result in substantial losses for investors.

Some of the factors that may cause the market price of our common stock to fluctuate include:

- results from, and any delays in, our clinical trials for our clinical-stage product candidates or any other future clinical development programs, including any delays related to the COVID-19 pandemic;
- the success of existing or new competitive products or technologies;
- commencement or termination of collaborations for our product candidates;
- failure or discontinuation of any of our product candidates;
- failure to develop our Therapeutic Vector Evolution platform technology;
- results of preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the commencement of litigation;
- the level of expenses related to any of the research programs or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- expiration of market standoff or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Further, the stock market in general has been highly volatile due to the COVID-19 pandemic and political uncertainty in the United States. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We currently have research coverage by three financial analysts. If one or more of these analysts should drop research coverage of us or if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, upon the expiration of the market standoff and lock-up agreements, the early release of these agreements or the perception in the market that the holders of a large number of shares of our common stock intend to sell shares, could reduce the market price of our common stock. As of December 31, 2020 we have 26,681,983 shares of our common stock outstanding. Of these shares, the 9,660,000 shares we sold in our initial public offering ("IPO") in December 2020, may be sold in the public market immediately, unless purchased by our affiliates. The remaining 17,021,983 shares, or 63.8% of our outstanding shares as of December 31, 2020, are currently prohibited or otherwise restricted under securities laws, market standoff agreements entered into by our stockholders with us, or lock-up agreements entered into by our stockholders with the underwriters. However, subject to applicable securities law restrictions and excluding shares of restricted stock that will remain unvested, prohibitions and restrictions on the sale of these shares in the public market will be lifted beginning June 9, 2021. Goldman Sachs & Co. LLC, BofA Securities, Inc. and Evercore Group L.L.C. may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. Shares issued upon the exercise of stock options outstanding under our equity incentive plans, or pursuant to future awards granted under those plans, will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act of 1933, as amended (the "Securities Act").

Moreover, holders of an aggregate of 11.6 million shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have registered all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described in our final prospectus related to our IPO. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We will seek additional capital through one or a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future offerings. To the extent that we raise additional capital through the sale of equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Insiders have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.

Our directors, executive officers, holders of more than 5% of our outstanding stock and their respective affiliates beneficially own shares representing approximately 49.8% of our outstanding common stock as of December 31, 2020. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

We are an "emerging growth company" and a "smaller reporting company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, 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 stockholder approval of any golden parachute payments not previously approved. In addition, as an "emerging growth company" the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. 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 (1) the last day of the year following the fifth anniversary of the consummation of our IPO, (2) the last day of the year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if 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 or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

Even after we no longer qualify as an “emerging growth company,” we may still qualify as a “smaller reporting company,” which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including, among other things, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, presenting only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and reduced disclosure obligations.

We will incur significant costs as a result of operating as a public company, and our management will devote substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would seriously harm our business.

We will incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of the Nasdaq Global Select Market and the rules of the Securities and Exchange Commission (“SEC”) require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 (“Section 404”) and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Beginning with the second annual report that we will be required to file with the SEC, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting.

To date, we have never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. In order to report our results of operations and financial statements on an accurate and timely basis, we will depend in part on CROs to provide timely and accurate notice of their costs to us.

Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would seriously harm our business.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our Company may deem advantageous. These provisions, among other things:

- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- provide that our directors may be removed only for cause;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- provide for a staggered board, which will result in only a few directors being up for re-election in each calendar year;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws;
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of our common stock to amend many of the provisions described above; and
- limit the liability of, and provide indemnification to, our directors and officers.

In addition, Section 203 of the General Corporation Law of the State of Delaware (“DGCL”) prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our certificate of incorporation, bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for certain 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 and amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, in the event that the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws will also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act. Nothing in our amended and restated certificate of incorporation and amended and restated bylaws precludes stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could seriously harm our business.

We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

General Risk Factors

Any legal proceedings or claims against us could be costly and time-consuming to defend and could harm our reputation regardless of the outcome.

We are and may in the future become subject to legal proceedings and claims that arise in the ordinary course of business, such as disputes or employment claims made by our current or former employees. Any litigation, whether meritorious or not, could harm our reputation, will increase our costs and may divert management's attention, time and resources, which may in turn seriously harm our business. Insurance might not cover such claims, might not provide sufficient payments to cover all the costs to resolve one or more such claims, and might not continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs and could seriously harm our business.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical 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, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to cease commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased or interrupted demand for our products;
- substantial monetary awards to trial participants or patients;

- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Our employees, independent contractors, consultants, research or commercial partners or collaborators and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, research or commercial partners or other collaborators, including the foundations we work with, and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA, EMA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA and other comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third parties, 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 be in compliance with such laws. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could seriously harm our business, including the imposition of significant fines or other sanctions.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could seriously harm our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could seriously harm our business.

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.

Reliance on third parties to conduct clinical trials, assist in research and development and to manufacture our product candidates, will at times require us to share trade secrets with them. We seek to protect our proprietary technology by in part 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 seriously harm our business.

We may fail to comply with any of our obligations under existing or future agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

We are party to various agreements that we depend on to operate our business. Our rights to use currently licensed intellectual property, or intellectual property to be licensed in the future, are or will be subject to the continuation of and our compliance with the terms of these agreements. These agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations which could lead to disputes, including but not limited to those regarding:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our proprietary technology and product candidates infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us or our counterparties, alone or jointly;
- the scope and duration of our payment obligations;
- rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

The resolution of any contractual interpretation dispute that may arise, if unfavorable to us, could seriously harm our business. Such resolution could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, increase what we believe to be our financial or other obligations under the relevant agreement, or decrease the third party's financial or other obligations under the relevant agreement.

If disputes over intellectual property rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current license agreements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future license agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements.

Litigation or other proceedings or third-party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our products.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. We cannot assure you that our operations do not, or will not in the future, infringe existing or future patents or other proprietary rights of third parties.

Third parties may have or obtain patents or other proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and future approved products, if any, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, *inter partes* review proceedings and post-grant review proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and

pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates.

Furthermore, 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 and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent 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, which may negatively impact our ability to develop and market our product candidates.

As the biotechnology 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. 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. 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 United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These 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 product candidates. As a result, we may be unaware of third-party patents that may be infringed by commercialization of our product candidates, and cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, 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. In addition, identification of third-party patent rights that may be relevant to our technology 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. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing; and/or

- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this report, others may hold proprietary rights that could prevent our product candidates or any future products from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or proprietary technologies could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates or any future products. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be time-consuming and a substantial diversion of management and employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Even if such licenses are available, we could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins, and the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. In addition, we cannot be certain that we could redesign our product candidates or proprietary technologies to avoid infringement, if necessary, or on a cost-effective basis. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates or any future products which could seriously harm our business. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. Also, we may be obligated under our agreements with our collaborators, licensors, suppliers and others to indemnify and hold them harmless for damages arising from intellectual property infringement by us.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged.

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court or administrative tribunal may decide that a patent we own or license is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and may result in the revocation, cancellation, or amendment of any foreign patents we hold in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we could lose at least part, and perhaps all, of the patent protection on an affected product candidate. Such a loss of patent protection would seriously harm our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO, or equivalent actions brought in foreign jurisdictions, may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be seriously harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract 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 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 conduct such litigation or proceedings adequately. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace and seriously harm our business.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. 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 our common stock.

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

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will depend in part on our ability to acquire, license or use these proprietary rights. We may be unable to acquire or 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 are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We have collaborated with, and are currently collaborating with, U.S. academic institutions and may in the future collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution’s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified

timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

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 that program and our business could be seriously harmed.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we, our employees or consultants have wrongfully used or disclosed alleged confidential information or trade secrets of their former or concurrent employers or former or current clients.

As is common in the biotechnology and biopharmaceutical industries, 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 biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees or consultants, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer or former or current client. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, which could seriously harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management and other employees.

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

Our agreements with employees and consultants provide that any inventions conceived by an individual in the course of rendering services to us shall be our exclusive property. Although our policy is to have all such individuals complete these agreements, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property may not be self-executing and despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. We may also be subject to claims that former employees, consultants, or other third parties have an ownership interest in our patents or other intellectual property. In addition, we may face claims by third parties that our agreements with employees or consultants obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could seriously harm our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to our management and other employees.

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

Depending upon the timing, duration and specifics of FDA marketing approval of any of our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five

years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration of the applicable product, and our business may be seriously harmed.

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

Our patent rights may be affected by developments or uncertainty in the U.S. or foreign patent statutes, patent case laws, USPTO rules and regulations or in the rules and regulations of foreign patent offices.

There are a number of recent changes to the U.S. patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, the Leahy-Smith America Invents Act ("Leahy-Smith Act") was signed into law. The Leahy-Smith Act includes a number of significant changes to the U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. This could have a negative impact on some of our intellectual property and could increase uncertainties surrounding obtaining and enforcement or defense of our issued patents. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, 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 we might obtain in the future. Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

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

Filing, prosecuting and defending all current and future patents 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 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.

The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, 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. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our business may be seriously harmed.

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.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own, and if we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located in Emeryville, California, where we lease approximately 51,000 square feet of office, research and development, engineering and laboratory space pursuant to lease agreements that expire in September 2026 and December 2029. We believe that our facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

Item 3. Legal Proceedings.

We are not currently a party to any material legal proceedings.

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of its business. If applicable, the Company records a liability for such matters when it believes that it is both probable that a liability may be imputed, and the amount of the liability can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount. Regardless of outcome litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

None.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "FDMT" since December 11, 2020. Prior to this date, there was no public market for our common stock.

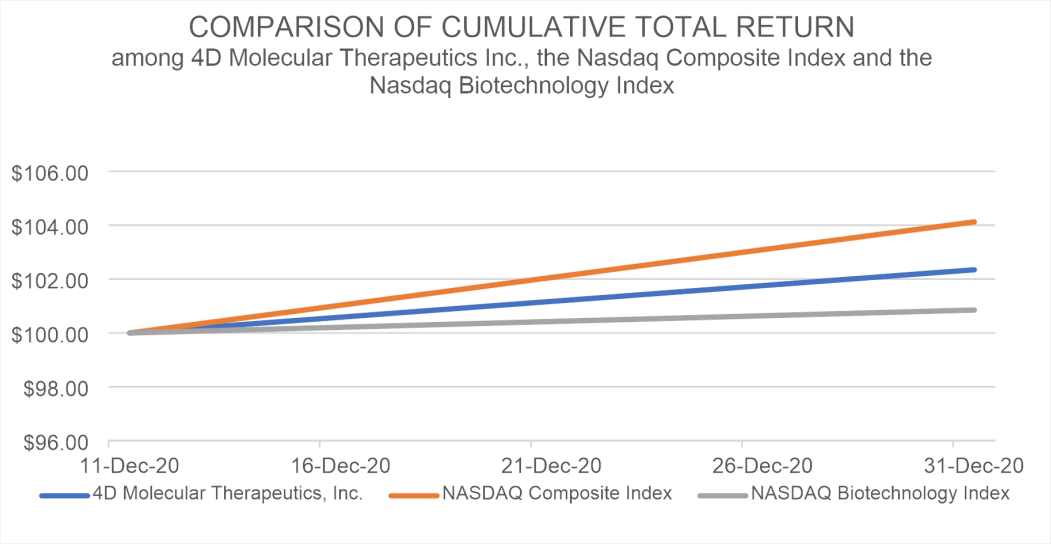
Holders of Common Stock

As of March 15, 2021, there were approximately 96 holders of record of our common stock. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in "street name" or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

Stock Performance Graph

The following graph is not "soliciting material" or deemed "filed" with the SEC for purposes of Section 18 of the Exchange Act, or otherwise subject to liabilities under that Section, and shall not be deemed incorporated by reference into any filing of 4D Molecular Therapeutics Inc. under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following graph compares the cumulative total stockholder return on our common stock with the cumulative total return of the Nasdaq Composite Index and the Nasdaq Biotechnology Index for an investment of $100, between December 11, 2020 (the date of our IPO) and December 31, 2020. The stockholder returns shown in the graph below are based on historical results and are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



Dividend Policy

We have never declared or paid any cash dividends on our common stock and do not anticipate paying cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Securities Authorized for Issuance under Equity Compensation Plans

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

Recent Sales of Unregistered Securities

From April to June 2020, we issued in a series of transactions an aggregate of 4,200,353 shares of our Series C convertible preferred stock at $18.00 per share for aggregate proceeds of $75.6 million. All of our Series C convertible preferred stock automatically converted into shares of our common stock immediately prior to our IPO in December 2020. The sale and issuance of these securities was exempt from registration requirements under the Securities Act, pursuant to Section 4(a)(2) thereof and/or Regulation D promulgated thereunder as transactions not involving any public offering. All of the purchasers of unregistered securities for which we relied on Section 4(a)(2) and/or Regulation D represented that they were accredited investors as defined under the Securities Act. We claimed such exemption on the basis that (a) the purchasers in each case represented that they intended to acquire the securities for investment only and not with a view to the distribution thereof and that they either received adequate information about the registrant or had access, through employment or other relationships, to such information and (b) appropriate legends were affixed to the stock certificates issued in such transactions.

In December 2020, immediately prior to our IPO, all convertible preferred shares then outstanding automatically converted into 11,575,984 shares of common stock. The issuance of such common stock upon conversion of the redeemable convertible preferred stock was exempt from the registration requirements of the Securities Act, pursuant to Section 3(a)(9) thereof, involving an exchange of securities exchanged by the issuer with its existing security holders exclusively where no commission or other remuneration is paid or given directly or indirectly for soliciting such exchange.

Use of Proceeds from Initial Public Offering

On December 15, 2020, we closed our IPO, in which we issued and sold 9,660,000 shares of common stock at a price to the public of $23.00 per share. We received net proceeds of $204.7 million, after deducting underwriting discounts and commissions of $15.6 million and offering costs of $1.9 million.

None of the expenses associated with the IPO were paid to directors, officers, or persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates, other than payments in the ordinary course of business to officers for salaries. Goldman Sachs & Co. LLC, BofA Securities and Evercore ISI acted as book-running managers for the offering.

Shares of our common stock began trading on the Nasdaq Global Select Market on December 11, 2020. The shares were registered under the Securities Act on a Registration Statement on Form S-1 (File No. 333-250150), which was declared effective by the SEC on December 11, 2020.

There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus dated December 11, 2020, filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act.

Purchases of Equity Securities by the Issuer and Affiliated Purchases

None.

Item 6. Selected Financial Data.

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

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included elsewhere in this Annual Report on Form 10-K (this "report"). This discussion and analysis and other parts of this report contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section titled "Risk Factors" and elsewhere in this report.

Overview

We are a clinical-stage gene therapy company pioneering the development of product candidates using our targeted and evolved AAV vectors. We seek to unlock the full potential of gene therapy using our platform, Therapeutic Vector Evolution, which combines the power of directed evolution with our approximately one billion synthetic capsid sequences to invent evolved vectors for use in targeted gene therapy products. Our targeted and evolved vectors are invented with the goal of being delivered through clinically routine, well-tolerated and minimally invasive routes of administration, of transducing diseased cells in target tissues efficiently, of having reduced immunogenicity and, where relevant, of having resistance to pre-existing antibodies. We believe these key design features will help us to potentially create targeted gene therapy product candidates with improved therapeutic profiles, and address a broad range of diseases from rare to large patient populations, including those that other gene therapies are unable to address. Each of our product candidates is created with our targeted and evolved AAV vectors. Our platform is designed to be modular, in that an evolved vector invented for a given set of diseases can be equipped with different transgene payloads to treat other diseases affecting the same tissue types. We believe this modularity will help inform the clinical development of subsequent product candidates using the same vector.

We have built a deep portfolio of gene therapy product candidates initially focused in three therapeutic areas: ophthalmology (intravitreal vector), cardiology (intravenous vector) and pulmonology (aerosol vector). We have three product candidates that are in clinical trials. We are developing 4D-125 for the treatment of X-linked retinitis pigmentosa ("XLRP"), currently in Phase 1/2 clinical trial with initial clinical data expected in the second half of 2021. We are advancing 4D-110 for the treatment of choroideremia, currently in a Phase 1 clinical trial with initial clinical data expected in 2022. Roche holds an exclusive worldwide license to 4D-110 and has the exclusive option to in-license 4D-125 prior to initiation of pivotal clinical trials. We received FDA Fast Track designation for 4D-310 for the treatment of Fabry disease, which is currently in a Phase 1/2 clinical trial, with initial clinical data expected in the second half of 2021. Our two IND candidates are 4D-150 for the treatment of wet age-related macular degeneration ("wet AMD"), and 4D-710 for the treatment of cystic fibrosis lung disease. We expect to file the IND and to initiate clinical trials for both of these programs in the second half of 2021.

We have funded our operations primarily through the sale and issuance of equity securities and to a lesser extent from cash received pursuant to our collaboration and license agreements. In December 2020, we completed our IPO and issued and sold 9,660,000 shares of common stock at a price to the public of $23.00 per share. The aggregate net proceeds from our IPO were $204.7 million after deducting underwriting discounts and commissions and other offering costs. As of December 31, 2020, we had cash and cash equivalents of $276.7 million.

We have incurred significant operating losses and expect that our operating losses will increase significantly as we, among other things, continue to advance our product candidates through preclinical and clinical development, seek regulatory approval, and prepare for, and, if approved, proceed to commercialization; broaden and improve our platform; acquire, discover, validate and develop additional product candidates; maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, we expect to incur additional costs associated with operating as a public company.

Our net losses were $56.7 million and $49.3 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $135.7 million. We do not expect positive cash flows from operations in the foreseeable future. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We do not have any products approved for sale and have not generated any revenue from product sales since our inception. Our ability to generate product revenue will depend on the successful development, regulatory approval and eventual commercialization of one or more of our product candidates, if approved.

We will require substantial additional funding to support our continuing operations and further the development of our product candidates. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which could include income from collaborations, strategic partnerships or other strategic arrangements, for the foreseeable future. Adequate funding may not be available when needed or on terms acceptable to us, or at all. If we are unable to raise additional capital as needed, we may have to significantly delay, scale back or discontinue development of our product candidates. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic and otherwise. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations. Insufficient liquidity may also require us to relinquish rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

The global COVID-19 pandemic continues to rapidly evolve, and we will continue to monitor the COVID-19 situation closely. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, CROs, third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. To the extent possible, we are conducting business as usual, with necessary or advisable modifications to employee travel and the majority of our employees working remotely. We will continue to actively monitor the rapidly evolving situation related to the COVID-19 pandemic and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. At this point, the extent to which the COVID-19 pandemic may affect our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain.

Components of Results of Operations

Revenue

Our revenue to date has been generated through payments from our collaboration and license agreements, primarily from upfront and milestone payments and expense reimbursement. We have not generated any revenue from the sale of approved products and do not expect to do so for the foreseeable future. The primary drivers for revenue consist of the following:

- Roche: In November 2017, we entered into a collaboration and license agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together, "Roche"). We received an upfront payment of $21.0 million in 2017 and are reimbursed for our internal and third-party costs and are entitled to contingent payments, including milestone payments. In 2020, we received milestone payments totaling $10.0 million, which was comprised of a $5.0 million milestone payment upon the release of clinical trial material for our Phase 1 clinical trial for 4D-110 to treat choroideremia in the second quarter of 2020 and an additional $5.0 million milestone payment upon dosing our first patient in the trial in the third quarter of 2020. We began recognizing revenue related to this in 2017 and expect to continue to recognize revenue over the next three to four years. See Note 6 to our financial statements included elsewhere in this report for further discussion regarding the accounting treatment of this agreement.
- uniQure: In August 2019, we amended our agreement with uniQure and entered into a separate new collaboration and license agreement with uniQure. Neither party was required to pay monetary consideration in connection with the amendment or new agreement. We determined the incremental transaction price of the amendment and new agreement to be $5.1 million and recorded the amount as deferred revenue. We began recognizing revenue related to this in 2020 and expect to recognize revenue over the next two to three years. See Note 6 to our financial statements included elsewhere in this report for further discussion regarding the accounting treatment of this transaction.

Future collaboration and license revenue is highly dependent on the successful development and commercialization of products by our collaboration partners, which is uncertain, and revenue may fluctuate significantly from period to period. Additionally, we may never receive the consideration from our license agreements that is contemplated for option fees, development and sales-based milestone payments or royalties on sales of licensed products, given the contingent nature of these payments. We expect that our collaboration and license revenue in 2021 will primarily be from Roche and uniQure. If our agreements with Roche or uniQure were terminated, it may materially impact the amount of license revenue we recognize in future periods.

Operating Expenses

Research and Development

Our research and development expenses primarily consist of costs incurred for the discovery and preclinical and clinical development of our product candidates. These expenses include salaries and personnel-related costs, including stock-based compensation of our scientific personnel performing research and development activities; laboratory supplies; research materials; fees paid to CROs to execute preclinical studies and clinical trials; fees paid to CMOs to manufacture materials for preclinical studies and clinical trials; fees related to obtaining technology licenses; consulting costs; costs related to seeking regulatory approval of our product candidates; and allocated facility-related costs, information technology costs, depreciation expense and other overhead.

We expense all research and development costs in the periods in which they are incurred. We have entered into various agreements with CROs and CMOs. Costs of certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Payments made prior to the receipt of goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses and other current assets on our balance sheet. The

capitalized amounts are recognized as expense as the goods are delivered or the related services are performed.

We do not allocate our costs by product candidate, as a significant amount of research and development expenses includes internal costs, such as payroll and other personnel expenses, laboratory supplies and allocated overhead, and external costs, such as fees paid to third parties to conduct research and development activities on our behalf, none of which are tracked by product candidate. In particular, with respect to internal costs, several of our departments support multiple product candidate research and development programs, and therefore the costs cannot be allocated to a particular product candidate or development program.

At this time, we cannot reasonably estimate or know the nature, timing or estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, as our product candidates advance into later stages of development, as we begin to conduct larger clinical trials, as we seek regulatory approvals for any product candidates that successfully complete clinical trials, and incur expenses associated with hiring additional personnel to support our research and development efforts. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. See the section titled “Risk Factors” for additional risks regarding regulatory development and approval.

General and Administrative

Our general and administrative expenses consist primarily of personnel-related expenses, including salaries, employee benefit costs and stock-based compensation expense for our personnel in executive, finance and accounting, human resources, business development and other administrative functions. General and administrative expenses also include professional fees for legal, patent, consulting, accounting and tax services, allocated overhead, including rent, equipment, depreciation, information technology costs and utilities, and other general operating expenses not otherwise classified as research and development expenses.

We expect our general and administrative expenses to increase as a result of increased personnel-related costs, patent costs for our product candidates, consulting, legal and accounting services associated with maintaining compliance with stock exchange listing and requirements of the SEC, investor relations costs, director and officer insurance premiums and other costs associated with being a public company.

Other Income (Expense)

Our other income (expense) primarily consists of interest income earned on our cash equivalents and adjustments for the change in the fair value of our derivative liability which must be remeasured at each reporting period.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the periods indicated (dollars in thousands):

	Year Ended December 31,			
	2020	2019	$ Change	% Change
Revenue:				
Collaboration and license revenue	$ 13,363	$ 6,960	$ 6,403	92%
Collaboration and license revenue, related parties	249	26	223	*
Total revenue	13,612	6,986	6,626	95%
Operating Expenses:				
Research and development	53,038	38,718	14,320	37%
Acquired in-process research and development	—	5,137	(5,137)	*
General and administrative	17,238	13,895	3,343	24%
Total operating expenses	70,276	57,750	12,526	22%
Loss from operations	(56,664)	(50,764)	(5,900)	12%
Other Income (Expense)	(29)	1,458	(1,487)	*
Net loss and comprehensive loss	$ (56,693)	$ (49,306)	$ (7,387)	15%

* Percentage is not meaningful

Revenue

Revenue increased $6.6 million, or 95%, from the year ended December 31, 2019 to the year ended December 31, 2020 due to a $6.6 million increase in revenue recognized under our collaboration and license agreement with Roche and a $0.7 million increase in revenue recognized under our collaboration and license agreement with uniQure, which was partially offset by a decline in revenue recognized from other collaboration and license agreements.

Research and Development Expenses

The following table provides a breakout of research and development expenses for the periods indicated (dollars in thousands):

	Year Ended December 31,			
	2020	2019	$ Change	% Change
External expenses	$ 29,455	$ 21,342	8,113	38%
Payroll and personnel expenses	16,064	12,206	3,858	32%
Other research and development expenses	7,519	5,170	2,349	45%
Total research and development expenses	$ 53,038	$ 38,718	$ 14,320	37%

Research and development expense increased $14.3 million, or 37%, from the year ended December 31, 2019 to the year ended December 31, 2020. The increase was due to the following:

- an $8.1 million increase in external costs as we continue to develop novel vectors, identify potential product candidates and progress our preclinical studies and clinical trials;
- a $3.9 million increase in payroll and personnel expenses due to increased headcount of research and development personnel, including a $0.5 million increase in employee stock-based compensation expense; and

- a $2.3 million increase in other research and development expenses primarily for allocated overhead, including rent, equipment, depreciation, information technology costs and utilities.

Acquired In-Process Research and Development Expenses

We recorded acquired in-process research and development expenses of $5.1 million in the year ended December 31, 2019. This was due to the acquisition of in-process research and development from uniQure as a result of the execution of an Amended and Restated Collaboration and License Agreement and a separate Collaboration and License Agreement with uniQure. See Note 6 to our financial statements included elsewhere in this report for further discussion regarding the accounting treatment of this transaction. We did not incur any acquired in-process research and development expenses in 2020.

General and Administrative Expenses

General and administrative expenses increased $3.3 million, or 24%, from the year ended December 31, 2019 to the year ended December 31, 2020. The increase was due to the following:

- a $3.0 million increase for personnel costs including a $1.2 million increase in employee and nonemployee director stock-based compensation expense;
- a $2.2 million increase for professional services, including legal, accounting and other advisory services; and
- a $0.8 million increase for allocated overhead, including rent, equipment, depreciation, information technology costs and utilities.

These increases were partially offset by a $2.6 million decrease for public offering costs expensed in the year ended December 31, 2019, as a result of delays in the IPO process in 2019. We completed our IPO in December 2020 and the related offering costs were recorded within additional paid-in capital and reduced the IPO gross proceeds.

Other Income (Expense)

Other income (expense) decreased $1.5 million from the year ended December 31, 2019 to the year ended December 31, 2020 primarily due to lower interest income because of lower interest rates.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations primarily through the sale and issuance of our equity securities, including from the sale of our common stock in our IPO and the sale of our Series A, Series A-1, Series B and Series C redeemable preferred stock, and to a lesser extent from cash received pursuant to our collaboration and license agreements.

In December 2020, we completed our IPO. We issued and sold 9,660,000 shares of common stock at a price to the public of $23.00 per share. The aggregate net proceeds from our IPO were $204.7 million after deducting underwriting discounts and commissions and other offering costs. As of December 31, 2020, we had cash and cash equivalents of $276.7 million.

Future Funding Requirements

We have experienced recurring net losses and had an accumulated deficit of $135.7 million for the year ended December 31, 2020. Our transition to profitability is dependent upon the successful development, approval and commercialization of our product candidates and those of our collaboration partners and achieving a level of revenue adequate to support our cost structure. We expect to continue to incur losses for the foreseeable future.

We expect that our research and development and general and administrative expenses will continue to increase for the foreseeable future. Additionally, we expect our capital expenditures will increase significantly in the future for costs associated with building additional manufacturing capacity. As a result, we will need significant additional capital to fund our operations, which we may obtain through one or more equity offerings, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements.

Because of the numerous risks and uncertainties associated with the development and commercialization of gene therapy product candidates, we are unable to estimate the amount of increased capital we will need to raise to support our operations and the outlays and operating expenditures necessary to complete the development of our product candidates and build additional manufacturing capacity, and we may use our available capital resources sooner than we currently expect.

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

- the progress of our current and future product candidates through preclinical and clinical development;
- potential delays in our preclinical studies and clinical trials, whether current or planned, due to the COVID-19 pandemic, or other factors;
- expanding our manufacturing facilities and working with our contract manufacturers to scale up the manufacturing processes for our product candidates;
- continuing our research and discovery activities;
- continuing the development of our Therapeutic Vector Evolution platform;
- initiating and conducting additional preclinical, clinical or other studies for our product candidates;
- changing or adding additional contract manufacturers or suppliers;
- seeking regulatory approvals and marketing authorizations for our product candidates;
- establishing sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval;
- acquiring or in-licensing product candidates, intellectual property and technologies;
- making milestone, royalty or other payments due under any current or future collaboration or license agreements;
- obtaining, maintaining, expanding, protecting and enforcing our intellectual property portfolio;
- attracting, hiring and retaining qualified personnel;
- potential delays or other issues related to our operations;
- meeting the requirements and demands of being a public company;
- defending against any product liability claims or other lawsuits related to our products; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

We believe that our existing cash and cash equivalents will allow us to fund our planned operations for at least one year from the date of the issuance of the financial statements for the year ended December 31, 2020.

We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing sooner than

currently projected, which may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. See the section titled “Risk Factors” for additional risks associated with our substantial capital requirements.

We do not have any committed external sources of funds. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to complete the clinical development for the product candidates in treatment of Fabry disease, XLRP or choroideremia or any other indication we may pursue. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter would result in fixed payment obligations and may involve agreements that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, granting liens over our assets, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. Any debt financing or additional equity that we raise may contain terms that could adversely affect our common stockholders. Further, additional funds may not be available when we need them, on terms that are acceptable to us, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic.

If we are unable to obtain additional funding, we expect to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or investment in internal manufacturing capabilities, which could adversely affect our business. If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Summary Statement of Cash Flows

The following is a summary of cash flows for the periods indicated below (in thousands):

	Year Ended December 31,	
	2020	**2019**
Net cash used in operating activities	$ (50,909)	$ (36,711)
Net cash used in investing activities	(1,000)	(3,203)
Net cash provided by (used in) financing activities	278,983	(2,195)
Net increase (decrease) in cash and cash equivalents	$ 227,074	$ (42,109)

Net Cash Used in Operating Activities

Net cash used in operating activities was $50.9 million for the year ended December 31, 2020. This was primarily due to the net loss of $56.7 million and an increase in prepaid expenses of $2.6 million, which were partially offset by stock-based compensation expense of $5.0 million and depreciation and amortization expense of $1.4 million and an increase in accrued and other liabilities of $1.9 million.

Net cash used in operating activities was $36.7 million for the year ended December 31, 2019. This was primarily due to the net loss of $49.3 million, which was partially offset by the acquisition of in-process research and development of $5.1 million, stock-based compensation expense of $3.5 million, write-off of public offering costs of $2.6 million and depreciation and amortization expense of $1.0 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was $1.0 million for the year ended December 31, 2020, all of which was used to purchase property and equipment.

Net cash used in investing activities was $3.2 million for the year ended December 31, 2019, all of which was used to purchase property and equipment.

Net Cash Provided by (Used in) Financing Activities

Net cash provided by financing activities was $279.0 million for the year ended December 31, 2020, which was primarily due to $205.7 million of proceeds from our IPO net of paid underwriting discounts and commissions and offering costs and $72.5 million of net proceeds received from the issuance of our Series C redeemable convertible preferred stock in April and June 2020.

Net cash used in financing activities was $2.2 million for the year ended December 31, 2019, which was primarily for payments of public offering costs of $2.3 million.

Contractual Obligations, Commitments and Contingencies

Our commitments include obligations under vendor contracts to provide research services and other purchase commitments with our vendors. In the normal course of business, we enter into services agreements with contract research organizations, contract manufacturing organizations and other third parties. Generally, these agreements provide for termination upon notice, with specified amounts due upon termination based on the timing of termination and the terms of the agreement. The actual amounts and timing of payments under these agreements are uncertain and contingent upon the initiation and completion of the services to be provided. These amounts are not fixed and determinable and therefore are not included in the table below.

The following table summarizes our contractual obligations, commitments and contingencies as of December 31, 2020 (in thousands):

		Payments Due by Period			
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating lease payments	$ 27,389	$ 2,956	$ 6,150	$ 6,463	$ 11,820
Total contractual obligations	$ 27,389	$ 2,956	$ 6,150	$ 6,463	$ 11,820

In October 2018, we entered into a long-term lease for additional office and laboratory space in Emeryville, California, at a cost of $9.3 million over an 87-month term (the “Second Lease”). We concurrently amended our existing lease to extend the lease term to end at the same time as the Second Lease.

In May 2019, we amended the Second Lease (the “Second Lease Amendment”) to add 17,497 square feet to the space being leased pursuant to the Second Lease. The Second Lease Amendment extended the term of the Second Lease to December 31, 2029.

Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements have prepared in accordance with generally accepted accounting principles in the United States. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, as well as the reported revenue and expenses during the reported periods. We evaluate these estimates and assumptions on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are

reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in Note 2 to our financial statements included elsewhere in this report. We believe the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements and understanding and evaluating our reported financial results.

Revenue Recognition

We determine revenue recognition for arrangements within the scope of ASC 606 by performing the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Our revenue is primarily derived through our license, research, development and commercialization agreements. The terms of these types of agreements may include (i) licenses to our technology, (ii) research and development services, and (iii) services or obligations in connection with participation in research or steering committees. Payments to us under these arrangements typically include one or more of the following: nonrefundable upfront and license fees, research funding, milestone and other contingent payments to us for the achievement of defined collaboration objectives and certain preclinical, clinical, regulatory and sales-based events, as well as royalties on sales of any commercialized products. Arrangements that include upfront payments are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until performance obligations are met. The event-based milestone payments, royalties and cost reimbursements represent variable consideration, and we use the most likely amount method to estimate this variable consideration. Royalty payments are recognized when earned or as the sales occur. We record cost reimbursements as accounts receivable when right to consideration is unconditional.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC 606. We allocate the total transaction price to each performance obligation based on the estimated selling price and recognize revenue when, or as, the performance obligation is satisfied. We include the unconstrained amount of estimated variable consideration in the transaction price. At the end of each reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price.

Significant management judgment is required to determine the level of effort required under an arrangement, and the period over which the Company expects to complete its performance obligations under the arrangement. Changes in these estimates can have a material effect on revenue recognized.

Accrued Research and Development Expenses

We estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing contracts and purchase orders with service providers, identifying services that have been performed on our behalf and estimating the level of service performed, the expected remaining period of performance and the associated expenses incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. Depending on the timing of payments to the service providers and the estimated expenses incurred, we may record net prepaid or accrued research and development expenses relating to these costs.

Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with preclinical development and clinical studies; and
- CMOs and other vendors related to process development and manufacturing of materials for use in preclinical development and clinical studies.

Our understanding of the status and timing of services performed relative to the actual status and timing may vary and may result in us reporting changes in estimates in any particular period. To date, there have been no material differences from our estimates to the amounts actually incurred.

Stock-Based Compensation Expense

We use a fair value-based method to account for all stock-based compensation arrangements with employees and nonemployees including stock options and stock awards. Our determination of the fair value of stock options on the date of grant utilizes the Black-Scholes option pricing model.

The fair value of the option granted is recognized on a straight-line basis over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period, which usually is the vesting period. Prior to January 1, 2020, the stock-based compensation expense for nonemployees was subject to remeasurement until the related vesting conditions were met. Effective January 1, 2020, the measurement date for nonemployee awards is the date of grant without changes in the fair value of the award. We account for forfeitures as they occur for both employees and nonemployees.

Estimates of the fair value of equity awards as of the grant date using valuation models such as the Black-Scholes option pricing model are affected by assumptions with a number of complex variables.

Changes in the following assumptions can materially affect the estimate of fair value and ultimately how much stock-based compensation expense is recognized; and the resulting change in fair value, if any, is recognized in our statement of operations and comprehensive loss during the period the related services are rendered. These inputs are subjective and generally require significant analysis and judgment to develop:

- *Expected Term*—The expected term for employee options is calculated using the simplified method as we do not have sufficient historical information to provide a basis for estimate. The simplified method is based on the average of the vesting tranches and the contractual life of each grant.
- *Expected Volatility*—For all stock options granted to date, the expected volatility was estimated based on a study of publicly traded industry peer companies as we did not have sufficient trading history for our common stock. We selected the peer group based on similarities in industry, stage of development, size and financial leverage with our principal business operations. For each grant, we measured historical volatility over a period equivalent to the expected term.
- *Risk-Free Interest Rate*—The risk-free interest rate is based on the yield available on U.S. Treasury zero-coupon issues whose term is similar in duration to the expected term of the respective stock option.
- *Expected Dividend Yield*—We have not paid and do not currently anticipate paying any dividends on our common stock. Accordingly, we have estimated the dividend yield to be zero.

As of December 31, 2020, the unrecognized stock-based compensation expense related to stock options was $19.4 million and is expected to be recognized as expense over a weighted-average period of approximately 3.1 years. The intrinsic value of all outstanding stock options as of December 31, 2020 was approximately $97.1 million, of which approximately $44.8 million related to vested options and approximately $52.3 million related to unvested options.

Common Stock Valuations

Prior to our IPO in December 2020, the estimated fair value of the common stock underlying our stock options and stock awards was determined at each grant date by our board of directors, with assistance from management and external appraisers. All options to purchase shares of our common stock were intended to be exercisable at a price per share not less than the per-share fair value of our common stock underlying those options on the date of grant. The approach to estimate the fair value of our common stock was consistent with the methods outlined in the American Institute of Certified Public Accountants' Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Subsequent to our IPO, the fair value of our common stock is determined based on its closing market price as reported on the Nasdaq Global Select Market.

Income Taxes

We account for income taxes under the asset and liability method, which requires, among other things, that deferred income taxes be provided for temporary differences between the financial statement reporting and tax basis of our assets and liabilities. In addition, deferred tax assets are recorded for the future benefit of utilizing net operating losses and research and development credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. A valuation allowance is provided against deferred tax assets unless it is more likely than not that they will be realized.

We account for uncertain tax positions by assessing all material positions taken in any assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. Our policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (IRS) and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code, which could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on our value immediately prior to the ownership change. We have experienced ownership changes in the past. As a result of the ownership changes, we determined that $0.9 million of our NOLs will expire unutilized for federal income tax purposes and such amounts are excluded from our NOLs as of December 31, 2020. Subsequent ownership changes may result in additional limitations.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

JOBS Act

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, emerging growth companies may 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 elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, while we are an emerging growth company, we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earlier of (i) the last day of the year following the fifth anniversary of the completion of our IPO, (ii) the last day of the year in which we have total annual gross revenue of at least $1.07 billion, (iii) the last day of the year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if 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, or (iv) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. An emerging growth company may take advantage of specified reduced reporting requirements and is relieved of certain other significant requirements that are otherwise generally applicable to public companies. As an emerging growth company:

- we will present only two years of audited financial statements for any interim period, and related management’s discussion and analysis of financial condition and results of operations;
- we will avail ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002 (the “Sarbanes-Oxley Act”);
- we will provide less extensive disclosure about our executive compensation arrangements;
- we will not require stockholder non-binding advisory votes on executive compensation or golden parachute arrangements; and
- we will take advantage of extended transition periods to comply with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies.

As a result, the information in this report in the future may be different than what you might receive from other public reporting companies.

Recent Accounting Pronouncements

See Note 2 to our financial statements included elsewhere in this report for information.

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

Interest Rate Sensitivity and Effects of Inflation

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2020, we had cash and cash equivalents of $276.7 million, consisting of bank deposits and interest-bearing money market funds, for which the fair value would be affected by changes in the general level of U.S. interest rates. However, due to the short-term maturities of our cash equivalents, an immediate 10% change in interest rates would not have a material effect on the fair value of our cash equivalents.

We do not believe that inflation or interest rate changes have had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data.

The financial statements required by this item are set forth beginning on page F-1 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Management's Evaluation of our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial and accounting officers, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures at the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our principal executive officer and principal financial and accounting officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2020, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

Item 9B. Other Information.

On March 19, 2021, William Burkoth notified our board of directors that he would not stand for reelection at our 2021 annual meeting of stockholders (the "Annual Meeting"). Mr. Burkoth will serve on our board of directors through the Annual Meeting. Mr. Burkoth's decision to not stand for reelection was not related to any disagreement he had with us or any matter relating to our operations, policies (including accounting or financial policies) or practices.

On March 20, 2021, Tony Yao, M.D., Ph.D., notified our board of directors that he was resigning from the board effective as of the date of his notification. Dr. Yao's decision to resign was not related to any disagreement he had with us or any matter relating to our operations, policies (including accounting or financial policies) or practices.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with the Annual Meeting within 120 days after December 31, 2020 (the “Proxy Statement”) and is incorporated in this Annual Report on Form 10-K by reference.

Item 11. Executive Compensation.

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The financial statements schedules and exhibits filed as part of this Annual Report on Form 10-K are as follows:

(1) Financial Statements;

Reference is made to the financial statements included in Item 8 of Part II hereof.

(2) Financial Statement Schedules

All financial statement schedules are omitted because they are not required or the required information is included in the financial statements or notes thereto.

(3) Exhibits

The exhibits required to be filed as part of this report are listed in the Exhibit List attached hereto and are incorporated herein by reference.

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation, as currently in effect.	8-K	12/15/20	3.1	
3.2	Amended and Restated Bylaws, as currently in effect.	8-K	12/15/20	3.2	
4.1	Description of Securities of the Registrant.				X
4.2	Form of Common Stock Certificate.	S-1/A	12/7/20	4.2	
4.3	Amended and Restated Investors' Rights Agreement, dated as of April 29, 2020, among the Registrant and the investors party thereto.	S-1/A	12/7/20	4.3	
10.1(a)#	2015 Equity Incentive Plan.	S-1	11/17/20	10.1(a)	
10.1(b)#	Form of Stock Option Agreement under 2015 Equity Incentive Plan.	S-1	11/17/20	10.1(b)	
10.2(a)#	2020 Incentive Award Plan.	S-8	12/15/20	99.2(a)	
10.2(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2020 Incentive Award Plan.	S-1/A	12/7/20	10.2(b)	
10.2(c)#	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2020 Incentive Award Plan.	S-1/A	12/7/20	10.2(c)	
10.2(d)#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2020 Incentive Award Plan.	S-1/A	12/7/20	10.2(d)	
10.3#	2020 Employee Stock Purchase Plan.	S-8	12/15/20	99.3	
10.4†	Form of Indemnification Agreement for directors and officers.	S-1/A	12/7/20	10.4	
10.5†	Collaboration and License Agreement, dated November 16, 2017, among the Registrant, F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.	S-1	11/17/20	10.5	
10.6†	Amended and Restated Collaboration and License Agreement, dated August 6, 2019, between the Registrant and uniQure biopharma B.V.	S-1	11/17/20	10.6	
10.7†	Collaboration and License Agreement, dated August 6, 2019, by and between the Registrant and uniQure biopharma B.V.	S-1	11/17/20	10.7	
10.8†	Exclusive License and Bailment Agreement, dated December 19, 2013, between the Registrant and The Regents of the University of California.	S-1/A	12/7/20	10.8	
10.9†	Exclusive License and Bailment Agreement, dated December 19, 2013, between the Registrant and The Regents of the University of California.	S-1/A	12/7/20	10.9	
10.10#	Offer Letter, dated March 20, 2015 between David Kirn, M.D. and the Registrant.	S-1/A	12/7/20	10.10	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.11#	Employment Agreement, dated January 15, 2019 between Peter Francis, M.D., Ph.D. and the Registrant.	S-1/A	12/7/20	10.11	
10.12#†	Offer Letter, dated January 4, 2019 between August Moretti and the Registrant.	S-1/A	12/7/20	10.12	
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.				X
24.1	Power of Attorney (included on the signature page of this Form 10-K).				X
31.1	Certification of the Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of the Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1*	Certifications of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
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.				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				X

# Indicates management contract or compensatory plan.

† Certain confidential portions (indicated by brackets and asterisks) have been omitted form this exhibit.

* The certifications attached as Exhibit 32.1 that accompany this Annual Report on Form 10-K are deemed furnished and not filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of 4D Molecular Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

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**.**

4D Molecular Therapeutics, Inc.

Date: March 25, 2021

By: /s/ David Kirn

David Kirn, M.D.
Chief Executive Officer and Director
(Duly Authorized Officer and Principal Executive Officer)

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints David Kirn and August Moretti, jointly and severally, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place, and 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 attorneys-in-fact and agents 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 might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or his or their substitute or substitutes, 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
/s/ David Kirn **David Kirn, M.D.**	Chief Executive Officer and Director *(Principal Executive Officer)*	March 25, 2021
/s/ August J. Moretti **August J. Moretti**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 25, 2021
/s/ John F. Milligan **John F. Milligan, Ph.D.**	Executive Chairman	March 25, 2021
/s/ William Burkoth **William Burkoth, MBA**	Director	March 25, 2021
/s/ Jacob Chacko **Jacob Chacko, M.D., MBA**	Director	March 25, 2021
/s/ Susannah Gray **Susannah Gray, MBA**	Director	March 25, 2021
/s/ Nancy Miller-Rich **Nancy Miller-Rich**	Director	March 25, 2021
/s/ David Schaffer **David Schaffer, Ph.D.**	Director	March 25, 2021
/s/ Charles P. Theuer **Charles P. Theuer, M.D., Ph.D.**	Director	March 25, 2021
/s/ Shawn Cline Tomasello **Shawn Cline Tomasello, MBA**	Director	March 25, 2021

4D Molecular Therapeutics, Inc.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of 4D Molecular Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of 4D Molecular Therapeutics, Inc. (the “Company”) as of December 31, 2020 and 2019, and the related statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders’ equity (deficit) and of cash flows for the years then ended, including the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

We conducted our audits of these financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the 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/ PricewaterhouseCoopers LLP
San Jose, California
March 25, 2021

We have served as the Company’s auditor since 2016.

4D Molecular Therapeutics, Inc.

Balance Sheets
(In thousands, except share and per share amounts)

	As of December 31,	
	2020	**2019**
Assets		
Current assets:		
Cash and cash equivalents	$ 276,726	$ 49,652
Accounts receivable	1,486	978
Prepaid expenses and other current assets (includes $169 and $149 at December 31, 2020 and 2019, respectively, attributable to related parties)	4,444	1,878
Total current assets	282,656	52,508
Property and equipment, net	5,073	5,049
Other assets	602	677
Total assets	$ 288,331	$ 58,234
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities		
Accounts payable	$ 1,787	$ 1,744
Accrued and other current liabilities	8,371	5,347
Deferred revenue (includes $0 and $1,122 at December 31, 2020 and 2019, respectively, attributable to related parties)	6,586	5,864
Total current liabilities	16,744	12,955
Deferred revenue, net of current portion (includes $0 and $4,015 at December 31, 2020 and 2019, respectively, attributable to related parties)	13,226	13,603
Derivative liability	122	101
Other liabilities	1,852	1,565
Total liabilities	31,944	28,224
Commitments and contingencies (Note 8)		
Redeemable convertible preferred stock, $0.0001 par value; 0 and 7,375,638 shares authorized shares at December 31, 2020 and 2019, respectively; 0 and 7,375,631 shares issued and outstanding at December 31, 2020 and 2019, respectively. Liquidation value of $0 and $108,596 at December 31, 2020 and 2019, respectively.	—	102,980
Stockholders' equity (deficit)		
Preferred stock, $0.0001 par value, 10,000,000 shares authorized as of December 31, 2020 and no shares authorized as of December 31, 2019; no shares issued and outstanding as of December 31, 2020 and 2019, respectively.	—	—
Common stock, $0.0001 par value, 300,000,000 and 50,000,000 shares authorized at December 31, 2020 and 2019, respectively; 26,681,983 and 5,178,955 shares issued and outstanding at December 31, 2020 and 2019, respectively.	3	1
Additional paid-in-capital	392,063	6,054
Accumulated deficit	(135,679)	(79,025)
Total stockholders' equity (deficit)	256,387	(72,970)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 288,331	$ 58,234

The accompanying notes are an integral part of these financial statements

4D Molecular Therapeutics, Inc.

Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2020	**2019**
Revenue:		
Collaboration and license revenue	$ 13,363	$ 6,960
Collaboration and license revenue, related parties	249	26
Total revenue	13,612	6,986
Operating expenses:		
Research and development (includes $579 and $350 for the years ended December 31, 2020 and 2019, respectively, attributable to related parties)	53,038	38,718
Acquired in-process research and development, related parties	—	5,137
General and administrative	17,238	13,895
Total operating expenses	70,276	57,750
Loss from operations	(56,664)	(50,764)
Other income (expense):		
Interest income	152	1,504
Other income (expense), net	(181)	(46)
Total other income (expense)	(29)	1,458
Net loss and comprehensive loss	$ (56,693)	$ (49,306)
Net loss per share attributable to common stockholders, basic and diluted	$ (8.82)	$ (9.59)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	6,430,555	5,142,560

The accompanying notes are an integral part of these financial statements

4D Molecular Therapeutics, Inc.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Deficit
Balances at December 31, 2018	7,375,631	$ 102,980	5,126,344	$ 1	$ 2,438	$ (30,026)	$ (27,587)
Cumulative effect of adoption of ASC 606	—	—	—	—	—	307	307
Issuance of common stock upon exercise of stock options	—	—	52,611	—	75	—	75
Stock-based compensation	—	—	—	—	3,541	—	3,541
Net loss	—	—	—	—	—	(49,306)	(49,306)
Balances at December 31, 2019	7,375,631	$ 102,980	5,178,955	$ 1	$ 6,054	$ (79,025)	$ (72,970)
Cumulative effect of adoption of ASU 2018-07	—	—	—	—	(39)	39	—
Issuance of redeemable convertible preferred stock, net of $3,138 of issuance cost	4,200,353	72,468	—	—	—	—	—
Conversion of redeemable convertible preferred stock into common stock	(11,575,984)	(175,448)	11,575,984	1	175,447	—	175,448
Issuance of common stock upon initial public offering, net of $17,468 issuance cost	—	—	9,660,000	1	204,712	—	204,713
Issuance of common stock upon exercise of stock options	—	—	267,044	—	857	—	857
Stock-based compensation	—	—	—	—	4,984	—	4,984
Vesting of common stock warrant issued for services	—	—	—	—	48	—	48
Net loss	—	—	—	—	—	(56,693)	(56,693)
Balances at December 31, 2020	—	—	26,681,983	$ 3	$ 392,063	$ (135,679)	$ 256,387

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

4D Molecular Therapeutics, Inc.

Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2020	**2019**
Cash flows from operating activities		
Net loss	$ (56,693)	$ (49,306)
Adjustments to reconcile net loss to net cash used in operating activities		
Stock-based compensation expense	4,984	3,541
Vesting of common stock warrant in return for services	48	—
Change in fair value of derivative liability	21	37
Depreciation and amortization	1,443	1,004
(Gain) loss on disposition of property and equipment	(1)	7
Write-off of public offering costs	—	2,610
In-process research and development acquired and expensed in non-monetary related party transaction	—	5,137
Changes in operating assets and liabilities		
Accounts receivable	(508)	146
Prepaid expenses and other current assets	(2,566)	(695)
Other assets	75	(220)
Accounts payable	43	533
Accrued and other liabilities	1,900	3,841
Deferred revenue	345	(3,346)
Net cash used in operating activities	(50,909)	(36,711)
Cash flows from investing activities		
Acquisition of property and equipment	(1,000)	(3,203)
Net cash used in investing activities	(1,000)	(3,203)
Cash flows from financing activities		
Issuance of redeemable convertible preferred stock, net of issuance costs	72,468	(10)
Issuance of common stock in initial public offering, net of issuance costs	205,658	(2,260)
Issuance of common stock upon exercise of stock options	857	75
Net cash provided by (used in) financing activities	278,983	(2,195)
Net increase (decrease) in cash and cash equivalents	227,074	(42,109)
Cash and cash equivalents, beginning of period	49,652	91,761
Cash and cash equivalents, end of period	$ 276,726	$ 49,652
Supplemental disclosures of non-cash investing and financing information		
Conversion of redeemable convertible preferred stock into common stock	$ 175,448	$ —
Purchases of property and equipment in accounts payable and accrued and other liabilities	$ 466	$ 385
Unpaid offering costs	$ 946	$ 368

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

1. The Company

4D Molecular Therapeutics, Inc. (the “Company”) was formed as a limited liability company in September 2013 under the name 4D Molecular Therapeutics, LLC. The Company changed its name and converted into a corporation which was incorporated in the state of Delaware in March 2015. The Company is a clinical-stage gene therapy company pioneering the development of product candidates using its targeted and evolved adeno-associated viruses (“AAV”) vectors.

Initial Public Offering

In December 2020, the Company sold and issued 9,660,000 shares of common stock at a price to the public of $23.00 per share, which included shares sold upon the underwriters’ exercise of their overallotment option to purchase 1,260,000 additional shares. The Company received an aggregate of $204.7 million in net proceeds, after deducting underwriting discounts and commissions and offering costs.

Upon the closing of the IPO, all outstanding shares of redeemable convertible preferred stock automatically converted into 11,575,984 shares of common stock. Subsequent to the closing of the IPO, there were no shares of redeemable convertible preferred stock outstanding.

Liquidity

The Company has incurred significant losses and negative cash flows from operations and had an accumulated deficit of $135.7 million as of December 31, 2020. The Company believes that its cash and cash equivalents as of December 31, 2020 are sufficient for the Company to fund planned operations for at least one year from the issuance date of these financial statements for the year ended December 31, 2020. The Company has historically financed its operations primarily through the sale of equity securities and, to a lesser extent from cash received pursuant to its collaboration and license agreements. To date, none of the Company’s product candidates have been approved for sale and therefore, the Company has not generated any revenue from product sales. Management expects operating losses and negative cash flows from operations to continue for the foreseeable future. The Company currently plans to raise additional funding as required based on the status of its clinical trials and projected cash flows. There can be no assurance that, in the event the Company requires additional financing, such financing will be available at terms acceptable to the Company, if at all. Failure to generate sufficient cash flows from operations, raise additional capital and reduce discretionary spending should additional capital not become available could have a material adverse effect on the Company’s ability to achieve its business objectives.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with United States Generally Accepted Accounting Principles (“U.S. GAAP”).

Use of Estimates and Judgements

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and judgements that affect the reported amounts of assets, liabilities, revenue and expenses; and disclosure of contingent assets and liabilities as of the date of the financial statements. Such estimates include the determination of useful lives for property and equipment, the contract term, transaction price and costs of collaboration agreements, as well as estimates of the fair value of common

stock (prior to the IPO), stock options and derivative instruments and income tax uncertainties. Actual results could differ from those estimates.

Due to the coronavirus ("COVID-19") pandemic, there has been uncertainty and disruption in the global economy and financial markets. The Company is not aware of any specific event or circumstance that would require an update to its estimates or judgments or a revision of the carrying value of its assets or liabilities as of December 31, 2020. While there was not a material impact to the Company's financial statements as of December 31, 2020, these estimates may change, as new events occur and additional information is obtained, as well as other factors related to the COVID-19 pandemic that could result in material impacts to the financial statements in future reporting periods.

Segment Information

The Company operates and manages its business as one reportable and operating segment. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on a company-wide basis for purposes of allocating resources and assessing financial performance.

As of and for the years ended December 31, 2020 and 2019, all of the Company's long-lived assets were located in the United States and all revenue was earned in the United States.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents and accounts receivable. The Company's cash is held at two financial institutions in the United States of America. The Company's cash equivalents are invested in money market funds. The Company has not experienced any losses on its deposits of cash and cash equivalents. Such deposits may, at times, exceed federally insured limits.

The Company's partners in collaboration and license agreements who represent 10% or more of the Company's total revenue are as follows:

	Year Ended December 31, 2020	Year Ended December 31, 2019
Customer A	95%	90%
Customer B	*	*
Total	95%	90%

* Less than 10%

The Company's partners in collaboration and license agreements who represent 10% or more of the Company's total accounts receivable are as follows:

	December 31, 2020	December 31, 2019
Customer A	74%	64%
Customer B	26%	36%
Total	100%	100%

The Company's total revenues by geographic region, based on the location of the customer, are as follows (in thousands):

	Year Ended December 31, 2020	Year Ended December 31, 2019
Australia	$ —	$ 7
Netherlands	742	26
Switzerland	12,897	6,287
United States	(27)	666
	$ 13,612	$ 6,986

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Cash equivalents consist of money market funds.

Other Risks and Uncertainties

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, protection of proprietary technology, dependence on key personnel, suppliers for key raw materials, contract manufacturing organizations ("CMOs") and contract research organizations ("CROs"), compliance with government regulations and the need to obtain additional financing to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical studies, clinical trials and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance and reporting.

There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained or maintained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from other pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees, consultants and other third parties (including for clinical trials and some aspects of research and preclinical testing).

The extent of the impact of the COVID-19 pandemic on the Company's business will depend upon the duration and spread of the outbreak and the extent and severity of the impact on the Company's clinical trial activities, research activities and suppliers, all of which are uncertain and cannot be predicted. The extent to which the coronavirus outbreak may materially impact the Company's financial condition, liquidity or results of operations is uncertain.

Fair Value Measurements

The Company applies fair value accounting for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis. Fair value is 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, a three-level fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

- *Level 1*—Observable inputs, such as quoted prices in active markets for identical assets and liabilities.
- *Level 2*—Observable inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- *Level 3*—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The Company accounts for transfers of financial instruments between levels of the fair value hierarchy on the date of the event or change in circumstance that caused the transfer.

Accounts Receivable—Allowance for Doubtful Accounts

The Company regularly reviews accounts receivable for collectability and establishes an allowance for probable credit losses and writes off uncollectible accounts as necessary. The Company has determined that no allowance was required at December 31, 2020 and 2019. The Company did not have any write-offs relating to uncollectible accounts receivable during the years ended December 31, 2020 and 2019.

Property and Equipment, net

Property and equipment are stated at cost less accumulated depreciation for acquired assets. Depreciation is computed using the straight-line method over the estimated useful lives of assets, ranging from three to five years. Leasehold improvements are amortized over the shorter of the useful life of the assets or the lease term. Upon sale or retirement of assets, the costs and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is reflected within operating expenses in the statements of operations and comprehensive loss. Maintenance and repairs are charged to expense as incurred.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount to the future undiscounted net cash flows, which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is typically measured by the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. There have been no such impairments of long-lived assets in the years ended December 31, 2020 and 2019.

Redeemable Convertible Preferred Stock

The Company recorded all shares of redeemable convertible preferred stock at their respective fair values on the dates of issuance, net of issuance costs. The redeemable convertible preferred stock was recorded outside of permanent equity because while it was not mandatorily redeemable, in certain events considered not solely within the Company's control, such as a merger or consolidation, sale, lease, or license of substantially all of the Company's assets (each, a "deemed liquidation event"), the convertible preferred stock would become redeemable at the option of the holders of a majority of the outstanding series of redeemable convertible preferred stock. The Company did not adjust the carrying values of the redeemable convertible preferred stock to the liquidation preference of such shares because a deemed liquidation event obligating the Company to pay the liquidation preference did not occur. All outstanding

shares of the redeemable convertible preferred stock converted into common stock upon the closing of the IPO in December 2020.

Common Stock Warrants

The Company accounts for common stock warrants which meet the definition of a derivative as liabilities if the warrant requires net cash settlement or gives the holder the option of net cash settlement. The Company accounts for common stock warrants as equity if the contract requires physical settlement or net physical settlement or if the Company has the option of physical settlement or net physical settlement. Common stock warrants classified as liabilities are initially recorded at fair value and remeasured at fair value each balance sheet date with the offset adjustments recorded in other income (expense), net within the statements of operations and comprehensive loss. Common stock warrants classified as equity are initially measured at fair value on the grant date and are not subsequently remeasured.

Revenue Recognition

Effective January 1, 2019, the Company adopted Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASC 606"), using the modified retrospective transition method. The Company determines revenue recognition for arrangements within the scope of ASC 606 by performing the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

The Company's revenue is primarily derived through its license, research, development and commercialization agreements. The terms of these types of agreements may include (i) licenses to the Company's technology, (ii) research and development services, and (iii) services or obligations in connection with participation in research or steering committees. Payments to the Company under these arrangements typically include one or more of the following: nonrefundable upfront and license fees, research funding, milestone and other contingent payments to the Company for the achievement of defined collaboration objectives and certain preclinical, clinical, regulatory and sales-based events, as well as royalties on sales of any commercialized products. Arrangements that include upfront payments are recorded as deferred revenue upon receipt or when due and are recognized as revenue as performance conditions are met. The event-based milestone payments, royalties and cost reimbursements represent variable consideration, and the Company uses the most likely amount method to estimate this variable consideration. Royalty payments are recognized when earned or as the sales occur. The Company records cost reimbursements as accounts receivable when right to consideration is unconditional.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC 606. The Company allocates the total transaction price to each performance obligation based on the estimated standalone selling price and recognizes revenue when, or as, the performance obligation is satisfied. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. At the end of each reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price.

Significant management judgment is required to determine the level of effort required under an arrangement and the period over which the Company expects to complete its performance obligations under the arrangement. Changes in these estimates can have a material effect on revenue recognized.

Research and Development Expenses

Costs related to research, design and development of programs are charged to research and development expense as incurred. Research and development costs include, but are not limited to, payroll and personnel expenses including stock-based compensation, materials, laboratory supplies, outside services and allocated overhead, including rent, insurance, repairs and maintenance, depreciation and utilities. The Company expenses all research and development costs in the period in which they are incurred.

Costs incurred in obtaining technology licenses are charged to research and development expense as acquired in-process research and development if the technology licensed has not reached technological feasibility and has no alternative future use.

Accrued Research and Development

The Company has entered into various agreements with CROs and CMOs. The Company's research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development provided, but not yet invoiced, are included in accrued and other current liabilities on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made to CROs or CMOs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered.

Stock-Based Compensation

As of January 1, 2020, the Company adopted ASU 2018-07, *Compensation - Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, which aligns the measurement and classification guidance for share-based payments to nonemployees with the guidance for share-based payments to employees. As of January 1, 2020, the Company accounts for stock-based compensation for stock options granted to employees, directors and nonemployees as measured at grant date, based on the fair value of the award. The Company measures the fair value of awards granted using the Black-Scholes option pricing model and recognizes the expense in the statements of operations and comprehensive loss over the requisite service period using the straight-line method. Forfeitures are accounted for as they occur. The Company's policy for issuing stock upon stock option exercise is to issue new common stock.

Prior to the adoption of ASU 2018-07 on January 1, 2020, stock-based compensation expense related to stock options granted to nonemployees was recognized based on the vesting date fair value of options as the stock options were earned. The Company remeasured the stock-based compensation at each reporting period end with the resulting change in fair value being recognized in the statements of operations and comprehensive loss over the period the related services were rendered. The Company estimated the service period for the options based on the time that would be required to satisfy the service condition, assuming the service condition would be satisfied. Stock-based compensation expense was recognized over the estimated service period but was accelerated if the performance condition was achieved earlier than estimated.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires, among other things, that deferred income taxes be provided for temporary differences between the tax basis of the Company's assets and liabilities and their financial statement reported amounts. In addition, deferred tax assets are recorded for the future benefit of utilizing net operating losses and research and development credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. A valuation allowance is provided against deferred tax assets unless it is more likely than not that they will be realized.

The Company accounts for uncertain tax positions by assessing all material positions taken in any assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Embedded Derivative

Embedded derivatives that are required to be bifurcated from the underlying host instrument are accounted for and valued as a separate financial instrument. An embedded derivative exists in the award agreement with the Cystic Fibrosis Foundation ("CFF"). As described in Note 15, the embedded derivative has been bifurcated and is classified as a liability on the balance sheet and separately accounted for at its fair value. The derivative liability is subject to remeasurement to fair value each reporting period. Changes in the fair value of the derivative liability are recognized as a component of other income (expense), net within the statements of operations and comprehensive loss.

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly related to the Company's in-process financings, until such financings are consummated. After consummation of the financing, these costs are recorded as a reduction of the proceeds received as a result of the offering. In the event that a planned offering does not occur or is significantly delayed, all related deferred offering costs will be expensed immediately within the Company's statements of operations and comprehensive loss.

Net Loss Per Share Attributable to Common Stockholders

The Company calculates basic and diluted net loss per share to common stockholders in conformity with the two-class method required for companies with participating securities. The Company considers all series of redeemable convertible preferred stock to be participating securities as the holders are entitled to receive non-cumulative dividends on a pari passu basis in the event the dividend is paid on common shares. Under the two-class method, the net loss attributable to common stockholders is not allocated to the redeemable convertible preferred stock as the holders of redeemable convertible preferred stock do not have a contractual obligation to share in losses.

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, less shares subject to repurchase. Diluted net loss per share attributable to common stockholders is computed by giving effect to all potentially dilutive common shares outstanding for the period. For purposes of this calculation, redeemable convertible preferred shares, stock options to acquire shares of common stock, common stock warrants, and unvested common stock subject to repurchase, are considered potentially dilutive common shares, but have been excluded from the calculation of diluted net loss per share attributable to common stockholders as their effect is antidilutive.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued ASC 606. This standard outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. The Company adopted ASC 606 effective January 1, 2019 using the modified retrospective method only to contracts not completed as of this date. The Company recognized the cumulative effect of initially applying ASC 606 as an adjustment to the balance of

accumulated deficit at January 1, 2019 with a cumulative effect adjustment of $0.3 million reflected as a decrease to the opening balance of accumulated deficit and a decrease to deferred revenue.

In June 2018, FASB issued ASU 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*. This ASU aligns the measurement and classification guidance for share-based payments to nonemployees with the guidance for share-based payment to employees. Under this ASU, the measurement of equity-classified nonemployee awards will be fixed at the grant date, which may lower their cost and reduce volatility in the statement of operations and comprehensive loss. The transition method provided by this ASU is on a modified retrospective basis, which recognizes a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. This ASU is effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020, with early adoption permitted, but no earlier than a company's adoption date of ASC 606. The Company adopted this guidance effective January 1, 2020 using the modified retrospective method. The Company recorded a less than $0.1 million cumulative-effect adjustment reflected as a decrease to the opening balance of accumulated deficit and a decrease to additional paid-in capital.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820), Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. This ASU amends the disclosure requirement in ASC 820, Fair Value Measurement, by adding, changing, or removing certain disclosures. This ASU applies to all entities that are required under this guidance to provide disclosure about recurring or nonrecurring fair value measurements. The amendments require new disclosures related to: (i) changes in unrealized gains and losses for the period included in other comprehensive income for recurring Level 3 fair value measurements held at the end of the reporting period; and (ii) the range and weighted-average of significant unobservable inputs used to develop Level 3 fair value measurements. In addition, there are certain changes in disclosure requirements in the existing guidance. For all entities, this ASU is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted. The Company adopted this guidance effective January 1, 2020 with relevant updates made to disclosures.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic 260) Distinguishing Liabilities from Equity (Topic 480) Derivatives and Hedging (Topic 815) (Part I) Accounting for Certain Financial Instruments with Down Round Features, (Part II) Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception*. This ASU simplifies the accounting for certain financial instruments with down round features, a provision in an equity-linked financial instrument (or embedded feature) that provides a downward adjustment of the current exercise price based on the price of future equity offerings. Down round features are common in warrants, preferred shares, and convertible debt instruments issued by private companies and early-stage public companies. This ASU requires companies to disregard the down round feature when assessing whether the instrument is indexed to its own stock, for purposes of determining liability or equity classification. The amendments in Part I of this ASU are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted. The amendments in Part I should be applied (1) retrospectively to outstanding financial instruments with a down round feature by means of a cumulative-effect adjustment to the balance sheet as of the beginning of the first fiscal year and interim periods; (2) retrospectively to outstanding financial instruments with a down round feature for each prior reporting period presented. The amendments in Part II of this ASU do not require any transition guidance because those amendments do not have an accounting effect. The Company adopted this guidance effective January 1, 2020. The adoption did not have an impact on the Company's financial statements and related disclosures.

New Accounting Pronouncements Not Yet Adopted

As an "emerging growth company," the Jumpstart Our Business Startups Act ("JOBS Act") allows the Company to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. The Company has

elected to use this extended transition period under the JOBS Act. The adoption dates discussed below reflects this election.

In November 2018, the FASB issued ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606*. This ASU clarifies that certain transactions between participants in a collaborative arrangement should be accounted for under ASC 606, *Revenue from Contracts with Customers*, when the counterparty is a customer. This ASU also precludes an entity from presenting consideration received from a transaction as revenue from contracts with customers if the counterparty is not a customer for that transaction. This ASU is effective for fiscal years beginning after December 15, 2020, and interim periods within fiscal years beginning after December 15, 2021. Early adoption is permitted for entities that have adopted ASC 606, *Revenue from Contracts with Customers*. The Company is currently evaluating the impact the adoption of this standard will have on its financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. This ASU is effective for fiscal years beginning after December 15, 2020, and interim periods within fiscal years beginning after December 15, 2021. The Company is currently evaluating the impact the adoption of this standard will have on its financial statements and related disclosures.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842) ("ASC 842")*, which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e. lessees and lessors). In July 2018, the FASB issued ASU 2018-10, *Codification Improvements to Topic 842, Leases*, which provides clarification to ASU 2016-02. These ASUs (collectively the "new leasing standard") require lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. ASC 842 supersedes the previous leases standard, ASC 840, *Leases*. In July 2018, the FASB issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements,* which allows entities to elect an optional transition method where entities may continue to apply the existing lease guidance during the comparative periods and apply the new lease requirements through a cumulative effect adjustment in the period of adoption rather than in the earliest period presented. ASU 2016-02 is effective for the Company in the fiscal year beginning after December 15, 2021, and for interim periods within fiscal years beginning after December 15, 2022. Early adoption is permitted. The Company is currently evaluating the impact the adoption of this standard will have on its financial statements and related disclosures.

3. Fair Value Measurements

The following tables represent the Company's fair value hierarchy for financial assets and financial liabilities measured at fair value on a recurring basis as of December 31, 2020 and 2019 (in thousands):

	Basis for Fair Value Measurements			Fair Value as of December 31, 2020
	(Level 1)	(Level 2)	(Level 3)	
Assets				
Money market funds	$ 276,726	$ —	$ —	$ 276,726
Total	$ 276,726	$ —	$ —	$ 276,726
Liabilities				
Derivative liability	$ —	$ —	$ 122	$ 122
Total	$ —	$ —	$ 122	$ 122

	Basis for Fair Value Measurements			Fair Value as of December 31, 2019
	(Level 1)	(Level 2)	(Level 3)	
Assets				
Money market funds	$ 15,876	$ —	$ —	$ 15,876
Total	$ 15,876	$ —	$ —	$ 15,876
Liabilities				
Derivative liability	$ —	$ —	$ 101	$ 101
Total	$ —	$ —	$ 101	$ 101

Level 3 Inputs

The fair value of the derivative liability is based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The fair value of the derivative liability was determined using a present value analysis with multiple scenarios. In determining the fair value of the derivative liability, the inputs impacting fair value include the change of control payment to CFF, the probability of a change of control event, the product status at time of a change of control event and the discount rate. See Note 15 for further discussion on embedded derivative.

There were no transfers between Level 1, 2 and 3 during the periods presented.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial instruments (in thousands):

	Derivative Liability
Balance as of December 31, 2018	$ 64
Change in fair value included in other income (expense), net	37
Balance as of December 31, 2019	$ 101
Change in fair value included in other income (expense), net	21
Balance as of December 31, 2020	$ 122

4. Property and Equipment, Net

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

	December 31, 2020	December 31, 2019
Machinery and equipment	$ 4,911	$ 3,761
Leasehold improvements	2,527	2,405
Furniture and fixtures	473	541
Office equipment	101	98
Computer equipment and software	366	306
Construction in progress	539	563
Total property and equipment	8,917	7,674
Less: Accumulated depreciation and amortization	(3,844)	(2,625)
Property and equipment, net	$ 5,073	$ 5,049

All property and equipment are maintained in the United States. Depreciation expense was $1.4 million and $1.0 million for the years ended December 31, 2020 and 2019, respectively.

5. Accrued and Other Liabilities, Current and Noncurrent

Accrued liabilities consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Payroll and related	$ 3,437	$ 2,133
Accrued clinical and preclinical study costs	869	494
Consulting and professional	3,574	2,239
Other accrued expenses	491	481
Total accrued and other current liabilities	$ 8,371	$ 5,347

Other liabilities, noncurrent consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Deferred rent, noncurrent	$ 1,237	$ 1,023
Other payable, noncurrent	615	542
Total other liabilities, noncurrent	$ 1,852	$ 1,565

6. Research and Collaboration Arrangements

Collaboration and license revenue for each period was as follows (in thousands):

	Year Ended December 31,	
	2020	**2019**
uniQure	$ 742	$ 26
Benitec	—	7
CRF	—	—
Roche	12,897	6,287
CFF	(27)	118
AstraZeneca	—	548
	$ 13,612	$ 6,986

Deferred revenue for each period was as follows (in thousands):

	Deferred Revenue	
	As of December 31, 2020	**As of December 31, 2019**
uniQure	$ 4,396	$ 5,137
Benitec	—	—
CRF	—	—
Roche	14,318	13,640
CFF	1,098	690
AstraZeneca	—	—
	$ 19,812	$ 19,467

The total amount of revenue in the year ended December 31, 2020, which was included in deferred revenue at January 1, 2020, was $3.2 million. The total amount of revenue in the year ended December 31, 2019, which was included in deferred revenue at January 1, 2019, was $3.6 million.

uniQure

In January 2014, the Company and uniQure biopharma B.V. (“uniQure”) entered into a Collaboration and License Agreement (the “uniQure Agreement”) to collaborate on the discovery and non-clinical research activities related to the Company’s Therapeutic Vector Evolution platform in order to generate and validate vectors for gene delivery to treat diseases within the central nervous system and liver (together, the “uniQure Field”).

The uniQure Agreement provided uniQure with a research license as well as an exclusive development and commercialization license for each project variant selected for further development. The initial research term is three years with an option for uniQure to extend the research term one time for an additional year. Once the Company’s research plan has concluded, uniQure is solely responsible for the continued development, manufacturing and commercialization of the project variants as potential product candidates. In October 2016, uniQure exercised its option to extend the research term for an additional year to January 2018. The Company was also required to work exclusively with uniQure in the uniQure Field (the “uniQure Exclusivity Clause”).

Pursuant to the uniQure Agreement, the Company received upfront payments of $0.2 million, and was entitled to receive (i) contingent payments for the achievement of research and development milestones of up to $5.0 million for each licensed product selected under the arrangement, and (ii) royalties in the single digit range on future sales of the potential product candidates and sublicense

consideration in the low teens to low thirties range on any future sublicensing arrangements. The Company also received capped research and development service fees based on contractual full-time employee rates per year. In connection with the performance obligations under the uniQure Agreement, the founders of 4D Molecular Therapeutics, LLC received equity options to purchase an aggregate of 609,744 of uniQure ordinary shares that vest over the initial three-year term of the agreement.

The upfront payment of $0.2 million was recorded as deferred revenue and was recognized on a ratable basis over the estimated performance period of four years. Payments and reimbursements for research costs were recognized on an as-incurred basis. The options to purchase uniQure shares were deemed to be a noncash component of the arrangement consideration, as the vesting of options is linked to the uniQure Agreement and there is a requirement for the holders of the options to provide services under the agreement. The fair value of the uniQure options, which was estimated to be $10.6 million, was recognized ratably as revenue over the estimated performance period of four years and the associated compensation expense related to the stock options were recorded as research and development expense.

In August 2019, the Company and uniQure entered into an Amended and Restated Collaboration and License Agreement (the "Amended uniQure Agreement"), which amended and restated the uniQure Agreement, and a separate Collaboration and License Agreement (the "Second uniQure Agreement"). Under these agreements, the Company agreed to transfer incremental rights and services to uniQure in exchange for uniQure eliminating the uniQure Exclusivity Clause and transferring other rights back to the Company.

Under the Amended uniQure Agreement, uniQure continues to have an exclusive license to select AAV capsid variants (the "Selected Variants") in the uniQure Field. uniQure continues to be solely responsible, at its cost, to develop and commercialize the compounds and products containing the Selected Variants. The amended uniQure Agreement eliminated the uniQure Exclusivity Clause in the uniQure Agreement. Furthermore, the contingent payments that the Company was entitled to from uniQure for the achievement of research and development milestones of up to $5.0 million for each licensed product selected under the uniQure Agreement were eliminated and sublicense consideration on any future sublicensing arrangements was reduced from the low teens to low thirties percentages to mid-single digit to mid-twenties percentages.

Under the Second uniQure Agreement, the parties agreed to research and develop new AAV capsid variants (the "New Variants") that are not Selected Variants that affect certain targets selected by uniQure (the "uniQure Targets") in the uniQure Field. The Company is solely responsible, at its cost, for the research of the New Variants. The Company granted uniQure an exclusive license to a certain number of the New Variants (the "uniQure New Variants") that affect the uniQure Targets. uniQure is solely responsible, at its cost, to develop and commercialize the compounds and products containing the uniQure New Variants that affect the uniQure Targets (the "Licensed Products"). The Company retains all rights to New Variants in the uniQure Field that affect targets other than the uniQure Targets.

Under both the Amended uniQure Agreement and the Second uniQure Agreement, uniQure will be required to pay the Company royalties on worldwide annual net sales of Licensed Products at a mid-single digit percentage rate, subject to certain specified reductions. uniQure will also be required to pay the Company sublicensing consideration for sublicensing the Company's intellectual property rights licensed under the Amended uniQure Agreement or the Second uniQure Agreement to third parties at a rate between the mid-single digit to mid-twenties. The Company has reciprocal obligations, at the same percentage rates as uniQure, to pay uniQure royalties and sublicensing consideration for sublicensing certain intellectual property rights licensed under the Amended uniQure Agreement or the Second uniQure Agreement to third parties.

The Company concluded that the Amended uniQure Agreement and the Second uniQure Agreement should be accounted for as one combined contract that should be accounted for as a separate contract from the uniQure Agreement given that the incremental licensed intellectual property rights and research and development services are distinct from the rights and services previously

transferred to uniQure under the uniQure Agreement and the transaction price increased by an amount that equals the standalone selling price of the incremental rights and services to be transferred to uniQure under the Amended uniQure Agreement and Second uniQure Agreement.

Neither party was required to pay monetary consideration in connection with the execution of the Amended uniQure Agreement or the Second uniQure Agreement or for subsequent performance by the parties under those agreements, notwithstanding the potential future royalty and sublicense consideration described above. The fair value of the non-monetary consideration given by uniQure to the Company, for the intellectual property right is $5.1 million. This intellectual property right is considered to be an in-process research and development asset with no alternative future use and, accordingly, was written off as acquired in-process research and development expense in the year ended December 31, 2019.

The incremental transaction price described in the paragraph above was recorded as deferred revenue given that the Company identified one single combined performance obligation under ASC 606, which includes the licenses to the New Variants, research services and participation in the joint steering committee ("JSC"). Revenue is being recognized using the input method based on actual costs incurred as a percentage of total budgeted costs as the Company completes its performance obligation. Based on the current estimated timelines, the deferred revenue is expected to be recognized as revenue over approximately two to three years from December 31, 2020.

The Company determined the transaction price using the risk adjusted net present value analysis ("rNPV") methodology to value the elimination of the uniQure exclusivity clause and other material rights received by the Company, including the potential royalties the Company would receive from uniQure. The rNPVs incorporate estimates and assumptions including the number of products the Company and uniQure would develop, the risk-adjusted probability of successfully developing a biopharmaceutical product, the probability that uniQure will develop a product, the research and development costs, the potential worldwide sales and associated commercialization costs, corporate tax rate, and discount rate.

During the years ended December 31, 2020 and 2019 the Company recognized revenue of $0 and less than $0.1 million under the uniQure Agreement, respectively. During the years ended December 31, 2020 and 2019 the Company recognized revenue of $0.7 million and $0 under the Amended uniQure Agreement and the Second uniQure Agreement, respectively. As of December 31, 2020 and 2019, deferred revenue relating to uniQure was $4.4 million and $5.1 million, respectively. There were no amounts due from uniQure under the uniQure Agreement, Amended uniQure Agreement or Second uniQure Agreement as of December 31, 2020 and 2019. As of December 31, 2020 and 2019, the aggregate amount of the transaction price allocated to the remaining performance obligation was $4.4 million and $5.1 million, respectively.

Benitec

In November 2014, the Company and Benitec Biopharma Limited ("Benitec") entered into a collaboration and license agreement to collaborate on the discovery and non-clinical research activities related to the Company's Therapeutic Vector Evolution platform in order to generate and validate vectors for gene delivery to treat certain ophthalmic diseases (the "Benitec Agreement"). Benitec had the option of nominating up to three project variants as part of the Benitec Agreement.

The Benitec Agreement provided Benitec with a temporary research license as well as an exclusive development and commercialization license for each project variant selected to further develop. The initial research term was two years and was automatically extended in six-month increments, if necessary, in order to complete additional required studies, for a maximum of five years. Once the Company's research plan concluded, Benitec was solely responsible for the continued development, manufacturing and commercialization of the project variants as potential product candidates.

Pursuant to the Benitec Agreement, the Company received as consideration (i) an upfront payment of $0.5 million, (ii) capped research and development service fees based in part on prescribed

full-time equivalent labor rates and (iii) reimbursements of pass-through and overhead costs incurred on behalf of Benitec.

On January 24, 2017, the Benitec Agreement was amended to give Benitec sole responsibility for the performance of certain research work which would have generated research services revenue for the Company under the original agreement. Pursuant to the amendment, the Company received $0.5 million as consideration. This $0.5 million was recorded as deferred revenue and was recognized over the same period as the upfront payment.

In March 2019, the Benitec Agreement was terminated based on mutual agreement between the Company and Benitec.

The Company identified one combined performance obligation to provide the research license, exclusive development and commercialization licenses for each project variance selected to further develop, research services and participation in the JSC. The transaction price included the $1.0 million non-refundable upfront fees and $2.4 million reimbursement for costs incurred and the value of labor hours expended. The Company excluded any consideration related to sales-based milestones, including royalties, which are recognized when the related sales occur. For the year ended December 31, 2019, there was no change in the transaction price.

During the years ended December 31, 2020 and 2019, the Company recognized revenue of $0 and less than $0.1 million, respectively. As of December 31, 2020 and 2019, deferred revenue relating to the Benitec Agreement was $0. There were no amounts due from Benitec under the Benitec Agreement as of December 31, 2020 and 2019. Upon termination of the Benitec Agreement in March 2019, the Company had no further obligations impacting revenue recognition.

CRF

In November 2015, the Company entered into a research funding and collaboration agreement (the “CRF Agreement”) with the Choroideremia Research Foundation (“CRF”), a non-profit organization dedicated to finding a cure for choroideremia, a rare inherited disorder that causes progressive vision loss, ultimately leading to complete blindness. The goal of the CRF Agreement is for CRF to contribute funding to help with the advancement of the Company’s choroideremia research program. The Company is responsible for all decision making and execution of any and all of the related activities to be completed in its sole discretion. The initial term of the CRF Research Plan is two years. The agreement includes contribution to CRF of up to $2.5 million upon certain development or approval milestones. The overall arrangement has automatic extensions of up to three additional years. As of December 31, 2020, no milestones have been achieved.

Revenue was fully recognized for this agreement in the year ended December 31, 2017. There was no deferred revenue relating to the CRF Agreement as of December 31, 2020 and 2019. No amount was due from CRF under the CRF Agreement as of December 31, 2020 and 2019.

Roche

In November 2017, the Company entered into a collaboration and license agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together, “Roche”) to discover and develop products containing optimized next generation AAV Vectors focused on ophthalmological diseases and disorders excluding select criteria (the “2017 Roche Agreement”). The Company and Roche both have the ability to nominate products to discover, develop and commercialize.

At the effective date, choroideremia was designated a Roche product. The Company is responsible for conducting research and development services prior to pivotal clinical studies, and Roche is responsible for conducting subsequent development and commercialization activities. In addition, Roche agreed to pay for research and development services at the agreed upon full-time employee rate for work performed for choroideremia under the 2017 Roche Agreement, except for the costs associated with the manufacturing work for choroideremia.

For any product that the Company nominates and conducts research and development services under the 2017 Roche Agreement prior to pivotal clinical studies, including 4D-125 (for the treatment of XLRP), Roche has an option to convert the status of the product to a Roche product during the 90-day option period. If Roche chooses to not exercise its option, the Company can continue subsequent development and commercialization activities and Roche will have no further rights with respect to such product.

Pursuant to the 2017 Roche Agreement, the Company received an upfront payment of $21.0 million as consideration. In addition, the Company is entitled to contingent payments including (i) $1.0 million for each Roche nominated product beyond the first three, (ii) up to $30.0 million upon exercise of the option to convert a product the Company nominated and developed prior to pivotal clinical studies (iii) development milestone payments of up to $223.0 million, of which $86.0 million relates to choroideremia and the rest relate to other licensed products; and (iv) sales-based milestones of up to $123.0 million in connection with licensed products. The 2017 Roche Agreement also includes provisions that entitle the Company to receive royalty payments ranging from the mid-single digits to the mid-teens for the net sales of the licensed products, in each case subject to the reductions in accordance with the terms of the agreement.

Under ASC 606, the Company identified a single combined performance obligation for the license, research services and participation in the JSC. Furthermore, the Company concluded that at the inception of the agreement, Roche's option, exercisable prior to pivotal clinical study initiation, does not represent a material right and should be allocated to the single performance obligation and recognized as revenue upon Roche's exercise of the option. The transaction price related to the agreement upon adoption of ASC 606 included the $21.0 million non-refundable upfront fee and $10.7 million for estimated reimbursements for research and development services at the agreed upon full-time employee rate and third party costs. The Company's contract with Roche does not include a significant financing component. The Company concluded that the transaction price should not include the variable consideration related to development milestones as they were considered to be constrained as it is probable that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in the future. The Company excluded any consideration related to sales-based milestones, including royalties, which are recognized when the related sales occur. The transaction price and estimated period of performance will be re-evaluated at each reporting period. For the year ended December 31, 2020, an adjustment of $17.0 million was made to the transaction price to reflect an increase of $7.0 million in the scope of the project and expected reimbursable costs and the addition of $10.0 million of variable consideration as the uncertainty associated with two development milestones was resolved. The adjustments to the transaction price and total budgeted costs in 2020 resulted in a $4.6 million increase in revenue recognized in the year ended December 31, 2020 related to performance obligations partially satisfied in periods prior to January 1, 2020. For the year ended December 31, 2019, an adjustment of $4.5 million was made to the transaction price to reflect an increase in the scope of the project and expected reimbursable costs. The increase in the transaction price and total budgeted costs in 2019 resulted in a $1.6 million decrease in revenue recognized in the year ended December 31, 2019 related to performance obligations partially satisfied in periods prior to January 1, 2019.

During the years ended December 31, 2020 and 2019, the Company recognized revenue of $12.9 million and $6.3 million, respectively. As of December 31, 2020 and 2019, deferred revenue relating to the Roche Agreement was $14.3 million and $13.6 million, respectively. Accounts receivable from Roche under this agreement as of December 31, 2020 and 2019 was $1.1 million and $0.6 million, respectively. As of December 31, 2020 and 2019, the aggregate amount of the transaction price allocated to the remaining performance obligation was $25.8 million and $21.6 million, respectively. Based on current timelines, the deferred revenue is expected to be recognized as revenue over the next three to four years as the Company continues to develop nominated products until the initiation of pivotal studies.

CFF

In September 2016, the Company entered into an award agreement for the Optimized Adeno-Associated Virus for Lung Epithelia Gene Delivery Development Program with CFF, a non-profit organization dedicated to finding a cure for cystic fibrosis, an inherited disorder that causes disease in the pulmonary airways leading to morbidity and mortality. Under this agreement, CFF contributes funding to help advance the Company's CF research program. The agreement was subsequently amended in September 2017 and August 2018 (all three agreements are collectively referred to as the "CFF Agreement"). The total amount of the award under the CFF Agreement is $3.5 million. As of December 31, 2020 and 2019, the Company achieved milestones totaling $1.3 million and $0.9 million under the CFF Agreement, respectively. The remaining award amount will be paid by CFF based on achievement of certain development milestones by the Company.

The Company expects to make payments to CFF equal to six times the actual award received by the Company in three installments within the first four years of the first commercial sale of a product developed under this agreement. The Company also has agreed to make future sales-based milestone payments to CFF of up to three times the actual award received upon achieving specified commercialization milestones with respect to the first of any product developed utilizing any compound covered under the CFF Agreement. The CFF Agreement also requires the Company to pay to CFF royalties of a mid-single digit percentage, up to six times the actual award received, on any amounts received by the Company from the sale, license or transfer to a third-party of rights in the technology developed as a result of this collaboration. Any such royalty payments shall be credited against the payments owed by the Company upon first commercial sale. In the event of a change of control of the Company, CFF will receive certain payments, depending on the timing of the change of control and the size of the transaction.

To date, the Company has not developed a commercial product in connection with the CFF Agreement, and it has not licensed, sold or otherwise transferred to another party the product developed under the CFF Agreement or the underlying technology.

If at any time prior to the first commercial sale of a product developed as a result of the CFF Agreement, the Company ceases to use commercially reasonable efforts to develop or commercialize any product under the CFF Agreement for a continuous period of 180 consecutive days and fails to present a reasonable plan to resume commercially reasonable efforts, the Company will grant to CFF an irrevocable, exclusive worldwide interruption license under all of the Company's interest in the research plan technology to exploit such product. Any third-party license granted by the Company shall be subject to such interruption license.

Under ASC 606, the Company identified one performance obligation within the CFF grant agreement for research activities. The Company's contract with CFF does not include a significant financing component.

The Company concluded that the transaction price should not include the variable consideration related to future research milestones as they were considered to be constrained as it is probable that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in the future. The Company re-evaluates the transaction price and estimated period of performance at each reporting period. For the year ended December 31, 2020, an adjustment of $0.4 million was made to the transaction price to reflect the achievement of the third milestone related to in-vitro screenings under the CFF Agreement.

During the years ended December 31, 2020 and 2019, the Company recognized revenue of less than $(0.1) million and $0.1 million, respectively. As of December 31, 2020 and 2019, deferred revenue relating to the CFF Agreement was $1.1 million and $0.7 million, respectively. Accounts receivable from CFF under the CFF Agreement as of both December 31, 2020 and 2019 was $0.4 million. As of December 31, 2020 and 2019, the aggregate amount of the transaction price allocated to the remaining performance obligation was $1.1 million and $0.7 million, respectively. Based on current timelines, the deferred revenue is expected to be recognized as revenue over the next two to three years as the Company performs research services through the completion of IND-enabling studies.

The obligation to make payments to CFF upon a change of control meets the definition of an embedded derivative that is required to be bifurcated and separately accounted for as a derivative liability. The Company determined the estimated fair value of this derivative liability to be $0.1 million as of both December 31, 2020 and 2019. See Note 15 for further discussion of the embedded derivative.

AstraZeneca

In December 2017, the Company entered into a collaboration and option agreement with MedImmune, Inc., the global biologics research and development arm of AstraZeneca ("AstraZeneca") to discover and develop optimized AAV vectors to treat specific lung disease indications (the "AstraZeneca Agreement"). The AstraZeneca agreement included both a research funding component as well as a licensing component, wherein AstraZeneca was granted the option to license up to three resulting project vector variants for further development and commercialization.

The initial research term was approximately twelve months with AstraZeneca's option to extend the term for an additional six months. AstraZeneca requested the six-month extension in October 2018. AstraZeneca's option to license the resulting project variants expires twelve months after the conclusion of the research phase. Once the Company's research activities concluded, AstraZeneca was solely responsible for the continued development, manufacturing and eventual commercialization of the project variants as potential product candidates.

Pursuant to the AstraZeneca Agreement, the Company received an upfront payment of $1.5 million as consideration.

The Company identified a single combined performance obligation within the AstraZeneca agreement for the research program license, research and development activities and participation in the joint project team and JSC. The Company concluded that these activities are not distinct and, therefore, should be combined into a single combined performance obligation. Furthermore, the Company concluded that at the inception of the agreement, AstraZeneca's license option, did not represent a material right and should be allocated to the single performance obligation and recognized as revenue upon AstraZeneca's exercise of the option.

The transaction price related to the agreement consists of the $1.5 million non-refundable upfront fee. The Company concluded that the transaction price should not include the variable consideration related to developmental milestones as they were considered to be constrained as it is probable that the inclusion of such variable consideration could result in a significant reversal of cumulative revenue in the future. The Company excluded any consideration related to sales-based milestones, including royalties, which are recognized when the related sales occur. The Company re-evaluates the transaction price and estimated period of performance at each reporting period. The Company's contract with AstraZeneca does not include a significant financing component.

Under ASC 606, the Company used the input method to measure progress toward completion of the performance obligation and concluded that revenue will be recognized based on actual resources consumed, labor hours expended and costs incurred as a percentage of total budgeted costs.

In June 2019, the research phase concluded and the Company delivered its final report to AstraZeneca. In June 2020, AstraZeneca's option to obtain the license of up to three project vector variants under the AstraZeneca Agreement expired unexercised.

During the years ended December 31, 2020 and 2019, the Company recognized revenue of $0 and $0.5 million, respectively. As of December 31, 2020 and 2019, deferred revenue relating to the AstraZeneca Agreement was $0. No amount was due from AstraZeneca under this agreement as of December 31, 2020 and 2019.

7. License Arrangements

The Company has exclusive, worldwide license agreements (the "UC Agreements") with the Regents of the University of California (the "UC Regents") relating to the use of certain patents and intellectual property surrounding its core technologies, including Therapeutic Vector Evolution. Pursuant to each of the UC Agreements executed prior to January 2019, the Company was obligated to pay a (i) non-refundable license fee of $5,000 upon execution, (ii) a non-refundable license fee of $5,000 each year thereafter, until sales of a licensed product are made and royalties are paid to the UC Regents, (iii) reimbursement of domestic and foreign patent filing, prosecution and maintenance fees, and (iv) either $50,000 or issuance of a 3% equity interest in the Company upon the closing of the first qualified financing at the option of the UC Regents. The Company's first qualified financing occurred in 2015 and at the election of the UC Regents, the Company issued the UC Regents in January 2016 an amount of common stock equal to 6% of the equity interests in the Company pursuant to the applicable clause in each of the UC Agreements.

Pursuant to an agreement with the UC Regents executed in January 2019 the Company paid a non-refundable license fee of $50,000 to the UC Regents upon execution of the agreement. The Company is obligated to pay a non-refundable license fee of $5,000 on the one-year anniversary of the contract effective date and each year thereafter, until sales of a licensed product are made and royalties are paid to the UC Regents.

In addition, the Company is obligated to make certain contingent payments including (i) development milestones up to $3.1 million, (ii) low single digit royalties on the net sales of its developed products that consists of a minimum annual royalty of up to $0.1 million per year for the term of the Agreement beginning in the first calendar year after the year in which net sales first occurred, and (iii) sublicense consideration in the mid-teens to the mid-twenties-range on any future sublicensing arrangements the Company may enter into with third-party licensees.

During the years ended December 31, 2020 and 2019, the Company incurred expenses of $0.2 million and $0.3 million, respectively, under the provisions of the UC Agreements.

8. Commitments and Contingencies

Operating Lease Commitments

In May 2015, the Company executed a lease agreement for office and laboratory space in Emeryville, California. In January 2016, the Company executed the first amendment to the lease agreement for additional rentable office and laboratory space which extended the lease to March 31, 2023. In October 2018, the Company executed a second amendment to extend the lease to September 2026. Additionally, the second amendment provided a tenant improvement allowance of $0.2 million, which was paid to the Company in November 2018. The Company amortizes the tenant improvement allowance on a straight-line basis over the remaining term of the lease as a reduction of rent expense.

In October 2018, the Company executed a second lease agreement for additional office and laboratory space in Emeryville, California. The new lease has an initial term of 87 months beginning on the rent commencement date with the option to renew the lease for one additional term of five years. The Company did not have to pay rent until October 2019. This lease agreement also provided for a tenant improvement allowance of $0.4 million, which was paid to the Company in December 2019. The Company amortizes the tenant improvement allowance on a straight-line basis over the remaining term of the lease as a reduction of rent expense.

In May 2019, the Company amended the second lease agreement executed in October 2018 to add additional office and laboratory space. The amendment extended the term of the lease to December 31, 2029. The Company did not have to pay rent until December 2019. The annual rent for the additional space is $1.0 million per annum and escalates at 3% annually. This lease agreement also provides for a tenant improvement allowance of at least $1.6 million.

The Company recognizes rent expense on a straight-line basis over the lease term with the difference between the rent payments and the straight-line rent expense recorded as deferred rent. Rent expense for the years ended December 31, 2020 and 2019 was $3.0 million and $1.3 million, respectively. Deferred rent as of December 31, 2020 and 2019 was $1.6 million and $1.2 million, respectively. In conjunction with the lease agreements and amendments, the Company paid total security deposits of $0.6 million, which is included in other assets within the balance sheets as of both December 31, 2020 and 2019.

The following table summarizes the Company's future minimum commitments under lease contracts (in thousands):

As of December 31, 2020		
2021	$	2,956
2022		3,035
2023		3,115
2024		3,205
2025		3,258
2026 and beyond		11,820
Total	$	27,389

Indemnification Agreements

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions, such as with vendors and other parties. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third-party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has never incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. The Company has also entered into indemnification agreements with its directors and officers that require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by Delaware corporate law. The Company currently maintains directors' and officers' liability insurance that would generally enable it to recover a portion of any future amounts paid. The Company believes the estimated fair value of its indemnification agreements in excess of applicable insurance coverage is not material.

Legal Proceedings

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of its business. If applicable, the Company records a legal liability when it believes that it is both probable that a liability may be imputed, and the amount of the liability can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount.

Included in Accrued and Other Current Liabilities within the balance sheet at December 31, 2020 is a $1.4 million accrual relating to the estimated settlement of a claim from a former employee.

9. Income Taxes

The Company did not record any income tax expense during the years ended December 31, 2020 and 2019. The Company has a net operating loss and has provided a valuation allowance against net deferred tax assets due to uncertainties regarding the Company's ability to realize these assets. All losses before income taxes arose in the United States.

The effective tax rate of the Company's income tax expense (benefit) differs from the federal statutory rate as follows:

	December 31, 2020	December 31, 2019
Federal statutory income tax rate	21.0%	21.0%
Research tax credit	2.8%	5.2%
Permanent differences	(1.7)%	(0.7)%
Valuation allowance	(22.1)%	(25.5)%
Provision for income taxes	0.0%	0.0%

The tax effects of temporary differences that give rise to significant components of the deferred taxes are as follows (in thousands):

	December 31, 2020	December 31, 2019
Deferred Tax Assets		
Net operating loss carryforwards	$ 21,132	$ 10,638
Other accrued liabilities	422	336
Deferred revenue	3,111	2,698
Research tax credits	6,018	4,457
Stock compensation	1,151	554
Intangible asset basis	977	1,591
Total deferred tax assets	$ 32,811	$ 20,274
Less: valuation allowance	(32,811)	(20,274)
Net deferred tax assets	$ —	$ —

ASC 740, *Income Taxes,* requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of the future tax benefits is dependent on the Company's ability to generate sufficient taxable income within the carryforward period. Because of the Company's recent history of operating losses, management believes that recognition of the deferred tax assets arising from future tax benefits is currently not likely to be realized and, accordingly, has provided a full valuation allowance. The valuation allowance increased by $12.5 million during each of the years ended December 31, 2020 and 2019. The increase in the valuation allowance for each of the years ended December 31, 2020 and 2019 was primarily driven by losses and tax credits generated in the U.S.

The Company had net operating loss ("NOL") carryforwards of $100.6 million and $50.7 million as of December 31, 2020 and 2019, respectively, available to reduce future taxable income, if any, for federal income tax purposes. $9.5 million of the federal NOL carryforwards expire in 2037 and the remaining $91.1 million carryforward indefinitely.

As of December 31, 2020 and 2019, the Company had federal research and development credit carryforwards of $5.7 million and $3.3 million, respectively, and state research and development credit carryforwards of $4.3 million and $3.3 million, respectively, available to reduce future taxable income, if any, for federal and California state income tax purposes, respectively. The federal credit carryforwards begin expiring in 2035 and the state credits carryforward indefinitely.

Utilization of the NOL carryforwards and research credit carryforwards may be subject to an annual limitation due to the ownership percentage change limitations provided by the Internal Revenue Code and similar state provisions. Annual limitations may result in the expiration of the NOL and tax credit carryforwards before they are utilized. The Company has experienced ownership changes in the past as a result of its Series B redeemable convertible preferred stock financing. As a result of the ownership changes, the Company has determined that $0.9 million of its NOLs will expire unutilized for federal income tax purposes and such amounts are excluded from its NOL carryforwards. The Company does not expect any ownership changes during the year ended December 31, 2020. Subsequent ownership changes may affect the limitation in future years.

The reconciliation of the beginning and ending unrecognized tax benefits amounts is as follows (in thousands):

	Unrecognized Income Tax Benefits
Balance as of December 31, 2018	$ 659
Additions for current year tax positions	907
Balance as of December 31, 2019	1,566
Additions for current year tax positions	1,729
Additions for tax positions of prior years	72
Balance as of December 31, 2020	$ 3,367

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized. During each of the years ended December 31, 2020 and 2019, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will materially increase or decrease during the next 12 months.

The Company files income tax returns in the U.S. federal and California tax jurisdictions. In general, the Company is no longer subject to tax examination by the Internal Revenue Service or state taxing authorities for years before 2016. Although the federal and state statutes are closed for purposes of assessing additional income tax in those prior years, the taxing authorities may still make adjustments to the NOL and credit carryforwards used in open years. Therefore, the tax statutes should be considered open as it relates to the NOL and credit carryforwards used in open years. The Company has no ongoing income tax examinations by tax authorities at this time.

In March 2020, the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") was signed into law. The CARES Act changed certain provisions of the Tax Act. Under the CARES Act, NOLs arising in taxable years beginning after December 31, 2017 and before January 1, 2021 may be carried back to each of the five taxable years preceding the tax year of such loss, but NOLs arising in taxable years beginning after December 31, 2020 may not be carried back. In addition, the CARES Act eliminated the limitation on the deduction of NOLs to 80% of current year taxable income for taxable years beginning before January 1, 2021 and increased the amount of interest expense that may be deducted to 50% of adjusted taxable income for taxable years beginning in 2019 or 2020. The Company evaluated the impact of the CARES act on its tax provision and concluded that there was not a material impact.

On December 21, 2020, the U.S. president signed into law the Consolidated Appropriations Act, 2021 which includes further COVID-19 economic relief and extension of certain expiring tax provisions. The relief package includes a tax provision clarifying that businesses with forgiven PPP loans can deduct regular business expenses that are paid for with the loan proceeds. Additional pandemic relief tax measures include an expansion of the employee retention credit, enhanced charitable contribution deductions, and a temporary full deduction for business expenses for food and beverages provided by a restaurant. The Company evaluated the impact of the Consolidated Appropriations Act, 2021 on its tax provision and concluded that there was not a material impact.

10. Redeemable Convertible Preferred Stock

As of December 31, 2020 and 2019, the Company's certificate of incorporation authorized the Company to issue 0 and 7,375,638 shares of redeemable convertible preferred stock, respectively at the par value of $0.0001 per share.

As of December 31, 2019, redeemable convertible preferred stock consisted of the following (in thousands, except per share and share amounts):

	Shares Authorized	Original Issuance Price	Shares Issued and Outstanding	Liquidation Value	Proceeds Net of Issuance Cost
Series A	909,312	$ 7.70	909,312	$ 7,001	$ 6,960
Series A-1	1,311,687	$ 8.84	1,311,687	11,595	11,548
Series B	5,154,639	$ 17.46	5,154,632	90,000	84,472
Total	7,375,638		7,375,631	$ 108,596	$ 102,980

In April and June of 2020, the Company issued a total of 4,200,353 shares of Series C redeemable convertible preferred stock at $18.00 per share for net proceeds of $72.5 million. Upon the closing of the Company's IPO on December 15, 2020, all outstanding redeemable convertible preferred stock automatically converted into shares of common stock and the related carrying value was reclassified to common stock and additional paid in capital. There were no shares of redeemable convertible preferred stock outstanding as of December 31, 2020.

Prior to the closing of the Company's IPO the holders of redeemable convertible preferred stock had various rights and preferences including the following:

Liquidation Preference—In the event of a liquidation event, the holders of the shares of Series C and Series B redeemable convertible preferred stock were entitled to receive any distribution of any of the assets of the Company in preference to the holders of the Series A-1 redeemable convertible preferred stock, Series A redeemable convertible preferred stock or common stock, an amount per share equal to the greater of (i) the sum of the original Series C issue price plus all declared but unpaid dividends thereon or the original Series B issue price plus all declared but unpaid dividends and (ii) such amount per share payable had all shares of Series C and Series B redeemable convertible preferred stock been converted into common stock. If upon the occurrence of a liquidation event, the available assets were insufficient to pay the holders of Series C and Series B redeemable convertible preferred stock the full amount to which they were entitled, then the available assets would be distributed to the holders of the shares of Series C and Series B redeemable convertible preferred stock, in proportion to the full preferential amount each holder was otherwise entitled to receive. After full payment to holders of the Series C and Series B redeemable convertible preferred stock, payment would be made to the holders of Series A-1 redeemable convertible preferred stock, in preference to the holders of the Series A redeemable convertible preferred stock or common stock, in an amount equal to the greater of (i) the original Series A-1 issue price plus all declared but unpaid dividends and (ii) such amount per share payable had all shares of Series A-1 redeemable convertible preferred stock been converted into common stock. After full payment to holders of the Series A-1 redeemable convertible preferred stock, payment would be made to the holders of Series A redeemable convertible preferred stock, in preference

to the holders of the common stock, in an amount equal to the greater of (i) the original Series A issue price plus all declared but unpaid dividends and (ii) such amount per share payable had all shares of Series A redeemable convertible preferred stock been converted into common stock. If upon the occurrence of a liquidation event, the available assets were insufficient to pay the holders of Series A-1 or Series A redeemable convertible preferred stock the full amount to which they are entitled, then the available assets would be distributed to the holders of such redeemable convertible preferred stock on a pro rata, on an equal priority, pari passu basis, in proportion to the full preferential amount such holder was otherwise entitled to receive.

Notwithstanding the above, for purposes of determining the amount each holder of shares of redeemable convertible preferred stock would be entitled to receive with respect to a Liquidation Event, each such holder of shares of a series of redeemable convertible preferred stock would be deemed to have converted such holder's shares of such series into shares of common stock immediately prior to the Liquidation Event if, as a result of an actual conversion, such holder would receive, in the aggregate, an amount greater than the amount that would be distributed to such holder if such holder did not convert such series of redeemable convertible preferred stock into shares of common stock. If any such holder was deemed to have converted shares of redeemable convertible preferred stock into common stock pursuant to this paragraph, then such holder would not be entitled to receive any distribution that would otherwise be made to holders of redeemable convertible preferred stock that had not converted into shares of common stock.

Conversion—Shares of any series of redeemable convertible preferred stock could be converted, at the option of the holder, into such number of fully paid and non-assessable shares of common stock using a conversion rate determined by dividing the applicable original issue price by the applicable conversion price, as adjusted for any anti-dilution adjustments. The Company's redeemable convertible preferred stock was convertible into the Company's shares of common stock on a one-for-one basis.

Prior to the issuance of Series C redeemable convertible preferred stock in April 2020, shares of redeemable convertible preferred stock would automatically be converted into shares of common stock at the then effective conversion price for such share, immediately prior to either: (i) the completion of an underwritten public offering of the Company's common stock at a price of at least 1.5 times the original Series B issuance price for any initial public offering consummated at any time prior to the first anniversary of the Series B original issuance date, or 1.25 times the original Series B issuance price for any such IPO thereafter and that provides at least $30.0 million of gross proceeds to the Company or (ii) the conversion by the holders of redeemable convertible preferred stock, which requires the vote of the holders of a majority of the then outstanding shares of redeemable convertible preferred stock, voting together as a single class on an as-converted to common stock basis.

After the issuance of the Series C redeemable convertible preferred stock in April 2020, shares of redeemable convertible preferred stock would automatically be converted into shares of common stock at the then effective conversion price for such share, immediately prior to either: (i) the completion of an underwritten public offering of the Company's common stock at a price of at least 1.25 times the original Series C issuance price, as adjusted for any stock splits, stock dividends, combinations, subdivisions, recapitalizations or the like that provides at least $50.0 million of gross proceeds to the Company or (ii) the conversion by the holders of redeemable convertible preferred stock, which requires the vote of the holders of a majority of the then outstanding shares of redeemable convertible preferred stock voting together as a single class on an as-converted to common stock basis; provided, however that any automatic conversion of the Series C and Series B redeemable convertible preferred stock under (ii) shall require the consent of the holders of a majority of Series C and Series B redeemable convertible preferred stock then outstanding voting together as a single class on an as-converted to common stock basis.

Dividends—The redeemable convertible preferred stock dividends were not cumulative and were payable only when declared by the board of directors. No such dividends were declared. Such dividends were in preference to any dividends to holders of common stock.

Voting Rights—Each holder of redeemable convertible preferred stock would be entitled to the number of votes equal to the number of shares of common stock into which the shares of redeemable convertible preferred stock held by such holder could be converted as of the record date.

Redemption and Balance Sheet Classification—The redeemable convertible preferred stock was recorded in mezzanine equity because while it was not mandatorily redeemable, it would become redeemable at the option of the stockholders upon the occurrence of a deemed liquidation event that was considered not solely within the Company's control.

Funding Agreement with CFF —In April 2020, CFF made a $10.0 million investment in the Company's Series C redeemable convertible preferred stock financing. In return for the investment, CFF received shares of Series C redeemable convertible preferred stock, and the Company and CFF entered into a Funding Agreement ("the Funding Agreement"). Pursuant to the terms of the Funding Agreement, except in the event of a technical failure, the $10.0 million received from CFF will be used to advance the development program for 4D-710, the Company's lead product in cystic fibrosis, or any other therapeutic approved by the Program Advisory Group ("PAG") to alleviate pulmonary complications of cystic fibrosis ("the Funding Agreement Product"). CFF is committed to provide an additional $4.0 million of funding upon acceptance of an Investigational New Drug application or its equivalent to allow for human testing of the Funding Agreement Product ("Acceptance"), except in the event of a change of control transaction occurring prior to Acceptance or Acceptance occurring after April 29, 2026. At the time of Acceptance, CFF will receive shares of common stock priced at the 10-day average reported closing price of the Company's common stock on the date of Acceptance.

Except in the event of a technical failure, the Company is committed to providing an amount equal to the funding provided by CFF to be used solely to advance the Funding Agreement Product. A technical failure is defined as a determination by the Company, after consultation with and approval of the PAG that (i) the Funding Agreement Product has failed to reach its intended endpoints due to safety issues, lack of sufficient transgene expression and/or efficacy, each despite commercially reasonable efforts and (ii) the exercise of further commercially reasonable efforts is unlikely to correct such failure. Under the terms of the Funding Agreement, neither the $10.0 million investment in the Series C redeemable convertible preferred stock, which converted to common stock as of December 31, 2020, nor the $4.0 million of funding upon Acceptance are restricted as to withdrawal or usage.

11. Common Stock

As of each of December 31, 2020 and 2019, the Company's certificate of incorporation authorized the Company to issue 300,000,000 and 50,000,000 shares of common stock, respectively, at the par value of $0.0001 per share. The holder of each share of common stock is entitled to one vote per share.

Common stockholders are entitled to dividends if and when declared by the board of directors, subject to the prior rights of the redeemable preferred stockholders. As of December 31, 2020 and 2019, no dividends on common stock had been declared by the board of directors.

As of December 31, 2020 and 2019, the Company has reserved common stock, on an as-converted basis, for future issuance as follows:

	December 31, 2020	December 31, 2019
Conversion of redeemable convertible preferred stock	—	7,375,631
Issuance of common stock under the 2015 Equity Incentive Plan	—	125,353
Issuance of common stock under the 2020 Equity Incentive Plan	2,606,546	—
Issuance of common stock under the Employee Stock Share Purchase Plan	252,337	—
Exercise of options issued and outstanding	3,194,113	2,474,152
Exercise of common stock warrants	98,669	68,669
Total common stock reserved	6,151,665	10,043,805

Restricted Common Stock

During 2015, the Company issued common stock to the Company founders of 4,710,060 shares, of which 4,473,374 were fully vested upon issuance. The remainder were deemed to be restricted based on their vesting conditions. The stock agreement contains certain provisions that allow the Company to repurchase unvested portions of stock from such founders in the event they depart from the Company. The repurchase rights on the restricted common stock lapsed over time and fully expired in March 2019. As of December 31, 2020 and 2019, no shares of restricted common stock remained subject to repurchase.

12. Stock-based Compensation

2020 Incentive Award Plan

In December 2020, the Company adopted the 2020 Incentive Award Plan (“2020 Plan”), which became effective on December 10, 2020. The 2020 Plan initially reserved 2,606,546 shares of common stock for the issuance of stock options, stock appreciation rights, restricted stock awards, restricted stock units, performance bonus awards, performance stock units, dividend equivalents or other stock or cash based award granted to employees, directors and consultants of the Company. All options are exercisable over a period not to exceed the contractual term of ten years from the date the stock options were issued. As of December 31, 2020, there were 2,606,546 shares available for grant under the 2020 Plan.

Following the effectiveness of the 2020 Plan, the Company will not make any further grants under the 2015 Equity Incentive Plan (the “2015 Plan”). However, the 2015 plan continues to govern the terms of options that remain outstanding under the 2015 Plan.

2015 Equity Incentive Plan

The 2015 Plan provided for grants of stock options, stock appreciation rights, restricted stock and restricted stock unit awards to employees, directors and consultants of the Company. As of December 31, 2020, options to purchase 3,194,113 shares of common stock were outstanding under the 2015 Plan. All options are exercisable over a period not to exceed the contractual term of ten years from the date the stock options were issued and are granted at prices not less than the estimated fair market value of the Company’s common stock on the grant date as determined by the board of directors. If an individual owns stock representing more than 10% of the Company’s outstanding shares, the exercise price of each share shall be at least 110% of the fair market value on the date of grant.

No additional grants will be made under the 2015 Plan, and all outstanding grants under the 2015 Plan that are repurchased, forfeited, expire or are cancelled will become available for grant under the 2020 Plan in accordance with its terms.

Employee Stock Purchase Plan

In December 2020, the Company adopted the 2020 Employee Stock Purchase Plan (the "2020 ESPP"). Under the 2020 ESPP, 252,337 shares of our common stock were initially reserved for employee purchases of our common stock under terms and provisions established by the Board of Directors and approved by our stockholders. Under the 2020 ESPP our employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value of the stock at the beginning of the offering period or at the end of each applicable purchase period. The 2020 ESPP provides for a series of overlapping 24-month offering periods comprising of four six-month purchase periods. The initial offering period under the ESPP will be longer than 24 months, commencing February 15, 2021 and ending on May 14, 2023. Contributions under the 2020 ESPP are limited to a maximum of 15% of an employee's eligible compensation.

Stock Options

The following table summarizes the stock options activity:

		Options Outstanding			
	Number of Shares Available for Grant	Number of Shares Underlying Outstanding Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balances at December 31, 2019	125,353	2,474,152	$ 6.77	8.46	$ 19,974
Options authorized	3,468,198	—	—		
Options granted	(1,321,743)	1,321,743	16.83		
Options exercised	—	(267,044)	3.21		10,212
Options expired	103,637	(103,637)	6.24		
Options forfeited	231,101	(231,101)	9.51		
Balances at December 31, 2020	2,606,546	3,194,113	$ 11.05	$ 8.46	$ 97,105
Shares exercisable, December 31, 2020		1,207,394	$ 6.24	$ 7.36	$ 42,515
Shares vested and expected to vest, December 31, 2020		3,194,113	$ 11.05	$ 8.46	$ 97,105

The following table is a summary of stock compensation expense for employees and nonemployees by function (in thousands):

	Year Ended December 31, 2020	Year Ended December 31, 2019
Research and development	$ 2,670	$ 2,191
General and administrative	2,314	1,350
Total stock-based compensation	$ 4,984	$ 3,541

During the years ended December 31, 2020 and 2019, the Company granted 1,267,743 and 1,101,840 stock options to employees with a weighted-average grant date fair value of $11.84 and $8.46 per share, respectively, and 54,000 and 35,000 stock options to nonemployees with a weighted-average grant date fair value of $11.05 and $8.43 per share, respectively. The total fair value of options vested during the years ended December 31, 2020 and 2019 was $5.0 million and $2.2 million, respectively. As of December 31, 2020, the unrecognized stock-based compensation of unvested options was $19.4 million and is expected to be recognized over a weighted-average period of 3.1 years.

Stock-based compensation expense recorded for employee options was $4.6 million and $2.8 million for the years ended December 31, 2020 and 2019, respectively. Stock-based compensation expense recorded for nonemployee consultants was $0.4 million and $0.7 million for the years ended December 31, 2020 and 2019, respectively.

Prior to the Company's IPO, the fair value of the shares of common stock underlying the stock options was estimated by the board of directors at various dates considering the Company's most recently available third-party valuations of common stock as well as a number of objective and subjective factors including valuation of comparable companies, sales of redeemable convertible preferred stock, operating and financial performance and general and industry specific economic outlook, amongst other factors. The fair value was determined in accordance with the guidance provided by the American Institute of Certified Public Accountants' Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Subsequent to the Company's IPO, the fair value of the Company's common stock is determined based on its closing market price.

The Company estimates the fair value of employee and nonemployee stock options using the Black-Scholes valuation model. The fair value of employee and nonemployee stock options is recognized on a straight-line basis over the requisite service period of the awards. The fair value of the Company's stock options was estimated using the following assumptions for the years ended December 31, 2020 and 2019.

	Year Ended December 31, 2020		Year Ended December 31, 2019	
	Employee	**Nonemployee**	**Employee**	**Nonemployee**
Expected term	5.5 –6.3 years	6.0 years	5.5 –6.3 years	6.1 –10.0 years
Expected volatility	82.1% – 83.8%	82.1% – 83.1%	81.9% – 83.0%	81.3% – 83.7%
Risk-free interest rate	0.4% – 0.7%	0.4% – 0.7%	1.5% – 2.3%	1.4% – 2.4%
Expected dividend yield	0%	0%	0%	0%

Expected Term. The expected term for employee options is calculated using the simplified method as the Company does not have sufficient historical information to provide a basis for estimate. The simplified method is based on the average of the vesting tranches and the contractual life of each grant. The expected term for nonemployee options is the contractual term of the options.

Expected Volatility. The expected volatility was estimated based on a study of publicly traded peer companies as the Company did not have sufficient trading history for its common stock. The Company selected the peer group based on similarities in industry, stage of development, size and financial leverage with the Company's principal business operations. For each grant, the Company measured historical volatility over a period equivalent to the expected term.

Risk-free Interest Rate. The risk-free interest rate is based on the yield available on U.S. Treasury zero-coupon issues whose term is similar in duration to the expected term of the respective stock option.

Expected Dividend Yield. The Company has not paid and does not anticipate paying any dividends on its common stock in the future. Accordingly, the Company has estimated the dividend yield to be zero.

13. Common Stock Warrants

In 2016, the Company issued a warrant for 45,000 shares of the Company's common stock to a service provider with an exercise price of $1.14 per share, of which 15,000 warrant shares become exercisable upon completion of an offering of securities in a private placement by the Company with net proceeds in excess of $25.0 million and 30,000 warrant shares become exercisable upon completion of an IPO by the Company. The warrant expires in 2023. As the services had been completed at the date the warrant had been issued, the fair value of the warrant was determined at the issuance date. 15,000 of these warrant shares became exercisable upon the completion of the Series B financing in 2018 and 30,000 of these warrants became exercisable upon completion of the IPO in 2020. The Company recorded less than $0.1 million fair value of these warrant shares, as determined under the Black-Scholes Model, within operating expenses in the statements of operations and comprehensive loss and within additional paid-in-capital in the balance sheets during the year ended December 31, 2018 and December 31, 2020.

In May 2018, the Company issued a warrant for 23,669 shares of the Company's common stock to a service provider with an exercise price of $3.19 per share and recorded $0.1 million within in additional paid-in-capital upon issuance of the warrant. The warrant expires in 2025.

In 2020, the Company issued a warrant for 30,000 shares of the Company's common stock to a service provider with an exercise price of $18.00 per share. This warrant vests over a period of four years and expires in 2027. The fair value of the warrant was determined at the issuance date using the Black-Scholes Model. In 2020, an expense of less than $0.1 million was recorded within operating expenses in the statements of operations and comprehensive loss and within additional paid-in-capital in the balance sheets in connection with the vested portion of warrant shares.

14. Net Loss Per Share Attributable to Common Stockholders

The following table sets forth the computation of basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data):

	Year Ended December 31, 2020	Year Ended December 31, 2019
Numerator		
Net loss attributable to common stockholders	$ (56,693)	$ (49,306)
Denominator		
Weighted-average shares outstanding	6,430,555	5,143,776
Less: Weighted-average shares subject to repurchase used in computing net loss per share attributable to common stockholders, basic and diluted	—	(1,216)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	6,430,555	5,142,560
Net loss per share attributable to common stockholders—basic and diluted	$ (8.82)	$ (9.59)

The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common stockholders for the period presented because including them would have been antidilutive:

	December 31, 2020	December 31, 2019
Redeemable convertible preferred stock	—	7,375,631
Options to purchase common stock	3,194,113	2,474,152
Common stock warrants	98,669	68,669
Total	3,292,782	9,918,452

15. Derivative Liability

The Company identified an embedded derivative resulting from the change of control provision in the CFF Agreement. Embedded derivatives that are required to be bifurcated from the underlying host instrument are accounted for and valued as separate financial instruments. At the inception of the derivative in 2017, the Company recognized this derivative as a liability and revenue was reduced by the initial fair value of the derivative liability. The Company remeasures the derivative liability to fair value at each reporting period and records the change in fair value of the derivative liability as other income (expense), net. The Company uses a present value analysis with multiple scenarios, which incorporates assumptions and estimates to value the derivative instrument. The Company assesses these assumptions and estimates on a periodic basis as additional information impacting the assumptions is obtained. Estimates and assumptions impacting the fair value measurement include the change of control payment to CFF (range of $0 to $10.6 million at December 31, 2020), the probability of a change of control event, the probability of the product achieving development or commercial status at time of change of control (range of 3.4% to 12.3% at December 31, 2020) and the discount rate (14% at December 31, 2020). The Company determined the estimated fair value of this liability as of the inception date of the CFF Agreement and concluded that the amount was immaterial. The Company determined the fair value of this derivative liability was $0.1 million as of December 31, 2020 and 2019.

16. Related Party Transactions

In August 2019, the Company and uniQure entered into the amended uniQure Agreement and the Second uniQure Agreement. Under these agreements, the Company agreed to transfer incremental rights and services to uniQure in exchange for uniQure eliminating the exclusivity clause in the uniQure Agreement and transferring other rights back to the Company. Further details and the accounting for these agreements is discussed in Note 6. As of June 17, 2020, uniQure is no longer a related party of the Company.

As of December 31, 2019, Pfizer owned 1,474,992 shares of the Company's redeemable convertible preferred stock and had a representative director on the Company's board of directors. In April 2020, as part of Series C Preferred Stock Purchase Agreement, Pfizer acquired 166,666 shares of the Company's redeemable convertible preferred stock. On December 11, 2020 upon completion of the IPO, Pfizer's 1,641,658 shares of redeemable convertible preferred stock were converted into 1,641,658 shares of common stock. Pfizer also acquired additional 25,000 shares of common stock at $23.00 per share during the IPO. As of December 31, 2020, Pfizer owns 1,666,658 shares of common stock and has a representative director on the Company's board of directors.

In the years ended December 31, 2020 and 2019, the Company paid $93,000 and $52,000, respectively, to David Schaffer, PhD, the co-founder and Chief Scientific Advisor of the Company for consulting services. In April 2019, the Company entered into two sponsored research agreements ("SRAs") with the UC Regents to conduct research in a research facility on the Berkeley campus, under the direction of Dr. Schaffer. The SRAs have a three year term ending in May 2022. Under the SRAs, the Company has an option to license (on a royalty-bearing basis) all intellectual property generated under

the SRAs. The total amount the Company is committed to pay to the UC Regents under the SRAs is $1.5 million, of which $1.0 million and $0.4 million was paid as of December 31, 2020 and 2019, respectively. In the years ended December 31, 2020 and 2019, the Company recorded $0.5 million and $0.3 million, respectively, of expense related to SRAs. As of December 31, 2020 and 2019, accounts payable related to the SRAs was $0.2 million and $0.3 million, respectively. Any patent prosecution costs incurred under the SRAs will also be borne by the Company. The Company can terminate the SRAs for convenience and without cause with 60 days' notice.

In 2016, the Chief Executive Officer and several other employees of the Company founded Ignite Immunotherapy ("Ignite"). From 2016 through October 2019, the Company's Chief Executive Officer served as the Chief Executive Officer and Executive Chairman of Ignite and certain executives of the Company held ownership interests in Ignite and were members of the board of directors of Ignite. Additionally, during this time period, Pfizer, which is a related party of the Company, held a significant equity stake in Ignite. There were no transactions between the Company and Ignite from 2016 to October 2019. As of October 18, 2019, Ignite was no longer a related party of the Company.

17. 401(k) Plan

In 2014, the Company adopted a 401(k) plan for all employees who have met certain eligibility requirements. The 401(k) plan allows employees to make pre-tax and post-tax contributions up to the maximum allowable amount set by the Internal Revenue Service. The Company made contributions to the Plan for eligible participants, and recorded contribution expenses of $0.4 million and $0.3 million for the years ended December 31, 2020 and 2019, respectively.

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2020, 4D Molecular Therapeutics, Inc. had one class of common stock registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation, our amended and restated bylaws, the amended and restated investors' rights agreement to which we and certain of our stockholders are parties, and the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws, and amended and restated investors' rights agreement, each of which is incorporated herein by reference as an exhibit to the Annual Report on Form 10-K filed with the Securities and Exchange Commission, of which this Exhibit 4.1 is a part.

Authorized Capital Stock

Our authorized capital stock consists of 300,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. Unless our board of directors determines otherwise, we will issue all shares of our capital stock in uncertificated form.

Common Stock

As of December 31, 2020, there were 93 holders of record of our common stock.

Voting Rights

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. In addition, the affirmative vote of holders of 66 2/3% of the voting power of all of the then outstanding voting stock will be required to take certain actions, including amending certain provisions of our amended and restated certificate of incorporation, such as the provisions relating to amending our amended and restated bylaws, the classified board and director liability.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely

affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are fully paid and nonassessable.

Redeemable Convertible Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control or other corporate action. As of December 31, 2020, no shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Registration Rights

Under our amended and restated investors' rights agreement, based on the number of shares outstanding as of December 31, 2020, the holders of 11.6 million shares of our common stock, or their transferees, have the right to require us to register their shares under the Securities Act of 1933 (the "Securities Act") so that those shares may be publicly resold, and the holders of 11.6 million shares of our common stock, or their transferees, have the right to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

Based on the number of shares outstanding as of December 31, 2020, the holders of 11.6 million shares of our common stock (on an as-converted basis), or their transferees, were entitled to certain demand registration rights. Beginning 180 days following our initial public offering completed December 11, 2020, the holders of at least 50% of these shares can, on not more than two occasions, request that we register all or a portion of their shares if the aggregate price to the public of the shares offered is at least $30.0 million (before deductions of underwriters' commissions and expenses). Additionally, we will not be required to effect a demand registration during the period beginning 60 days prior to the filing and ending 180 days following the effectiveness of a company-initiated registration statement relating to an initial public offering of our securities.

Piggyback Registration Rights

Based on the number of shares outstanding as of December 31, 2020, in the event that we determine to register any of our securities under the Securities Act (subject to certain exceptions), either for our own account or for the account of other security holders, the holders of 11.6 million shares of our common stock (on an as-converted basis), or their transferees, will be entitled to certain "piggyback" registration rights allowing the holders to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to employee benefit plans, the offer and sale of debt securities, or corporate reorganizations or certain other transactions, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration. In an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to exclude or limit the number of shares such holders may include.

Form S-3 Registration Rights

Based on the number of shares outstanding as of December 31, 2020, the holders of 11.6 million shares of our common stock (on an as-converted basis), or their transferees, will be entitled to certain Form S-3 registration rights. The holders of at least 30% of the registrable securities then outstanding of these shares can make a written request that we register their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least $5.0 million (before deductions of underwriters' commissions and expenses). These stockholders may make an unlimited number of requests for registration on Form S-3, but in no event shall we be required to file more than two registrations on Form S-3 in any given twelve-month period.

Expenses of Registration

We will pay the registration expenses of the holders of the shares registered pursuant to the demand, piggyback and Form S-3 registration rights described above, including the expenses in an amount not to exceed $25,000 of one special counsel for the selling holders.

Expiration of Registration Rights

The demand, piggyback and Form S-3 registration rights described above will expire, with respect to any particular stockholder, upon the earlier of five years after the consummation of our initial public offering or when that stockholder can sell all of its shares under Rule 144 of the Securities Act during any three-month period (and without the requirement for us to be in compliance with the current public information required under Section c(1) of Rule 144 of the Securities Act).

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation, Our Amended and Restated Bylaws and Delaware Law

Certain provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly-held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by our board of

directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock will make it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management.

Special Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called at any time by our board of directors, or our President or Chief Executive Officer, but such special meetings may not be called by our stockholders or any other person or persons.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of our board of directors.

Stockholder Action by Written Consent

Our amended and restated certificate of incorporation and our amended and restated bylaws do not provide for the right of stockholders to act by written consent without a meeting.

Classified Board; Election and Removal of Directors; Filling Vacancies

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of our common stock outstanding will be able to elect all of our directors. Our amended and restated certificate of incorporation provides for the removal of any of our directors only for cause and requires a stockholder vote by the holders of at least a 66 2/3% of the voting power of the then outstanding voting stock. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board of directors, may only be filled by a resolution of our board of directors unless our board of directors determines that such vacancies shall be filled by our stockholders. This system of electing and removing directors and filling vacancies may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Choice of Forum

Our amended and restated certificate of incorporation and amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: any derivative action or proceeding brought on our behalf; any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers or stockholders to us or to our stockholders; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws (as either may be amended from time to time); or any action asserting a claim against us that is governed by the internal affairs doctrine. As a result, any action brought by any of our stockholders with regard to any of these matters will need to be filed in the Court of Chancery of the State of Delaware and

cannot be filed in any other jurisdiction; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act. Nothing in our amended and restated certificate of incorporation and amended and restated bylaws preclude stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

If any action the subject matter of which is within the scope described above is filed in a court other than a court located within the State of Delaware, or a Foreign Action, in the name of any stockholder, such stockholder shall be deemed to have consented to the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to enforce the applicable provisions of our amended and restated certificate of incorporation and amended and restated bylaws and having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the Foreign Action as agent for such stockholder. Although our amended and restated certificate of incorporation and amended and restated bylaws contain the choice of forum provision described above, it is possible that a court could find that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder.

Amendment of Charter Provisions

The amendment of any of the above provisions in our amended and restated certificate of incorporation, except for the provision making it possible for our board of directors to issue undesignated preferred stock, would require approval by a stockholder vote by the holders of at least a 66 2/3% of the voting power of the then outstanding voting stock.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Limitations of Liability and Indemnification Matters

Our amended and restated certificate of incorporation contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;

- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or

- any transaction from which the director derived an improper personal benefit.

Each of our amended and restated certificate of incorporation and amended and restated bylaws provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws also obligate us to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damages.

Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "FDMT."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-251370) of 4D Molecular Therapeutics, Inc. of our report dated March 25, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 25, 2021

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULES 13a-14(a) AND
15d-14(a) UNDER THE EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David Kirn, certify that:

1. I have reviewed this Annual Report on Form 10-K of 4D Molecular Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. [Reserved];

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 25, 2021

4D MOLECULAR THERAPEUTICS, INC.

By: /s/ David Kirn
David Kirn
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO EXCHANGE ACT 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

I, August J. Moretti, certify that:

1. I have reviewed this Annual Report on Form 10-K of 4D Molecular Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. [Reserved];

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 25, 2021

4D MOLECULAR THERAPEUTICS, INC.

By: /s/ August Moretti

August J. Moretti
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K (the "Annual Report") of 4D Molecular Therapeutics, Inc. (the "Company") for the year ended December 31, 2020, David Kirn, as Chief Executive Officer of the Company, and August J. Moretti, as Chief Financial Officer of the Company, each hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

a) the Company's Annual Report for the year ended December 31, 2020 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

b) the information contained in such Annual Report fairly presents, in all material respects, the financial condition and results of operations of 4D Molecular Therapeutics, Inc.

Dated: March 25, 2021

By: /s/ David Kirn
David Kirn
Chief Executive Officer
(Principal Executive Officer)

Dated: March 25, 2021

By: /s/ August J. Moretti
August J. Moretti
Chief Financial Officer
(Principal Financial and Accounting Officer)