Confidential Draft Submission No. 2 submitted to the Securities and Exchange Commission on August 30, 2019. This draft registration statement has not been filed publicly with the Securities and Exchange Commission and all information contained herein remains confidential.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

4D Molecular Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**2836**	**47-3506994**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

5858 Horton Street #455
Emeryville, California 94608
(510) 505-2680
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

David Kirn, M.D.
Chairman and Chief Executive Officer
5858 Horton Street #455
Emeryville, California 94608
(510) 505-2680
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting 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 to Section 7(a)(2)(B) of the Securities Act. ☐

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	**Proposed maximum aggregate offering price(1)**	**Amount of registration fee(2)**
Common Stock, $0.0001 par value per share	$	$

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended. Includes shares that the underwriters have the option to purchase.
(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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Subject to Completion, Dated , 2019

Shares

4DMT

Common Stock

This is the initial public offering of shares of common stock of 4D Molecular Therapeutics, Inc. We are offering shares of our common stock.

Prior to this offering, there has been no public market for our common stock. It is currently estimated that the initial public offering price will be between $ and $ per share.

We intend to apply to list our common stock on The Nasdaq Global Market under the symbol “DDDD.”

We are an “emerging growth company” as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements in this prospectus and may elect to do so in future filings.

See the section titled “Risk Factors” beginning on page 13 to read about factors you should consider before deciding to invest in shares of our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to 4D Molecular Therapeutics, Inc.	$	$

(1) See the section titled “Underwriting” for a description of the compensation payable to the underwriters.

To the extent that the underwriters sell more than shares of common stock, the underwriters have an option to purchase up to an additional shares from us at the initial public offering price, less the underwriting discounts and commissions.

The underwriters expect to deliver the shares against payment in New York, New York on , 2019.

Goldman Sachs & Co. LLC **Evercore ISI** **William Blair**

Chardan

Prospectus dated , 2019.

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We and the underwriters have not authorized anyone to provide you any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: we have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

4D Molecular Therapeutics™, Therapeutic Vector Evolution™, and our logo are some of our trademarks and tradenames used in this prospectus. This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this prospectus may appear without the ® and ™ symbol, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before deciding to invest in our common stock, you should read this entire prospectus carefully, including the sections of this prospectus titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes included elsewhere in this prospectus. Unless the context otherwise requires or as otherwise noted, references in this prospectus to the “company,” “4D Molecular Therapeutics,” “4DMT,” “we,” “us” and “our” refer to 4D Molecular Therapeutics, Inc.

4D Molecular Therapeutics, Inc.

Overview

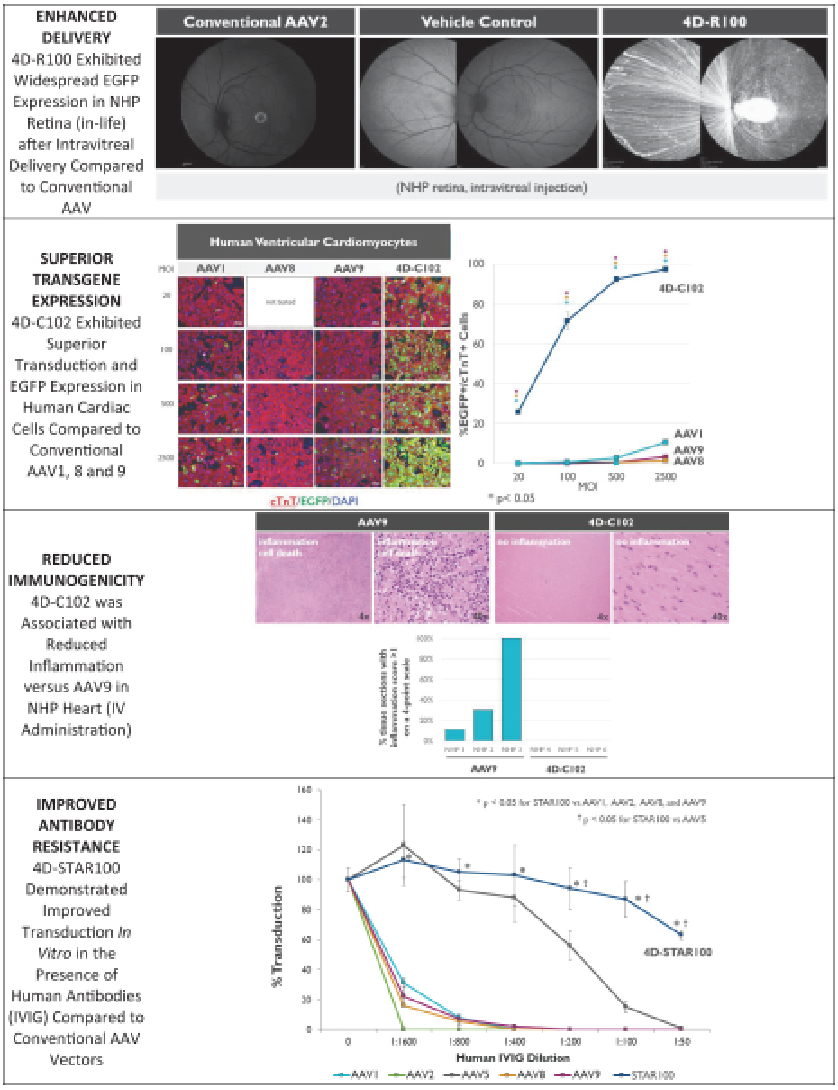
We are a development stage precision gene therapy company dedicated to pioneering the development of targeted therapies based on our next-generation AAV vectors. Our proprietary Therapeutic Vector Evolution platform enables our “disease first” approach to product discovery and development, thereby allowing us to customize our AAV vectors to target specific tissue types associated with the underlying disease. Our proprietary AAV vectors are designed to provide targeted delivery by routine clinical routes, efficient transduction, reduced immunogenicity and resistance to pre-existing antibodies, which we believe will enable us to develop gene therapies that could overcome known limitations of conventional AAVs. As a result, we believe these key attributes will enable us to develop gene therapies with improved therapeutic profiles, pursue previously untreatable diseases and address a broad range of rare and large market diseases.

Our product candidates that are in or have completed Investigational New Drug (IND)-enabling studies include a wholly-owned asset in development for the treatment of Fabry disease, as well as two assets in ophthalmology. In ophthalmology, our product candidate for the treatment of X-linked Retinitis Pigmentosa (XLRP) is wholly-owned subject to an exclusive option for Roche to develop and commercialize the asset, and our product candidate for the treatment of Choroideremia is licensed to Roche. In addition, our wholly-owned product candidate for the treatment of Cystic Fibrosis has completed lead optimization and we expect to initiate IND-enabling studies in the first half of 2020. We expect to initiate our first clinical trials in 2020. We also have a pipeline of product candidates in the lead optimization stage, including for the treatment of Duchenne Muscular Dystrophy (DMD) and Wet Age-Related Macular Degeneration (Wet AMD).

Our Therapeutic Vector Evolution Platform

While gene therapy holds tremendous promise as a transformative therapeutic class, the majority of gene therapeutic approaches utilize naturally-occurring or conventional AAV vectors that have encountered limitations such as high dose requirements, limited efficacy, inflammation and toxicity, and neutralization by pre-existing antibodies. As a result of these shortcomings, current efforts with conventional AAV vectors have focused on diseases in which a surgical technique is used for direct cell access such as subretinal injection for the retina, or a low level of gene expression may be sufficient for patient benefit, such as Hemophilia A or B treatment. Rather than using conventional AAV vectors for our products, we instead take a “disease first” approach by creating proprietary customized AAV vectors for each disease through our Therapeutic Vector Evolution platform. Our Therapeutic Vector Evolution platform is based on directed evolution, a high-throughput biological engineering and screening approach harnessing the power of natural selection to identify novel AAVs with desirable characteristics.

As of August 1, 2019, we have a total of 37 distinct libraries with an estimated over one billion vector sequences. We select customized AAVs based on the Target Vector Profile (TVP) for the disease, and we subsequently characterize each lead vector through extensive studies in non-human primates (NHPs) and proprietary human cell and organotypic tissue assays. Based on our preclinical data to date from NHPs and human cell models, including preclinical head-to-head comparisons with conventional AAVs, we observed that our precision gene therapy AAVs were well-tolerated and achieved enhanced delivery, increased transgene expression, reduced immunogenicity and/or improved antibody resistance when compared to conventional AAVs. Our preclinical data comparing vectors carrying and expressing a marker *GFP* transgene is summarized in the table below.



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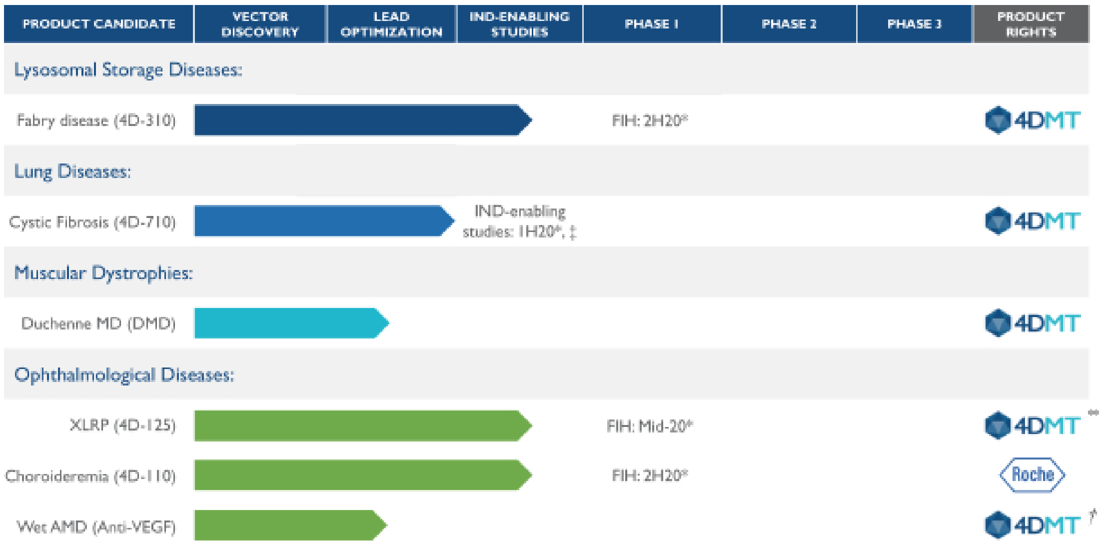
Our Pipeline

Our initial focus is on developing a broad pipeline of transformative gene therapy product candidates designed to treat patients suffering from lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological diseases. We are developing a diverse pipeline of wholly-owned and partnered programs for both rare and large market diseases. We have not conducted any clinical trials but we expect to initiate our first clinical trials by the middle of 2020. We believe our AAV products are modular, in that a single vector can be armed with different transgene payloads in order to treat multiple diseases within the same tissue types or therapeutic areas. Our pipeline is represented in the diagram below.



* *Expected timing of milestone. FIH refers to first-in-human, Phase 1 or Phase 1/2, clinical studies.*

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

† *We are independently optimizing lead assets in this field. If we elect to declare product candidates in the field specified in our collaboration and license agreement with Roche, Roche could exercise the option to license, further develop and commercialize this product candidate at any time prior to pivotal trial initiation. See the section titled "Business—Strategic Collaborations—Collaboration and License Agreement with F. Hoffman Ltd. and Hoffman-La Roche Inc." for further information.*

‡ *Proof of concept studies for 4D-710 were conducted in a pig model of Cystic Fibrosis and utilized a species-specific (i.e., pig-specific) vector rather than the primate-specific 4D-A101 vector, which is the vector for Cystic Fibrosis product candidate 4D-710.*

Lysosomal Storage Diseases

Our lead product candidate in lysosomal storage diseases, 4D-310, is wholly-owned and under development for the treatment of Fabry disease. Fabry disease affects at least 5,000 people in the United States and is progressive and fatal with cardiac complications being the leading cause of death. 4D-310 uses a proprietary vector designed for efficient, low dose intravenous delivery to cardiac and other relevant tissues and to have minimal toxicities, and potential resistance to pre-existing antibodies in the human population. The approved enzyme replacement therapies (ERT) reportedly do not adequately address Fabry cardiomyopathy, a leading cause of death in this disease. In 2019, we intend to advance 4D-310 to IND-enabling pharmacology and Good Laboratory Practices (GLP) toxicology and biodistribution studies. 4D-310 Phase 1/2 clinical trial initiation is planned for the second half of 2020. We expect initial human safety and biomarker data by .

Lung Diseases

Our lead product candidate in the lung therapeutic area, 4D-710, is wholly-owned and under development for the aerosol treatment of Cystic Fibrosis lung disease. Cystic Fibrosis is the most fatal inherited disease affecting more than 70,000 patients worldwide. 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, hospitalizations and eventual end stage respiratory failure. We produced 4D-710 using a proprietary vector designed for efficient aerosol delivery to the lung airway, with enhanced penetration through mucus, efficient airway cell transduction and transgene expression, and resistance to pre-existing antibodies in the patient population. While several products have been approved for Cystic Fibrosis, they fall short of restoring normal lung function in most patients, and these chronic therapies require daily dosing for the patient's lifetime. Additionally, approximately 10% of patients remain without a treatment option. We expect to initiate IND-enabling study activities with 4D-710 in the first half of 2020.

Muscular Dystrophies

We are currently in the lead optimization phase for our wholly-owned research candidates for the treatment of certain muscular dystrophies, including DMD. DMD, a progressive and fatal muscular-wasting disease, is one of the most prevalent rare genetic diseases, with an estimated prevalence between 10,000 to 15,000 cases in the United States. Our product candidates are engineered from proprietary vectors designed for efficient, low dose intravenous delivery to cardiac and skeletal muscle tissues with minimal toxicities, and potential resistance to pre-existing antibodies in the human population. Several companies are developing gene therapies for DMD using conventional AAVs. While early clinical data in some programs have been encouraging, AAV gene therapies using conventional AAV vectors have been subject to inflammation-related toxicity issues and manufacturing challenges. In addition to requiring high doses, patients have been excluded from clinical trials due to pre-existing antibodies. We expect to complete lead optimization in the first half of 2020.

Ophthalmological Diseases

We have two ophthalmology product candidates that utilize our proprietary intravitreal vector for rare monogenic blinding diseases: 4D-125 in development for the treatment of XLRP and 4D-110 in development for the treatment of Choroideremia. Our proprietary vector for these ophthalmological diseases is designed for intravitreal injection, potentially leading to transgene expression across the surface area of the retina. We have a broad partnership in ophthalmology with Roche, excluding DNA-directed RNA interference (ddRNAi) delivery. The partnership includes an option for Roche to license 4D-125 in XLRP, as well as other ophthalmology product candidates we may declare, prior to pivotal trial initiation. 4D-125 is expected to begin clinical trials in mid-2020. We expect initial human safety and biomarker data for 4D-125 by . In addition, Roche currently holds a license to 4D-110 in Choroideremia. We expect to initiate 4D-110 clinical trials in the second half of 2020.

We are currently in lead optimization for multiple product candidates that utilize our proprietary intravitreal vector for the treatment of Wet AMD, each of which is engineered to express a different protein to neutralize vascular endothelial growth factor (VEGF). We expect to complete lead optimization in the first half of 2020.

Manufacturing

Our team has extensive experience with the manufacturing and analytical testing of numerous unique AAV capsids. To date, our team has internally manufactured approximately 50 unique AAV vector capsids, including both proprietary evolved 4DMT capsid variants and naturally-occurring capsids. Our team has manufactured over 100 total lots of AAV vectors. This total includes 9 lots of material for GLP toxicology and biodistribution studies. We plan to initiate our first in-house manufacturing run for clinical trial material for use in patients, according to current Good Manufacturing Practices (cGMP), in 2019.

Our Team

We have an experienced team of biotherapeutics developers, innovative gene therapy scientists and clinicians to execute our strategy. Led by our Chief Executive Officer and co-founder, David Kirn, M.D., 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. Our Chief Technical Officer and Head of Regulatory and Quality, Fred Kamal, Ph.D., has over 20 years of industry experience in product manufacturing and quality, including most recently with AveXis where he was a key contributor to the development and writing of the quality and manufacturing sections of the biologics license application (BLA) for the AAV product Zolgensma. Our Chief Scientific Advisor and co-founder, David Schaffer, Ph.D., pioneered the application of directed evolution to the capsid of AAV vectors over 15 years ago.

Our Investors

We have raised $108.6 million from the sale and issuance of our preferred stock to leading investors including Viking Global Investors, Janus Henderson Investors, The Biotechnology Value Fund, Arrowmark Partners, Pfizer Ventures, Mirae Asset Financial Group, Perceptive Advisors, Ridgeback Capital Investments, Pappas Capital and Chiesi Ventures.

Our Strategy

To achieve our goal of unlocking the full potential of gene therapy for many patient populations, we strive to achieve the following:

- Develop transformative precision gene therapies using the power of directed evolution and our “disease first” approach.
- Design, develop and commercialize a diverse portfolio of product candidates in a broad range of therapeutic areas for both rare and large market diseases.
- Continue to expand our cGMP manufacturing capabilities.
- Protect, defend and expand our intellectual property portfolio of proprietary AAV vectors discovered through directed evolution or Therapeutic Vector Evolution.
- Selectively partner with leading pharmaceutical companies to harness the full potential of our platform while retaining product rights in key markets, and work closely with patient advocacy groups to inform our programs.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section titled "Risk Factors," immediately following this prospectus summary. These risks include the following, among others:

- We are in the early stages of drug development, and we 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 incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.
- Even if this offering is successful, we will require substantial additional capital to finance our operations. If we fail or 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, future commercialization efforts or other operations.
- All of our product candidates are based on a novel AAV gene therapy technology with which there is limited regulatory and no clinical experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.
- 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.

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. Our website address is www.4dmoleculartherapeutics.com. The information on, or that can be accessed through, our website is not part of this prospectus. We have included our website address as an inactive textual reference only.

Implications of Being an Emerging Growth Company

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). 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 this offering, (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 Securities Exchange Act of 1934, as amended (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, plus unaudited 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 prospectus and that we provide to our investors in the future may be different than what you might receive from other public reporting companies.

THE OFFERING

Common stock offered by us	shares.
Underwriters' option to purchase additional shares from us	We have granted the underwriters a 30-day option to purchase up to additional shares of our common stock.
Common stock to be immediately outstanding after the offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares in full, assuming an initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We currently expect to use the net proceeds from this offering to fund the ongoing and planned preclinical and clinical development of our product candidates, further the development and expansion of our pipeline, the continued expansion of our manufacturing and research and development capabilities and the remainder for working capital and general corporate purposes. See the section titled "Use of Proceeds" for a more complete description of the intended use of proceeds from this offering.
Risk factors	See the section titled "Risk Factors" and other information included in this prospectus for a discussion of factors that you should consider carefully before deciding to invest in our common stock.
Proposed Nasdaq Global Market trading symbol	"DDDD."

The number of shares of our common stock to be outstanding after this offering is based on 12,516,975 shares of our common stock (including our redeemable convertible preferred stock on an as-converted basis) outstanding as of June 30, 2019, and excludes:

- 2,192,230 shares of our common stock issuable upon the exercise of stock options to purchase common stock that were outstanding as of June 30, 2019, with a weighted-average exercise price of $6.10 per share;
- 68,669 shares of our common stock issuable upon the exercise of outstanding warrants with weighted-average exercise price of $1.85 per share;

- 399,886 shares of our common stock reserved for issuance pursuant to future awards under our 2015 Equity Incentive Plan (the Plan) and associated amendments as of June 30, 2019;
- shares of our common stock reserved for issuance pursuant to future awards under our 2019 Equity Incentive Award Plan (the 2019 Plan), as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering; and
- shares of our common stock reserved for issuance pursuant to future awards under our 2019 Employee Stock Purchase Plan (the ESPP), as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering.

In addition, unless we specifically state otherwise, all information in this prospectus reflects and assumes the following:

- a -for- forward stock split of our capital stock to be effected prior to the effectiveness of the registration statement of which this prospectus is a part;
- the conversion of 7,375,631 shares of our outstanding redeemable convertible preferred stock as of June 30, 2019 into an equivalent number of shares of our common stock immediately prior to the completion of this offering;
- the filing and effectiveness of our amended and restated certificate of incorporation in Delaware and the adoption of our amended and restated bylaws, each of which will occur immediately prior to the completion of this offering;
- no exercise of outstanding stock options or warrants described above; and
- no exercise of the underwriters' option to purchase additional shares of our common stock.

Unless otherwise specified and unless the context otherwise requires, we refer to our Series A, Series A-1 and Series B redeemable convertible preferred stock collectively as, redeemable convertible preferred stock in this prospectus, as well as for financial reporting purposes and in the financial tables included elsewhere in this prospectus, as more fully explained in Note 10 to our financial statements included elsewhere in this prospectus.

Summary Financial Data

The following tables summarize our financial data for the periods and as of the dates indicated. We derived the summary statements of operations and comprehensive loss data for the years ended December 31, 2017 and 2018 and the summary balance sheet data as of December 31, 2018 from our audited financial statements included elsewhere in this prospectus. We derived the summary statements of operations and comprehensive loss data for the six months ended June 30, 2018 and 2019 and the summary balance sheet data as of June 30, 2019 from our unaudited interim financial statements that are included elsewhere in this prospectus. Our unaudited interim financial statements are prepared in accordance with U.S. generally accepted accounting principles (GAAP) on the same basis as our audited financial statements and include, in the opinion of management, all adjustments, consisting of normal recurring adjustments, that are necessary for the fair statement of the financial information set forth in those financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future and our historical results for the six months ended June 30, 2019 are not necessarily indicative of the results that may be expected for the remainder of 2019.

You should read this data together with our financial statements and related notes included elsewhere in this prospectus and the information under the sections titled "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year Ended December 31,		Six Months Ended June 30,	
	2017	2018	2018	2019
	(in thousands, except share and per share data)			
Revenue:				
Collaboration and research revenue, related parties	$ 3,176	$ 5,143	$ 143	$ 26
Collaboration and research revenue	2,614	8,987	4,926	4,390
Total revenue	5,790	14,130	5,069	4,416
Operating expenses:				
Research and development	13,573	18,362	8,208	16,985
General and administrative	3,489	6,167	2,198	4,884
Total operating expenses	17,062	24,529	10,406	21,869
Loss from operations	(11,272)	(10,399)	(5,337)	(17,453)
Other income (expense):				
Interest income	89	850	147	945
Other income (expense), net	(40)	(2)	4	(8)
Total other income (expense)	49	848	151	937
Net loss and comprehensive loss	$ (11,223)	$ (9,551)	$ (5,186)	$ (16,516)
Net loss per share attributable to common stockholders, basic and diluted(1)	(2.27)	(1.89)	(1.03)	(3.22)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted(1)	4,953,419	5,049,203	5,021,003	5,132,714
Pro forma net loss per share, basic and diluted(1)				
Weighted-average shares outstanding used in computing pro forma net loss per share, basic and diluted(1)				

(1) See Notes 2 and 14 to our financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders, pro forma net loss per share, and the weighted-average number of shares of our common stock used in the computation of the per share amounts.

	As of June 30, 2019		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)(3)
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 72,869	$	$
Working capital(4)	66,842		
Total assets	80,500		
Redeemable convertible preferred stock	102,980		
Accumulated deficit	(46,235)		
Total stockholders' (deficit) equity	(42,304)		

(1) The pro forma column in the balance sheet data table above gives effect to (i) the conversion of 7,375,631 shares of our outstanding redeemable convertible preferred stock as of June 30, 2019 into an equivalent number of shares of our common stock immediately prior to the completion of this offering; and (ii) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur, in each case, immediately prior to the completion of this offering.

(2) The pro forma as adjusted column in the balance sheet data table above gives effect to (i) the pro forma adjustments set forth in footnote (i) above and (ii) the sale and issuance of shares of our common stock in this offering, assuming an initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, would increase or decrease, as applicable, each of the amount of our cash and cash equivalents, working capital, total assets and total stockholders' (deficit) equity by $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discount and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million in the number of shares we are offering would increase or decrease, as applicable, each of the amount of our cash and cash equivalents, working capital, total assets and total stockholders' (deficit) equity by approximately $ million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

(4) We define working capital as current assets less current liabilities. See our financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

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 prospectus, including our financial statements and the related notes and the section of this prospectus titled "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.

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 development-stage biopharmaceutical company specializing in the development of novel, precision AAV vectors, for gene therapies that are generated through our proprietary directed evolution platform. 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. We expect to begin our first clinical trial in the middle of 2020. If our product candidates are not successfully developed and approved, we may never generate any revenue. To date, we have not initiated or 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 incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred net losses in each reporting period since our inception, including net losses of $11.2 million and $9.6 million for the years ended December 31, 2017 and 2018, respectively. As of June 30, 2019, we had an accumulated deficit of $46.2 million.

We have devoted substantially all of our financial resources and efforts in 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;
- 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; and
- defend against any product liability claims or other lawsuits related to our products.

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.

Even if this offering is successful, we will require substantial additional capital to finance our operations. If we fail or 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, future commercialization efforts or other operations.

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, payments pursuant to our collaboration agreements. We expect to initiate clinical trials in the middle of 2020 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 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 additional funding beyond the net proceeds of this offering.

As of June 30, 2019, we had $72.9 million in cash and cash equivalents. Based on our current operating plan, we estimate that our existing cash and cash equivalents, together with the anticipated net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next months. Our estimate as to how long we expect our existing cash and cash equivalents to be available to fund our operations is based on assumptions that may prove inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. 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 significantly 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 or 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 lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological 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 all 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.

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 no clinical experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

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 products 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 have a negative impact on our business and financial condition.

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;
- 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;
- 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 future 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.

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. To date, neither we nor our collaborators have initiated any clinical trials for any product candidates. We cannot guarantee that any clinical trials will be initiated or conducted as planned or completed on schedule, if at all. For example, we delayed the initiation of our planned first-in-human trial of 4D-110 until the second half of 2020 after the batch of 4D-110 produced by our contract manufacturer failed to meet the specifications required for use in our planned clinical trial. 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;

- 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 raises 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.

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 studies, or may result in findings in our clinical studies that do not reach levels of statistical significance sufficient for marketing approval.

Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. 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 studies from reaching statistical significance or otherwise meeting their specified endpoints, which could require us to conduct additional clinical studies, 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.

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;
- 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 studies 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 studies 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 adversely affect our viability. 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, 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 studies 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.

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 clinical development 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 additional funding beyond the net proceeds of this offering 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 us.

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 Fabry disease, Cystic Fibrosis, XLRP and Choroideremia. 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 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 lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological diseases areas include large companies with significant financial resources, such as Allergan, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda and Vertex, and biopharmaceutical companies such as Avrobio, Freeline, Sangamo and Sarepta. In addition to competition from other companies targeting lysosomal storage, lung, muscular dystrophy and ophthalmologic indications, 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 lysosomal storage, lung, muscular dystrophy and ophthalmologic 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;
- 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.

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.

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 Paragon and Wuxi, 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, recently 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. As a result, we delayed the initiation of our planned first-in-human trial of 4D-110 until the second half of 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 agreements with Paragon or WuXi 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 current 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 for our second manufacturing facility in Emeryville, California, at which we plan to devote manufacturing activities for our clinical studies. 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 initiate our planned clinical studies. 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 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.

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 studies;
- 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.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also increase the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would seriously harm 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. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could seriously harm our business.

We have received orphan drug designation for 4D-110 for the treatment of Choroideremia, 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. 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. While the Texas District Court Judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

Since the enactment of the Tax Cuts and Jobs Act of 2017, there have been additional amendments to certain provisions of the ACA, and we expect the current Trump administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. It is uncertain the extent to which any such changes may harm 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 2027 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, our financial operations.

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. The Trump administration's budget proposals for fiscal years 2019 and 2020 contains further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of prescription drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services (HHS) has started soliciting feedback on some of these measures and, at the same time, is implementing others under its existing authority. While some measures 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.

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.

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.

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.

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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy and security of individually identifiable health information of covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers as well as their business associates, independent contractors of a covered entity that perform certain

services involving the use or disclosure of individually identifiable health information on their behalf;

- 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;
- 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; state and local laws requiring the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- similar healthcare laws and data protection laws in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information, such as the General Data Protection Regulation (GDPR), which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Economic Area (the EEA) and the United Kingdom (including health data).

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 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.

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 have a significant impact on 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 and radioactive 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.

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

Our research programs involve the use of hazardous materials and chemicals, which are currently only handled by third parties. 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 GCPs 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.

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 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, 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.

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 issues 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. 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, 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 in patent claims being narrowed, invalidated or held unenforceable, 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 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 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 and results of operations will be adversely affected.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be 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 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 is 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 The Regents of the University of California (the UC Regents) 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 suffer 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.

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 prospectus, 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.

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.

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.

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 US 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.

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. 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 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 restricted stock and 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 may 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 June 30, 2019, we had 57 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, the most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or international trade disputes could also strain our suppliers, some of which are located outside of the United States, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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

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

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.

Despite the implementation of security measures, 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 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 may 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 have a material adverse effect on our operations, financial performance and 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 imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. 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 takes 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 EU data subjects. 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.

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 adversely affect our business and results of operations.

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 and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. We have experienced ownership changes in the past. We may also experience ownership changes as a result of this offering or as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our pre-change net operating loss carryforwards 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 if we do not attain profitability sufficient to offset our available NOLs prior to their 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 This Offering and Ownership of Our Common Stock

We do not know whether an active market will develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of our common stock at an attractive price, or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors including those identified in this "Risk Factors" section, the price of our common stock may fall.

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

The initial public offering price for our common stock was determined through negotiations with the underwriters. This initial public offering price may differ from the market price of our common stock after the offering. As a result, you may not be able to sell your common stock at or above the initial public offering price. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- 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. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. 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 do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock could decrease. Even if we do obtain analyst coverage, 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. After this offering and after giving effect to the conversion of 7,375,631 outstanding shares of our redeemable convertible preferred stock into an equivalent number of   shares of our common stock immediately prior to the completion of this offering, we will have   shares of our common stock outstanding based on   shares of our common stock outstanding as of June 30, 2019. Of these shares, the   shares we are selling in this offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining   shares, or   % of our outstanding shares after this offering, 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 180 days after the date of this prospectus. Goldman Sachs & Co. LLC 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). See the section of this prospectus titled "Shares Eligible for Future Sale" for additional information.

Moreover, after this offering, holders of an aggregate of   shares of our common stock will 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 also plan to register all shares of our common stock that we may issue under our equity compensation plans. Once we register these shares, they 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 the section of this prospectus titled “Underwriters.” 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 will continue to have substantial influence over us after this offering, which could limit your ability to affect the outcome of key transactions, including a change of control.

After this offering, our directors, executive officers, holders of more than 5% of our outstanding stock and their respective affiliates will beneficially own shares representing approximately % of our outstanding common stock. 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 as a result of the reduced disclosure and governance requirements applicable to emerging growth 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 this offering, (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.

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 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.

After this offering, we will be 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 Market or other adverse consequences that would seriously harm our business.

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

The initial public offering price of our common stock is substantially higher than the pro forma net tangible book value per share of our common stock before giving effect to this offering. Accordingly, if you purchase our common stock in this offering, you will incur immediate substantial dilution of approximately $ per share, based on an assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, and our pro forma net tangible book value as of June 30, 2019. In addition, following this offering, purchasers in this offering will have contributed approximately   % of the total gross consideration paid by stockholders to us to purchase shares of our common stock, through June 30, 2019, but will own only approximately   % of the shares of our common stock outstanding immediately after this offering. Furthermore, if the underwriters exercise their option to purchase additional shares, or outstanding options and warrants are exercised, you could experience further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section titled “Dilution.”

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the uses of the majority of the net proceeds we will receive from this offering. Our management will have broad discretion in the application of the net proceeds, including for any of the purposes described in the section of this prospectus titled “Use of Proceeds.” Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could seriously harm our business. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Delaware law and provisions in our certificate of incorporation and bylaws that will become effective upon the closing of this offering might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our certificate of incorporation and bylaws that will become effective upon the closing of this offering may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents will:

- 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 couple 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 will 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 to be effective immediately prior to the completion of this offering and our indemnification agreements that we have entered into with our directors and officers will 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 our amended and restated bylaws will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and our amended and restated bylaws will provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a 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 Securities Act or 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. Nothing in our amended and restated bylaws precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

We believe these provisions may benefit us by providing increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. 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. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation 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.

We could be subject to securities class action litigation.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus 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 planned 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-710;
- the timing and success of lead optimization for our product candidates in lead optimization, including our product candidates for the treatment of DMD;
- 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 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, AstraZeneca 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;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- our anticipated use of the proceeds from this offering; and
- other risks and uncertainties, including those listed under the section titled "Risk Factors."

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 prospectus 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 prospectus. 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 prospectus. 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 prospectus. See the section titled "Where You Can Find More Information."

INDUSTRY AND MARKET DATA

This prospectus contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates, including data regarding the estimated patient population and market size for our product candidates, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

USE OF PROCEEDS

We estimate that the net proceeds from the issuance and sale of shares of our common stock in this offering will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares from us in full, based on the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, would increase or decrease, as applicable, the net proceeds to us from this offering by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same, and after deducting underwriting discounts and commissions. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares we are offering would increase or decrease, as applicable, the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, by approximately $ million, assuming the assumed initial public offering price stays the same. We do not expect that a change in the initial price to the public or the number of shares by these amounts would have a material effect on the uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

The principal purposes of this offering are to obtain additional capital to support our operations, to create a public market for our common stock and to facilitate our future access to the public equity markets. We intend to use the net proceeds from this offering, together with our cash and cash equivalents, as follows:

- approximately $ million to fund the ongoing and planned preclinical and clinical development of our product candidates, including the initiation of our planned Phase 1/2 clinical trial for 4D-310 and IND-enabling study activities for 4D-710, as well as the initiation of Phase 1 clinical trials for 4D-125 and 4D-110;
- approximately $ million to fund the further development and expansion of our pipeline including to complete lead optimization for our research candidates for the treatment of DMD and to complete toxicology studies for our research candidates for the treatment of Wet AMD;
- approximately $ million to fund the continued expansion of our manufacturing and research and development capabilities; and
- any remaining amounts for working capital and general corporate purposes.

Based on our current operating plan, we estimate that our current cash and cash equivalents, together with the anticipated net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next months.

The amounts and timing of our actual expenditures and the extent of our research and development activities may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from any preclinical or clinical trials we may commence in the future, our ability to take advantage of expedited programs or to obtain regulatory approval for any other product candidates we may identify and pursue, the timing and costs associated with the manufacture and supply of any other product candidates we may identify and pursue for clinical development or commercialization, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

We may also use a portion of the remaining net proceeds and our existing cash and cash equivalents to in-license, acquire, or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above.

Pending their use, we intend to invest the net proceeds of this offering in a variety of capital-preservation investments, including short and intermediate-term, interest-bearing, investment-grade securities, and government securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of June 30, 2019:

- on an actual basis;
- on a pro forma basis to give effect to: (i) the conversion of 7,375,631 shares of our outstanding redeemable convertible preferred stock as of June 30, 2019 into an equivalent number of shares of our common stock immediately prior to the completion of this offering, and (ii) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur, in each case, immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to sale and issuance of shares of our common stock in this offering, assuming an initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our financial statements and related notes included elsewhere in this prospectus and the information set forth in the sections titled "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of June 30, 2019		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
	(in thousands, except share and per share amounts)		
Cash and cash equivalents	$ 72,869	$	$
Redeemable convertible preferred stock, $0.0001 par value: 7,375,638 shares authorized; 7,375,631 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma or pro forma as adjusted	$102,980	$	$
Stockholders' (deficit) equity:			
Common stock, $0.0001 par value: 50,000,000 shares authorized; 5,141,344 shares issued and outstanding, actual; shares authorized, pro forma and pro forma as adjusted; shares issued and outstanding, pro forma; shares issued and outstanding, pro forma as adjusted	1		
Additional paid-in capital	3,930		
Accumulated deficit	(46,235)		
Total stockholders' (deficit) equity	(42,304)		
Total capitalization	$ 60,676	$	$

(1) Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, would increase or decrease, as applicable, each of the amount of our cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity and total capitalization by approximately $, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million in the number of shares offered by us would increase or decrease, as applicable, each of the amount of our cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity and total capitalization by approximately $, assuming the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, remains the same, and after deducting the estimated

underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

If the underwriters' exercise their option to purchase additional shares from us in full, our pro forma as adjusted cash and cash equivalents, and total capitalization as of June 30, 2019, would be $ million and $ million, respectively.

The number of shares of our common stock issued and outstanding, pro forma and pro forma as adjusted in the table above is based on 12,516,975 shares of our common stock (including our redeemable convertible preferred stock on an as-converted basis) outstanding as of June 30, 2019, which excludes:

- 2,192,230 shares of our common stock issuable upon the exercise of stock options to purchase common stock that were outstanding as of June 30, 2019, with a weighted-average exercise price of $6.10 per share;
- 68,669 shares of our common stock issuable upon the exercise of outstanding warrants with a weighted-average exercise price of $1.85 per share;
- 399,886 shares of our common stock reserved for issuance pursuant to future awards under our the Plan and associated amendments as of June 30, 2019;
- shares of our common stock reserved for issuance pursuant to future awards under our 2019 Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering; and
- shares of common stock reserved for issuance pursuant to future awards under our ESPP, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering.

DILUTION

If you invest in our common stock in this offering, your interest will be immediately diluted to the extent of the difference between the initial public offering price per share of our common stock in this offering and the pro forma as adjusted net tangible book value per share of our common stock immediately after the completion of this offering.

As of June 30, 2019, our historical net tangible book value (deficit) was $(42.7) million, or $(8.30) per share of our common stock. Our historical net tangible book value (deficit) per share represents total tangible assets less total liabilities and redeemable convertible preferred stock divided by the number of shares of our common stock outstanding on June 30, 2019.

Our pro forma net tangible book value as of June 30, 2019, before giving effect to this offering, was $ million, or $ per share of our common stock. Pro forma net tangible book value represents our historical net tangible book value (deficit), before the issuance and sale of shares in this offering, and gives effect to the conversion of 7,375,631 shares of our outstanding redeemable convertible preferred stock as of June 30, 2019 into an equivalent number of shares of our common stock immediately prior to the completion of this offering.

Our pro forma as adjusted net tangible book value represents our pro forma net tangible book value, plus the effect of the sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We determine dilution per share to investors participating in this offering by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by investors participating in this offering.

The following table illustrates this per share dilution:

Assumed initial public offering price per share		$
Historical net tangible book value (deficit) per share as of June 30, 2019	$(8.30)	
Pro forma increase in historical net tangible book value (deficit) per share		
Pro forma net tangible book value per share as of June 30, 2019		
Increase in pro forma net tangible book value per share attributable to new investors		
Pro forma as adjusted net tangible book value per share		
Dilution per share to new investors participating in this offering		$

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, would increase or decrease, as applicable, our pro forma as adjusted net tangible book value as of June 30, 2019 after this offering by approximately $ million, or approximately $ per share, and would decrease or increase dilution to investors in this offering by approximately $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares we are offering would increase or decrease, as applicable, our pro forma as adjusted net tangible book value as of June 30, 2019 after this offering by approximately $ million, or approximately $ per share, and would decrease or increase, as applicable, dilution to investors in this offering by approximately $ per share, assuming the assumed initial public offering price per share remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

If the underwriters fully exercise their option to purchase additional shares, pro forma as adjusted net tangible book value after this offering would increase to approximately $ per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors purchasing shares in this offering would be $ per share.

To the extent that outstanding options with an exercise price per share that is less than the pro forma as adjusted net tangible book value per share are exercised, new investors will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

The following table shows, as of June 30, 2019, on a pro forma as adjusted basis, the number of shares of our common stock purchased from us, the total consideration paid to us and the average price paid per share by existing stockholders and by new investors purchasing common stock in this offering, assuming an initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us (in thousands, except share and per share amounts and percentages):

	Shares Purchased		Total Consideration		Weighted-Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
New investors participating in this offering					$
Total		100%	$	100%	

If the underwriters were to fully exercise their option to purchase additional shares of our common stock from us, the percentage of shares of our common stock held by existing investors would be %, and the percentage of shares of our common stock held by new investors would be %.

The foregoing tables and calculations (other than the historical net tangible book value calculations) are based on 12,516,975 shares of our common stock (including our redeemable convertible preferred stock on an as-converted basis) outstanding as of June 30, 2019, which excludes:

- 2,192,230 shares of our common stock issuable upon the exercise of stock options to purchase common stock that were outstanding as of June 30, 2019, with a weighted-average exercise price of $6.10 per share;
- 68,669 shares of our common stock issuable upon the exercise of outstanding warrants with a weighted-average exercise price of $1.85 per share;
- 399,886 shares of our common stock reserved for issuance pursuant to future awards under our the Plan and associated amendments as of June 30, 2019;

- shares of our common stock reserved for issuance pursuant to future awards under our 2019 Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering; and
- shares of common stock reserved for issuance pursuant to future awards under our ESPP, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering.

To the extent that outstanding options or warrants are exercised, new options or other securities are issued under our equity incentive plans, or we issue additional shares of our common stock in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED FINANCIAL DATA

The following tables present our selected financial data for the periods and as of the dates indicated. We derived the selected statements of operations and comprehensive loss data for the years ended December 31, 2017 and 2018 and the selected balance sheet data as of December 31, 2018 from our audited financial statements included elsewhere in this prospectus. We derived the selected statements of operations and comprehensive loss data for the six months ended June 30, 2018 and 2019 and the selected balance sheet data as of June 30, 2019 from our unaudited interim financial statements that are included elsewhere in this prospectus. Our unaudited interim financial statements are prepared on the same basis as our audited financial statements and include, in the opinion of management, all adjustments, consisting of normal recurring adjustments, that are necessary for the fair statement of the financial information set forth in those financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future and our historical results for the six months ended June 30, 2019 are not necessarily indicative of the results that may be expected for the remainder of 2019. You should read this data together with our financial statements and related notes included elsewhere in this prospectus and the information under the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year Ended December 31,		Six Months Ended June 30,	
	2017	2018	2018	2019
	(in thousands, except share and per share data)			
Revenue:				
Collaboration and research revenue, related parties	$ 3,176	$ 5,143	$ 143	$ 26
Collaboration and research revenue	2,614	8,987	4,926	4,390
Total revenue	5,790	14,130	5,069	4,416
Operating expenses:				
Research and development	13,573	18,362	8,208	16,985
General and administrative	3,489	6,167	2,198	4,884
Total operating expenses	17,062	24,529	10,406	21,869
Loss from operations	(11,272)	(10,399)	(5,337)	(17,453)
Other income (expense):				
Interest income	89	850	147	945
Other income (expense), net	(40)	(2)	4	(8)
Total other income (expense)	49	848	151	937
Net loss and comprehensive loss	$ (11,223)	$ (9,551)	$ (5,186)	$ (16,516)
Net loss per share attributable to common stockholders, basic and diluted(1)	(2.27)	(1.89)	(1.03)	(3.22)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted(1)	4,953,419	5,049,203	5,027,197	5,132,714
Pro forma net loss per share, basic and diluted(1)				
Weighted-average shares outstanding used in computing pro forma net loss per share, basic and diluted(1)				

(1) See Notes 2 and 14 to our financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders, pro forma net loss per share, and the weighted-average number of common shares used in the computation of the per share amounts.

	December 31, 2018	June 30, 2019
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 91,761	$ 72,869
Working capital[1]	86,014	66,842
Total assets	96,969	80,500
Accumulated deficit	(30,026)	(46,235)
Total stockholders' deficit	(27,587)	(42,304)

(1) We define working capital as current assets less current liabilities. See our financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

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 related notes thereto included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the section titled "Risk Factors", our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. All amounts are expressed in thousands other than share and per share amounts. Please also see the section of this prospectus titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a development stage precision gene therapy company dedicated to pioneering the development of targeted therapies based on our next-generation AAV vectors. Our proprietary Therapeutic Vector Evolution platform enables our "disease first" approach to product discovery and development, thereby allowing us to customize our AAV vectors to target specific tissue types associated with the underlying disease. Our proprietary AAV vectors are designed to provide targeted delivery by routine clinical routes, efficient transduction, reduced immunogenicity and resistance to pre-existing antibodies, which we believe will enable us to develop gene therapies that could overcome known limitations of conventional AAVs. As a result, we believe these key attributes will enable us to develop gene therapies with improved therapeutic profiles, pursue previously untreatable diseases and address a broad range of rare and large market diseases.

Our product candidates that are in or have completed IND-enabling studies include a wholly-owned asset in development for the treatment of Fabry disease, as well as two assets in ophthalmology. In ophthalmology our product candidate for the treatment of XLRP is wholly-owned, subject to an exclusive option for Roche to develop and commercialize the asset, and our product candidate for the treatment of Choroideremia is licensed to Roche. In addition, our wholly-owned product candidate for the treatment of Cystic Fibrosis has completed lead optimization and we expect to initiate IND-enabling studies in the first half of 2020. We have not conducted any clinical trials to date but we expect to enter clinical trials for multiple of these programs in 2020. We also have a pipeline of product candidates in the lead optimization stage, including for the treatment of DMD and Wet AMD.

We do not have any products approved for sale and have not generated any revenue from product sales since our inception. From inception through June 30, 2019, we funded our operations primarily with an aggregate of $108.6 million in gross cash proceeds primarily from the sale and issuance of redeemable convertible preferred stock and to a lesser extent from cash received from our collaboration and license agreements. As of June 30, 2019, we had cash and cash equivalents of $72.9 million. Based on our current operating plan, we estimate that our cash and cash equivalents, together with the anticipated net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next   months.

Since our inception in September 2013, we have devoted substantially all of our resources to discovering and developing product candidates and manufacturing processes, building our Therapeutic Vector Evolution platform and assembling our core capabilities in drug development for genetic therapies.

Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates. Until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of our current product candidates or delay our efforts to advance and expand our product pipeline.

We have incurred significant operating losses to date and expect that our operating losses will increase significantly as we 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; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, upon the completion of this offering we expect to incur additional costs associated with operating as a public company.

Our net losses were $11.2 million, $9.6 million, $5.2 million and $16.5 million for the years ended December 31, 2017 and 2018 and the six months ended June 30, 2018 and 2019, respectively. As of June 30, 2019, we had an accumulated deficit of $46.2 million. We do not expect positive cash flows from operations in the foreseeable future. We expect to continue to incur net operating losses for at least the next several years as we advance our product candidates through clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization, continue our research and development efforts and invest in our manufacturing facility.

Components of Results of Operations

Revenue

Our revenue to date has been generated through payments from our collaboration and license agreements, primarily from upfront payments and expense reimbursement. We have not generated any revenue from the sale of approved products and do not expect to do so in the near future.

In 2018 we recognized $14.1 million of revenue from our collaboration and license agreements, principally from our agreements with Roche, Pfizer and AstraZeneca (previously MedImmune). For the six months ended June 30, 2019, we recognized $4.4 million of revenue, principally from our agreements with Roche and AstraZeneca (previously MedImmune).

- We expect payments from Roche for reimbursement of our internal and third-party costs as well as the recognition of the $21.0 million upfront payment received in 2017 to be our principal source of revenue in the second half of 2019. Upon initiation of our Phase 1/2 clinical trial for 4D-110 to treat Choroideremia, we expect to receive certain milestone payments. We expect this trial to initiate in the second half of 2020. If Roche continues the development of 4D-110, we will be entitled to further development and approval milestones, and, if the product candidate is approved, royalties on net sales and sales based milestones. Roche also has the option to assume the development and commercialization of 4D-125 to treat XLRP prior to pivotal trial initiation in return for an option payment and assumption of all future expenses. If Roche exercises such option, we would be entitled to future milestones upon development of the product candidate and, if approved, royalties on future net sales and sales based milestones.
- Pfizer terminated our agreement in 2018, and as a result we recognized $5.0 million of revenue in 2018 that we had previously deferred. We do not expect to recognize any revenue from Pfizer in 2019.

- AstraZeneca (previously MedImmune) is evaluating the results of the development work we performed. If AstraZeneca (previously MedImmune) decides to continue the program, we will be entitled to an option fee, development milestones, and if the product candidate is approved, we will be entitled to royalties on net sales.

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 license revenue in the second half of 2019 will be primarily from Roche. If our agreement with Roche was terminated, it may materially impact the amount of license revenue we recognize in future periods.

Operating Expenses

Our operating expenses consist of research and development and general and administrative expenses. Personnel costs including salaries, benefits, bonuses and stock-based compensation expense, comprise a significant component of research and development and general and administrative expenses. We allocate indirect expenses associated with our facilities, information technology costs, depreciation and other overhead costs between research and development and general and administrative categories based on employee headcount and the nature of work performed by each employee.

Research and Development

Our research and development expenses primarily consist of costs incurred for the discovery and development of our product candidates, which include:

- salaries and personnel-related costs, including benefits, stock-based compensation and travel, for our scientific personnel performing research and development activities;
- costs related to executing preclinical studies and clinical trials, including payments to CROs;
- costs related to acquiring, developing and manufacturing materials for preclinical studies and clinical trials including payments to CMOs;
- costs related to laboratory supplies, research materials and other costs related to development and characterization of new AAV vectors;
- fees paid to consultants and other third-parties who support our product candidate development, including CROs, CMOs, and other service providers;
- other costs in seeking regulatory approval of our product candidates; and
- allocated facility-related 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, and 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.

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 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 in the future as we increase our headcount to support our continued research activities and development of our programs. We also expect 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 Six Months Ended June 30, 2018 and 2019

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

	Six Months Ended June 30, 2018	Six Months Ended June 30, 2019	$ Change	% Change
Revenue:				
Collaboration and license revenue, related party	$ 143	$ 26	$ (117)	(82%)
Collaboration and license revenue	4,926	4,390	(536)	(11%)
Total revenue	5,069	4,416	(653)	(13%)
Operating Expenses:				
Research and development	8,208	16,985	8,777	107%
General and administrative	2,198	4,884	2,686	122%
Total operating expenses	10,406	21,869	11,463	110%
Loss from operations	(5,337)	(17,453)	(12,116)	227%
Other Income (Expense)	151	937	786	521%
Net loss and comprehensive loss	$ (5,186)	$(16,516)	$(11,330)	218%

Revenue

Revenue decreased from $5.1 million for the six months ended June 30, 2018 to $4.4 million for the six months ended June 30, 2019. The decrease of $0.7 million, or 13%, was primarily due to the following:

- a $0.3 million decrease in revenue recognized under our Collaboration and License Agreement with Applied Genetic Technologies Corporation;
- a $0.2 million decrease in revenue recognized under our Collaboration and License Agreement with Roche for the development and treatment of various ophthalmology diseases;
- a $0.1 million decrease in revenue recognized under our Collaboration and License Agreement with uniQure; and
- a $0.1 million decrease in revenue recognized under our Collaboration and License Agreement with Benitec Biopharma Limited.

Research and Development Expenses

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

	Six Months Ended June 30, 2018	Six Months Ended June 30, 2019	$ Change	% Change
External expenses	$4,415	$ 9,599	$ 5,184	117%
Payroll and personnel expenses	2,177	5,236	3,059	141%
Other research and development expenses	1,616	2,150	534	33%
Total research and development expenses	$8,208	$16,985	$ 8,777	107%

Research and development expenses increased from $8.2 million for the six months ended June 30, 2018 to $17.0 million for the six months ended June 30, 2019. The increase of $8.8 million, or 107%, was primarily due to the following:

- a $5.2 million increase in external costs as we continue to develop novel vectors and identify potential product candidates and progress our preclinical studies; and
- a $3.1 million increase in payroll and personnel expenses due to increased headcount to support the development of our and our partners' product candidates.

General and Administrative Expenses

General and administrative expenses increased from $2.2 million for the six months ended June 30, 2018 to $4.9 million for the six months ended June 30, 2019. The increase of $2.7 million, or 122%, was primarily due to the following:

- a $1.3 million increase for personnel costs as a result of increased headcount of general and administrative personnel, including a $0.2 million increase in employee stock-based compensation expense; and
- a $0.9 million increase for professional services, including legal, accounting and other advisory services.

Other Income (Expense)

Other income (expense) increased from $0.2 million for the six months ended June 30, 2018 to $0.9 million for the six months ended June 30, 2019. The increase was due to increased interest income in 2019 as a result of investing the $84.5 million net proceeds from our Series B redeemable convertible preferred stock financing in August 2018.

Comparison of the Years Ended December 31, 2017 and 2018

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

	Year Ended December 31,			
	2017	2018	$ Change	% Change
Revenue:				
Collaboration and license revenue, related party	$ 3,176	$ 5,143	$ 1,967	62%
Collaboration and license revenue	2,614	8,987	6,373	244%
Total revenue	5,790	14,130	8,340	144%
Operating Expenses:				
Research and development	13,573	18,362	4,789	35%
General and administrative	3,489	6,167	2,678	77%
Total operating expenses	17,062	24,529	7,467	44%
Loss from operations	(11,272)	(10,399)	873	(8%)
Other Income (Expense)	49	848	799	1,631%
Net loss and comprehensive loss	$(11,223)	$ (9,551)	$ 1,672	(15%)

Revenue

Revenue increased from $5.8 million for the year ended December 31, 2017 to $14.1 million for the year ended December 31, 2018. The increase of $8.3 million, or 144%, was primarily due to the following:

- a $6.6 million increase in revenue recognized under our Collaboration and License Agreement with Roche for the development and treatment of various ophthalmology diseases;
- a $5.0 million increase in revenue recognized upon termination of our Collaboration and License Agreement with Pfizer. This amount represented recognition of the upfront payment previously made by Pfizer that we had deferred; and
- which were both partially offset by a $3.0 million decrease in revenue relating to our Collaboration and License Agreement with uniQure.

We do not expect to recognize any revenue from Pfizer or uniQure in 2019.

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,			
	2017	2018	$ Change	% Change
External expenses	$ 4,009	$ 9,740	$ 5,731	143%
Payroll and personnel expenses	4,302	4,960	658	15%
Other research and development expenses	5,262	3,662	(1,600)	(30%)
Total research and development expenses	$13,573	$18,362	$ 4,789	35%

Research and development expenses increased from $13.6 million for the year ended December 31, 2017 to $18.4 million for the year ended December 31, 2018. The increase of $4.8 million, or 35%, was primarily due to the following:

- a $5.7 million increase in external costs as we continue to develop novel vectors and identify potential product candidates and progress our preclinical studies;
- a $0.7 million increase in payroll and personnel expenses due to increased headcount to support the development of our and our partners' product candidates; and
- which were both partially offset by a $1.6 million decrease for other research and development expenses, primarily due to a $2.5 million decrease in stock-based compensation for uniQure, which was fully expensed in the first quarter of 2018. See Note 6 to our financial statements included elsewhere in this prospectus for further discussion of the stock options received from uniQure.

General and Administrative Expenses

General and administrative expenses increased from $3.5 million for the year ended December 31, 2017 to $6.2 million for the year ended December 31, 2018. The increase of $2.7 million, or 77%, was primarily due to the following:

- a $1.0 million increase for personnel costs as a result of increased headcount of general and administrative personnel, including a $0.2 million increase in employee stock-based compensation expense;

- a $0.9 million increase for professional services, including legal, accounting and other advisory services; and
- a $0.2 million increase for allocated overhead, including rent, equipment, depreciation, information technology costs and utilities.

Other Income (Expense)

Other income (expense) increased from less than $0.1 million for the year ended December 31, 2017 to $0.8 million for the year ended December 31, 2018. The increase was due to increased interest income in 2018 as a result of investing the $84.5 million net proceeds from our Series B redeemable convertible preferred stock financing in August 2018.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2018 and June 30, 2019, we had cash and cash equivalents of $91.8 million and $72.9 million, respectively. We primarily generate cash and cash equivalents from the sale of our equity securities, including from the sale of our Series B redeemable convertible preferred stock, and to a lesser extent from cash received from our collaboration and license agreements.

In August 2018, we completed the private offering of 5,154,632 shares of our Series B redeemable convertible preferred stock at a price of $17.46 per share. The net proceeds from the offering were $84.5 million.

Future Funding Requirements

We have incurred net losses since our inception and had an accumulated deficit of $46.2 million as of June 30, 2019. 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 do not expect to achieve such revenue and expect to continue to incur losses for the foreseeable future.

We expect that our current cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months from the date of this prospectus.

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 scope, progress, results and costs of vector discovery, laboratory testing, preclinical development and clinical trials for our and our collaboration partner's product candidates;
- the timing of enrollment, commencement and completion of our clinical trials;
- the costs associated with building additional laboratory and manufacturing capacity;
- the costs, timing and outcome of regulatory review of our product candidates;
- the cost of manufacturing our product candidates or any future product candidates and any products we successfully commercialize, including costs associated with building-out our manufacturing capabilities
- the costs of future product sales, medical affairs, marketing, manufacturing and distribution activities for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- any product liability or other lawsuits related to our product candidates;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the extent to which we acquire or in-license other technologies;
- the payment of milestone or royalty payments owed under our existing collaboration and licensing agreements;
- our current collaboration and licensing agreements remaining in effect and our collaboration partners adhering to the terms of such collaboration and licensing agreements;
- our ability to establish and maintain additional licensing agreements or collaborations on favorable terms, if at all; and
- the costs associated with being a public company.

Many of these factors are outside of our control. Developing novel vectors and identifying potential product candidates and conducting preclinical testing and clinical trials are time-consuming, expensive and uncertain processes that take years to complete, and we and our collaboration partners may never generate the necessary data or results required to obtain regulatory and marketing approval and achieve product sales. In addition, our and our collaboration partner's product candidates, if approved, may not achieve commercial success. Our product revenue, if any, and any commercial milestones or royalty payments under our collaboration agreements, will be derived from or based on sales of products that may not be commercially available for many years, if at all.

Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline. Adequate additional financing may not be available to us on acceptable terms, or at all. We also could be required to seek funds through arrangements with collaboration partners or otherwise that may require us to relinquish rights to our intellectual property or our product candidates or otherwise agree to terms unfavorable to us. See the section titled "Risk Factors" for additional risks associated with our substantial capital requirements.

Summary Statement of Cash Flows

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

	Year Ended December 31,		Six Months Ended June 30,	
	2017	2018	2018	2019
Net cash provided by (used in) operating activities	$ 8,237	$(16,252)	$(6,422)	$(17,168)
Net cash provided by (used in) in investing activities	7,675	(414)	(33)	(1,662)
Net cash provided by (used in) financing activities	16	84,577	20	(62)
Net increase in cash and cash equivalents	$15,928	$ 67,911	$(6,435)	$(18,892)

Net Cash Provided by (Used in) Operating Activities

Net cash used in operating activities was $17.2 million for the six months ended June 30, 2019. This was primarily due to net loss of $16.5 million and a decrease in deferred revenue of $2.7 million, which were partially offset by stock-based compensation expense of $1.5 million and depreciation and amortization expense of $0.4 million.

Net cash used in operating activities was $6.4 million for the six months ended June 30, 2018. This was primarily due to net loss of $5.2 million and a decrease in deferred revenue of $1.4 million.

Net cash used in operating activities was $16.3 million for the year ended December 31, 2018. This was primarily due to net loss of $9.6 million and a decrease in deferred revenue of $8.6 million, which were partially offset by stock-based compensation expense of $1.4 million and depreciation and amortization expense of $0.7 million.

Net cash provided by operating activities was $8.2 million for the year ended December 31, 2017. This was due to an increase in deferred revenue of $19.0 million, primarily due to a $21.0 million upfront payment from Roche in December 2017, which was partially offset by net loss of $11.2 million.

Net Cash Provided by (Used in) Investing Activities

Net cash used in investing activities was $1.7 million for the six months ended June 30, 2019, all of which was used to purchase property and equipment.

Net cash used in investing activities was less than $0.1 million for the six months ended June 30, 2018, all of which was used to purchase property and equipment.

Net cash used in investing activities was $0.4 million for the year ended December 31, 2018, all of which was used to purchase property and equipment.

Net cash provided by investing activities was $7.7 million for the year ended December 31, 2017, which was due to the maturity of $8.2 million of marketable securities, which was partially offset by $0.6 million used to purchase property and equipment.

Net Cash Provided by (Used in) Financing Activities

Net cash used in financing activities was $0.1 million for the six months ended June 30, 2019, which was primarily due to deferred financing costs.

Net cash provided by financing activities was less than $0.1 million for the six months ended June 30, 2018, all of which was due to the issuance of our common stock.

Net cash provided by financing activities was $84.6 million for the year ended December 31, 2018, which was primarily due to $84.5 million of net proceeds received from the issuance of our Series B redeemable convertible preferred stock in August 2018.

Net cash provided by financing activities was less than $0.1 million for the year ended December 31, 2017, which was primarily due to the issuance of our common stock.

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, 2018 (in thousands):

		Payments Due by Period			
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating lease payments	$13,527	$ 850	$3,532	$3,766	$ 5,379
Total contractual obligations	$13,527	$ 850	$3,532	$3,766	$ 5,379

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 new lease, which has a remaining cost of $4.2 million.

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 lease to December 31, 2029. We do not have to pay rent until December 2019. The annual rent for the additional space is approximately $1.0 million per annum and escalates at 3% annually. The incremental increase in the Second Lease cost per annum due to the Second Lease Amendment is not reflected in the above table.

Critical Accounting Policies and Significant Judgments and Estimates

This Management's Discussion and Analysis of Financial Condition and Results of Operations is based on our financial statements, which we have prepared in accordance with accounting principles generally accepted 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 and recently announced accounting pronouncements, including the expected impact of such pronouncements, are described in Note 2 to our financial statements included elsewhere in this prospectus. 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

Effective January 1, 2019, we adopted ASC 606, using the modified retrospective transition method. As a result, we changed our accounting policies for revenue recognition as detailed below.

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 relative to standalone 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.

Prior to the adoption of ASC 606 on January 1, 2019, we recognized revenue when all of the following criteria were met: persuasive evidence of an arrangement exists; transfer of technology has been completed or services have been rendered; the price to the customer is fixed or determinable and collectability is reasonably assured.

In arrangements involving the delivery of more than one element, each required deliverable was evaluated to determine whether it qualified as a separate unit of accounting. The determination was based on whether the deliverable had “standalone value” to the customer. If a deliverable did not qualify as a separate unit of accounting, it was combined with the other applicable undelivered item(s) within the arrangement and these combined deliverables were treated as a single unit of accounting.

The arrangement's consideration that was fixed or determinable was allocated to each separate unit of accounting based on the relative selling price methodology in accordance with the selling price hierarchy, which included vendor-specific objective evidence (VSOE) of selling price, if available, or third-party evidence of selling price if VSOE was not available, or the best estimate of selling price, if neither VSOE nor third-party evidence was available.

Payments or reimbursements for our research and development efforts for the arrangements where such efforts were considered as deliverables were recognized as the services were performed and were presented on a gross basis. When upfront payments were received and if there was no discernible pattern of performance, we recognized revenue ratably over the associated period of performance.

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

We use a fair value-based method to account for all stock-based compensation arrangements with employees 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.

We use a fair value-based method to account for stock-based compensation arrangements with non-employees. Our determination of fair value of stock options utilizes the Black-Scholes option pricing model. The compensation expense for these arrangements is subject to remeasurement until the related vesting conditions are met. We account for forfeitures as they occur for both employees and non-employees.

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. The expected term for nonemployee options is the contractual term of the options.
- *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 any 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 , 2019, the unrecognized stock-based compensation expense related to stock options was $ million and is expected to be recognized as expense over a weighted-average period of approximately years. The intrinsic value of all outstanding stock options as of , 2019 was approximately $ million, based on the assumed initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, of which approximately $ million related to vested options and approximately $ million relate to invested options.

Common Stock Valuations

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 input from management. All options to purchase shares of our common stock are 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.

In the absence of a public trading market for our common stock, on each grant date, we develop an estimate of the fair value of our common stock based on the information known to us on the date of grant, upon a review of any recent events and their potential impact on the estimated fair value per share of our common stock, and in part on input from an independent third-party valuation firm.

Our valuations of our common stock were determined in accordance with the guidelines outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the Practice Aid).

The assumptions used to determine the estimated fair value of our common stock are based on numerous objective and subjective factors, combined with management's judgment, including:

- external market conditions affecting the pharmaceutical and biotechnology industry and trends within the industry;
- our stage of development and business strategy;

- the rights, preferences and privileges of our redeemable convertible preferred stock relative to those of our common stock;
- the prices at which we sold shares of our redeemable convertible preferred stock;
- our financial condition and operating results, including our levels of available capital resources;
- the progress of our research and development efforts;
- equity market conditions affecting comparable public companies;
- general U.S. market conditions; and
- the lack of marketability of our common stock.

The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of our common stock at each valuation date. In accordance with the Practice Aid, we considered the following methods:

- Option Pricing Method. Under the option pricing method (OPM) shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options.
- Probability-Weighted Expected Return Method. The probability-weighted expected return method (PWERM) is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

Based on our early stage of development and other relevant factors, we determined that a hybrid approach of the OPM and the PWERM methods was the most appropriate method for allocating our enterprise value to determine the estimated fair value of our common stock. In determining the estimated fair value of our common stock, our board of directors also considered the fact that our stockholders could not freely trade our common stock in the public markets. Accordingly, we applied discounts to reflect the lack of marketability of our common stock based on the weighted-average expected time to liquidity. The estimated fair value of our common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

Following the completion of this offering, our board of directors intends to determine the fair value of our common stock based on the closing quoted market price of our common stock on the date of grant.

Redeemable Convertible Preferred Stock

We record 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 is recorded outside of permanent equity because while it is not mandatorily redeemable, in certain events considered not solely within our control, such as a merger, acquisition, or sale of all or substantially all of our assets, each of which we refer to as a deemed liquidation event, the convertible preferred stock will become redeemable at the option of the holders of at least a majority of the then outstanding such shares. We have not adjusted the carrying values of the redeemable convertible preferred stock to its liquidation preference because a deemed liquidation event obligating us to pay the liquidation preferences to holders of shares of redeemable convertible preferred stock is not probable of occurring. Subsequent adjustments to the carrying values to the liquidation preferences will be made only when it becomes probable that such a deemed liquidation event will occur.

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 approximately $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, 2018. 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.

Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Sensitivity

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 June 30, 2019, we had cash and cash equivalents of $72.9 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.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and development costs. We do not believe that inflation has had a significant impact on our results of operations for any periods presented herein.

JOBS Act

We are an emerging growth company, as defined in 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 are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). 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 this offering, (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 Securities Exchange Act of 1934, as amended (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, plus unaudited 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 prospectus and that we provide to our investors 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 prospectus for information.

BUSINESS

Overview

We are a development stage precision gene therapy company dedicated to pioneering the development of targeted therapies based on our next-generation AAV vectors. Our proprietary Therapeutic Vector Evolution platform enables our "disease first" approach to product discovery and development, thereby allowing us to customize our AAV vectors to target specific tissue types associated with the underlying disease.

Our proprietary AAV vectors are designed to provide targeted delivery by routine clinical routes, efficient transduction, reduced immunogenicity and resistance to pre-existing antibodies, which we believe will enable us to develop gene therapies that could overcome known limitations of conventional AAVs. As a result, we believe these key attributes will enable us to develop gene therapies with improved therapeutic profiles, pursue previously untreatable diseases and address a broad range of rare and large market diseases. Our product candidates that are in or have completed Investigational New Drug (IND)-enabling studies include a wholly-owned asset in development for the treatment of Fabry disease, as well as two assets in ophthalmology. In ophthalmology our product candidate for the treatment of X-linked Retinitis Pigmentosa (XLRP), is wholly-owned subject to an exclusive option for Roche to develop and commercialize the asset, and our product candidate for the treatment of Choroideremia is licensed to Roche. In addition our wholly-owned product candidate for the treatment of Cystic Fibrosis has completed lead optimization and we expect to initiate IND-enabling studies in the first half of 2020. We expect to initiate our first clinical trials in 2020. We also have a pipeline of product candidates in the lead optimization stage, including for the treatment of Duchenne Muscular Dystrophy (DMD) and Wet Age-Related Macular Degeneration (Wet AMD).

While gene therapy holds tremendous promise as a transformative therapeutic class, the majority of gene therapeutic approaches utilize naturally-occurring or conventional AAV vectors that have encountered limitations such as high dose requirements, limited efficacy, inflammation and toxicity, and neutralization by pre-existing antibodies. As a result of these shortcomings, current efforts with conventional AAV vectors have focused on diseases in which a surgical technique is used for direct cell access, such as subretinal injection for the retina, or a low level of gene expression may be sufficient for patient benefit, such as Hemophilia A or B treatment. Rather than using conventional AAV vectors for our products, we instead take a "disease first" approach creating proprietary customized AAV vectors for each disease indication through our Therapeutic Vector Evolution platform. Our Therapeutic Vector Evolution platform is based on directed evolution, a high-throughput biological engineering and screening approach harnessing the power of natural selection to identify novel AAVs with desirable characteristics. As of August 1, 2019 we have a total of 37 distinct libraries, with an estimated over one billion vector sequences. We select customized AAVs based on the Target Vector Profile (TVP) for the disease and we subsequently characterize each lead vector through extensive studies in non-human primates (NHPs) and proprietary human cell and organotypic tissue assays. Based on our preclinical data to date from NHPs and human cell models, including preclinical head to head comparisons with conventional AAVs, we observed that our precision AAVs were well-tolerated and achieved enhanced delivery, increased transgene expression, reduced immunogenicity and/or improved antibody resistance when compared to therapies using conventional AAVs.

Our initial focus is on developing a broad pipeline of transformative gene therapy product candidates designed to treat patients suffering from lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological diseases. We are developing a diverse pipeline of wholly-owned and partnered programs for both rare and large market diseases. We have not conducted any clinical trials but expect to initiate our first clinical trials by the middle of 2020. Our pipeline is represented in the diagram below.

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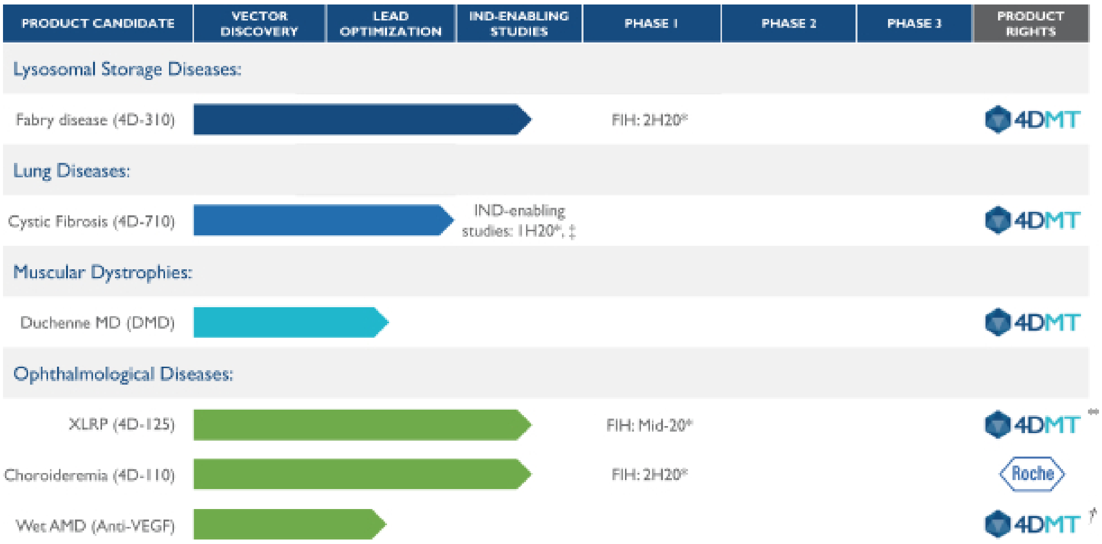


* *Expected timing of milestone. FIH refers to first-in-human, Phase 1 or Phase 1/2, clinical studies.*

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

† *We are independently optimizing lead assets in this field. If we elect to declare product candidate(s) in the field specified in our collaboration and license agreement with Roche, Roche could exercise the option to license, further develop and commercialize this product candidate at any time prior to pivotal trial initiation. See the section titled “Business—Strategic Collaborations—Collaboration and License Agreement with F. Hoffman Ltd. and Hoffman—La Roche Inc.” for further information.*

‡ *Proof of concept studies for 4D-710 were conducted in a pig model of Cystic Fibrosis and utilized a species-specific (i.e., pig-specific) vector rather than the primate-specific 4D-A101 vector, which is the vector for Cystic Fibrosis product candidate 4D-710.*

Lysosomal Storage Diseases

Our lead product candidate in lysosomal storage diseases is wholly-owned by 4DMT: 4D-310 under development for the treatment of Fabry disease. Fabry disease affects at least 5,000 people in the United States and is progressive and fatal with cardiac complications being the leading cause of death. 4D-310 uses a proprietary vector designed for efficient, low dose intravenous delivery to cardiac and other relevant tissues and to have minimal toxicities, and potential resistance to pre-existing antibodies in the human population. The approved enzyme replacement therapies (ERT) reportedly do not adequately address Fabry cardiomyopathy, a leading cause of death in this disease. In 2019 we intend to advance 4D-310 to IND-enabling pharmacology and Good Laboratory Practices (GLP) toxicology and biodistribution studies. 4D-310 Phase 1/2 clinical trial initiation is planned for the second half of 2020. We expect initial human safety and biomarker data by .

Lung Diseases

Our lead product candidate in the lung therapeutic area, 4D-710, is wholly-owned and under development for the aerosol treatment of Cystic Fibrosis lung disease. Cystic Fibrosis is the most fatal inherited disease affecting more than 70,000 patients worldwide. 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, hospitalizations and eventual end-stage respiratory failure. We produced 4D-710 using a proprietary vector designed for efficient aerosol delivery to the lung airway and to have with enhanced penetration through mucus, efficient airway cell transduction and transgene expression, and resistance to pre-existing antibodies in the patient population. While several products have been approved for the treatment of Cystic Fibrosis, they fall short of restoring normal lung function in most patients, and these chronic therapies require daily dosing for the patient's lifetime. Additionally, approximately 10% of patients remain without a treatment option. We expect to initiate IND-enabling study activities with 4D-710 in the first half of 2020.

Muscular Dystrophies

We are currently in the lead optimization phase for our wholly-owned research candidates for the treatment of certain muscular dystrophies, including DMD. DMD, a progressive and fatal muscular-wasting disease, is one of the most prevalent rare genetic disease, with an estimated prevalence between 10,000 to 15,000 cases in the United States. Our product candidates engineered from proprietary vectors designed for efficient, low dose intravenous delivery to cardiac and skeletal muscle tissues with minimal toxicities, and potential resistance to pre-existing antibodies in the human population. Several companies are developing gene therapies for DMD using conventional AAVs. While early clinical data in some programs have been encouraging, AAV gene therapies using conventional AAV vectors have been subject to inflammation-related toxicity issues and manufacturing challenges. In addition to requiring high doses, patients have been excluded from clinical trials due to pre-existing antibodies. We expect to complete lead optimization in the first half of 2020.

Ophthalmological Disorders

We have two ophthalmology product candidates that utilize our proprietary intravitreal vector for rare monogenic binding diseases: 4D-125 in development for the treatment of XLRP and 4D-110 in development for the treatment of Choroideremia. Our proprietary vector for these ophthalmological diseases is designed for intravitreal injection, potentially leading to transgene expression across the surface area of the retina. We have an exclusive partnership in ophthalmology with Roche that includes an option for Roche to license 4D-125 in XLRP, as well as other ophthalmology product candidates we may declare, prior to pivotal trial initiation. 4D-125 is expected to begin clinical trials in mid-2020. We expect initial human safety and biomarker data for 4D-125 by . In addition, Roche currently holds a license to 4D-110 in Choroideremia. We expect to initiate 4D-110 clinical trials in the second half of 2020.

We are currently in lead optimization for multiple product candidates that utilize our proprietary intravitreal vector for the treatment of Wet AMD, each of which is engineered to express a different protein to neutralize vascular endothelial growth factor (VEGF). We expect to complete lead optimization in the first half of 2020.

Our Team

We have an experienced team of biotherapeutics developers, innovative gene therapy scientists and clinicians to execute our strategy. Led by our Chief Executive Officer and co-founder, David Kirn, M.D., 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. Our Chief Technical Officer and Head of Regulatory and Quality, Fred Kamal, Ph.D., has over 20 years of industry experience in product manufacturing and quality, including most recently with AveXis where he was a key contributor to the development and writing of the quality and manufacturing sections of the biologics license application (BLA) for the AAV product Zolgensma. Our Chief Scientific Advisor and co-founder, Dr. David Schaffer, Ph.D., pioneered the application of directed evolution to the capsid of AAV vectors over 15 years ago.

Our Investors

We have raised $108.6 million from the sale and issuance of our preferred stock to leading investors including Viking Global Investors, Janus Henderson Investors, The Biotechnology Value Fund, Arrowmark Partners, Pfizer Ventures, Mirae Asset Financial Group, Perceptive Advisors, Ridgeback Capital Investments, Pappas Capital, and Chiesi Ventures.

Our Strategy

To achieve our goal of unlocking the full potential of gene therapy for many patient populations, we strive to achieve the following:

Develop transformative precision gene therapies using the power of directed evolution and our "disease first" approach.

Our Therapeutic Vector Evolution platform allows us to move beyond naturally-occurring conventional AAV vectors and select proprietary, customized AAV vectors based on a disease-specific Target Vector Profile (TVP). As a result, we believe we will be able to unlock the full potential of gene therapy by creating precision gene therapies with improved characteristics that enable us to treat broader patient populations and previously untreatable diseases, if approved.

We believe our AAV products are modular, in that a single vector can be armed with different transgene payloads in order to treat multiple diseases within the same tissue types or therapeutic areas. As a result, if clinical studies provide us with clinical proof-of-concept for a specific vector, we believe our likelihood of technical success may increase with each subsequent product leveraging the same vector.

Design, develop and commercialize a diverse portfolio of product candidates in a broad range of therapeutic areas for both rare and large market diseases.

We are developing product candidates in diseases and therapeutic areas in which we believe our proprietary AAV vectors may provide differentiating advantages to conventional approaches. Our initial focus is to develop a broad pipeline of potentially transformative gene therapy product candidates designed for patients suffering from lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological diseases. Additionally, we believe our customized vectors will allow us to create and, if approved, commercialize transformative therapies for rare and large market diseases that cannot be addressed with conventional AAV vectors.

Continue to expand our Good Manufacturing Practice manufacturing capabilities.

We believe a critical component to our success will be to leverage and expand our proprietary manufacturing know-how, expertise, and capacity. We currently operate an internal manufacturing facility in which we intend to produce clinical trial material according to current Good Manufacturing Practices (cGMP) requirements, along with material we have used for Good Laboratory Practices (GLP), toxicology studies and vectors for characterization studies in non-human primates and other animal models. We plan to continue expanding our internal manufacturing capabilities, while leveraging the experience of our chemistry, manufacturing and controls (CMC) team to support the development and, if approved, commercialization of our product candidates. We believe that focusing on internal manufacturing activities and control, supplemented by outside activities at CMOs, can mitigate CMC development and commercialization risks, limit reliance on CMOs and increase product development speed. We are dedicated to using the scalable unit operations we have designed for our product and vector manufacturing, which we believe have advantages for large-scale manufacturing versus those developed in academic laboratory settings.

Protect, defend, and expand our intellectual property portfolio of proprietary AAV vectors discovered through Therapeutic Vector Evolution platform.

We have issued patents and patent application filings on the composition-of-matter for over 300 unique AAV capsid sequences that were identified through our discovery efforts. In addition, we have product-specific patent application claims that include our capsids carrying codon-optimized transgenes. Through sponsored research agreements with the UC Regents, under the direction of Dr. Schaffer, we also hold options to exclusive licenses on future promoter-related intellectual property, as well as manufacturing-related technologies. We also hold trade secrets covering vector discovery and manufacturing methodologies. Finally, our intellectual property portfolio includes our vector libraries, consisting of an estimated one billion unique AAV capsid sequences.

Selectively partner with leading biopharmaceutical companies to harness the full potential of our platform while retaining product rights in key markets and work closely with patient advocacy groups to inform our programs.

We have retained rights to the majority of therapeutic areas and product opportunities within our proprietary platforms. We have entered into strategic partnerships with biopharmaceutical companies Roche, AstraZeneca (previously MedImmune) and uniQure in order to maximize the potential of the platform and broaden our therapeutic reach through their expertise and commercial capabilities. In addition, we have relationships with the Cystic Fibrosis Foundation, Foundation Fighting Blindness, Choroideremia Research Foundation and CureDuchenne. We will continue to evaluate new opportunities to partner with leading pharmaceutical and biotechnology companies, and with patient disease foundations and advocacy groups, that we believe maximize value and benefits for us and patients.

Gene Therapy and Limitations of Current Approaches

Gene therapy aims to address diseases caused by gene mutations and gene dysregulation, and it holds the promise of delivering transformative and durable benefit to the patient after a single administration. Genetic therapies are designed to address 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. These genetic 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 demonstrated therapeutic utility across multiple disease areas, with a focus on rare diseases. There has been significant progress in the area of gene and cell therapy, including with AAV based gene therapy, as well as chimeric antigen receptor T-cell therapies. 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, it 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 efficacy of gene therapy, as the vector must deliver the promoter and transgene to the diseased cells in sufficient quantities to result in clinical benefit. The majority of AAV gene therapy companies use conventional AAV vectors that are comprised of naturally-occurring AAV viruses of a few specific subtypes, including AAV2, AAV5, AAV8, AAV9, AAVrh10, and AAVrh74.

- *Promoter and Transgene:* The promoter is the DNA region that controls and initiates transcription of the transgene, while the transgene is the functional gene intended to be delivered into the cell and expressed at the RNA and protein levels.

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. While gene therapy holds tremendous promise as a transformative therapeutic class, the demonstrated hurdles with conventional vectors may limit the diseases that can be effectively addressed. There are four fundamental challenges that hinder gene therapies that utilize conventional vectors:

1. *Lack of efficient delivery to specific tissues and/or cell types due to physical barriers.* Conventional naturally-occurring AAVs have not been designed or engineered to circumvent natural barriers to viral vector delivery, such as clearance by the liver or the inner-limiting membrane of the retina, 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 skeletal muscle diseases) to achieve therapeutic benefit.

2. *Lack of efficient transduction of specific target cell types.* 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 AAVs are not designed or engineered for efficient transduction of specific target cells. As a consequence, conventional vectors may be associated with inefficient transduction and transgene expression which would limit efficacy.

3. *Potential to cause toxicity due to inflammation.* Conventional AAV vector based products 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, and the ability of these AAVs to transduce immune cells. For example, intravenous gene therapy programs in patients with DMD have been associated with acute inflammation and transient kidney dysfunction.

4. *Neutralization by pre-existing antibodies.* The human immune system has evolved to fight viruses, including conventional AAVs that are present in nature. Widespread exposure to these conventional AAVs has resulted in neutralizing antibodies in a large portion of the population (approximately 30% to 70% depending on the vector serotype and patient population); these antibodies can limit gene delivery and the addressable patient population with conventional vectors. In addition, re-dosing with the same vector is generally not feasible given the induction of neutralizing antibodies to the vector.

Attempts have been made to address some of these limitations by incorporating incremental modifications in naturally-occurring vectors, including through the following methods:

- engineered mutations to naturally occurring AAVs of a few specific subtypes to create new vectors; and

- acquisition of pools of novel AAV capsids generated using a single methodology, followed by screening and identification of capsids in small animal models (typically in mouse models) or *in vitro*.

While these latter conventional vectors are different from naturally-occurring AAV vectors, we do not believe these attempts at improvements to the naturally-occurring AAV have overcome each of the challenges encountered to date.

While gene therapy has the potential to treat previously intractable diseases, current efforts with conventional AAV vectors have focused on diseases in which a surgical technique is used for direct cell access (such as subretinal injection for the retina), or a low level of gene expression may be sufficient for patient benefit (such as Hemophilia A or B treatment).

Our Solution: Customized Vectors and "Disease First" Approach

We are pioneering the development of precision gene therapies based on our proprietary AAV vectors. We believe our customized AAV vectors have the potential to enable targeted delivery, efficient transduction, reduced inflammation and resistance to pre-existing antibodies. As a result, we believe we will be able to develop gene therapies with improved therapeutic profiles and also address previously untreatable diseases and patient populations.

Our Therapeutic Vector Evolution platform enables our "disease first" approach to product discovery, design and development. We use our platform to discover custom and proprietary AAVs designed for specific tissues and diseases, which we believe will allow us to overcome known limitations of conventional AAV vectors and potentially address a broad range of both rare and large market diseases. Based on our Target Vector Profile for a disease, we select customized capsids in non-human primates from an estimated over one billion vector capsid sequences in our 37 proprietary and diverse AAV vector libraries as of August 1, 2019. We subsequently characterize each vector through extensive studies in non-human primates and human cell and organotypic tissue assays.

Key Attributes of Our Proprietary and Customized AAVs

Through our proprietary Therapeutic Vector Evolution platform, we rigorously screen our vectors to select for the optimal AAV for a specific disease, or class of diseases. We focus on discovering and selecting vectors that we believe have the potential to display superiority to conventional vectors with four key attributes:

- Targeted delivery to specific tissues by routine clinical routes of administration;
- Improved transduction of target cell types and tissues;
- Lower toxicity with reduced inflammation; and
- Ability to avoid neutralization by pre-existing antibodies in humans.

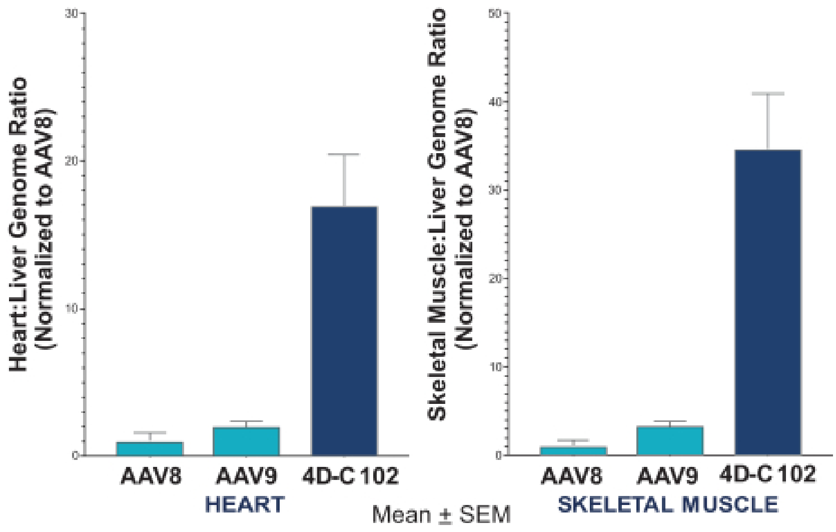
As shown below, while we have not initiated any clinical trials to date, we continue to generate animal proof-of-concept data in both primates *in vivo* and in human cells *in vitro* that we believe provide evidence regarding the potential for our precision AAVs to show superiority over conventional AAVs. As a result, we believe we have the potential to create products that are safer, more efficacious, 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 AAVs that are designed to be 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 a first example of targeted delivery in NHP *in vivo*, our investigational, novel and proprietary AAV vector for cardiac and muscle tissues, 4D-C102, was designed for IV administration, which we believe represents the optimal route of administration for systemic delivery. There are diverse barriers to IV delivery to muscle tissues, which include the liver, blood components, immune cells and antibodies. In NHPs we have observed that 4D-C102 was more efficiently delivered through IV administration to cardiac and skeletal muscle tissues than conventional AAV8 and AAV9. As shown below, 4D-C102 targeted the heart and skeletal muscle tissues (upper and lower extremities plus diaphragm) more efficiently than conventional IV vectors like AAV8 and AAV9, and showed up to 35-fold improvements, on average, in the ratio of vector reaching heart and skeletal muscle tissues versus the liver.

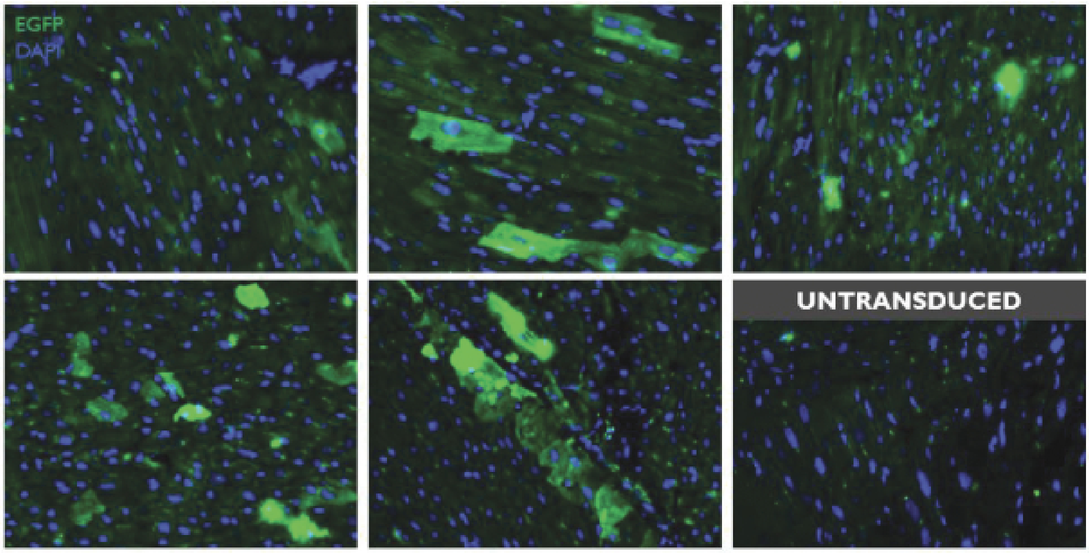
4D-C102 Intravenous Targeting to NHP
Skeletal Muscle and Cardiac Tissue Was Superior to AAV8 and AAV9



SEM = standard error of the mean, which denotes the standard deviation of the sampling distribution

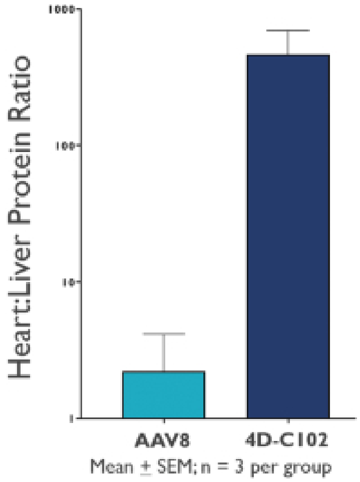
In a second example of targeted delivery in NHP *in vivo*, 4D-C102 delivered a marker gene (*EGFP*) which resulted in EGFP protein production in NHP cardiomyocytes *in vivo.* For example, 30 of 30 heart biopsy samples from three NHPs were positive for genomes and 29 of 30 samples were positive for EGFP protein expression.

Cardiac Muscle Tissue Transduction and Protein Expression Patterns Observed After Intravenous Injection of 4D-C102 in NHP Cardiomyocytes (EGFP Expression as Detected by Immunohistochemistry).
Five Panels Illustrate Gene Expression Patterns Observed in NHP Cardiac Muscle Tissue After Treatment with 4D-C102. Cardiomyocyte Cell Staining was Visible 8 Weeks Post-Injection.
The Lower-Right Panel Illustrates a Lack of Visible EGFP Staining in an Untransduced Control NHP.



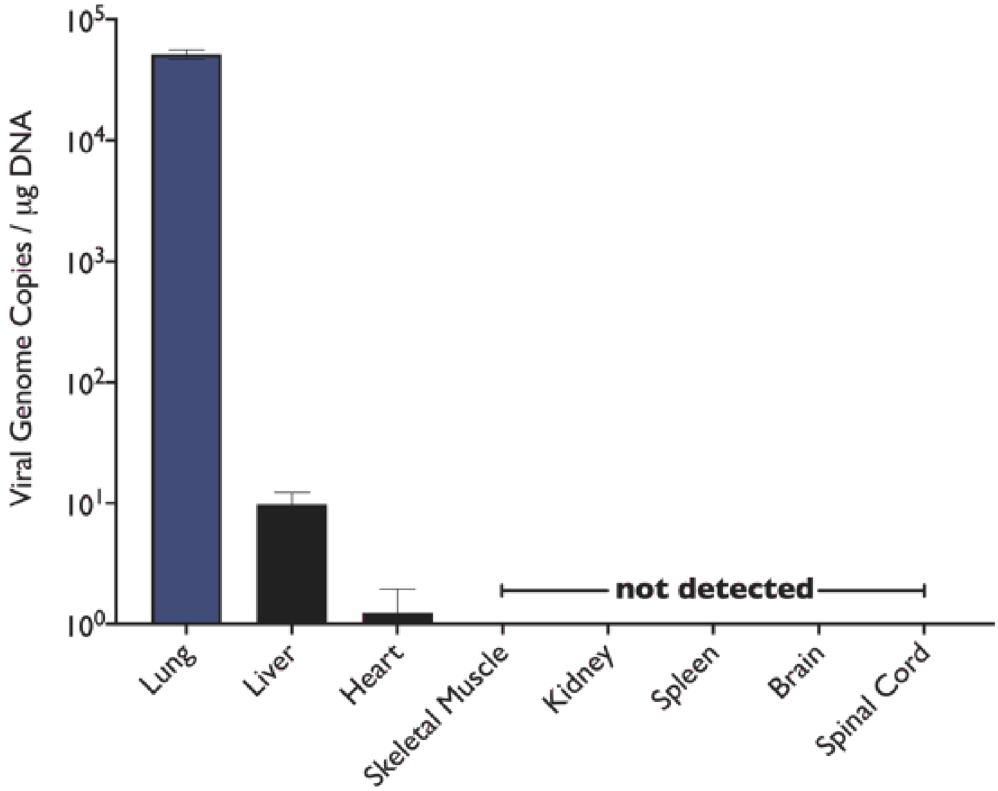
Further to this second example, 4D-C102 selectively induced protein expression in cardiac tissue. Specifically, in NHPs treated with 4D-C102, the ratio of cardiac protein expression to liver protein expression was estimated to be 190 fold higher than that ratio in NHPs treated with AAV8 (420:1 vs 2.2:1 for 4D-C102 vs AAV8, respectively).

Selective 4D-C102 Protein Expression in NHP (IV Administration):
Cardiac Tissue Protein Expression Versus Liver Was Superior to AAV8



In a third example of targeted delivery in NHP *in vivo*, our investigational, novel, proprietary AAV for lung tissues, 4D-A101, was designed for aerosol delivery to lung airway cells; this vector was also selected for potential antibody-resistance in humans. In NHPs, we observed that aerosol delivery of 4D-A101 via a standard nebulization device, approved for use in humans, resulted in delivery to, and transduction of, all 48 lung sites evaluated; lung tissue sites evaluated included proximal, medial and distal airways. In addition to efficient lung airway transduction, migration to organs outside the lung was either undetectable (91% of samples tested) or extremely low concentrations (less than 0.1% of the average genomes per microgram of DNA in the lung airway tissues) as shown below.

Aerosol Delivery with 4D-A101 in NHP Resulted in Genome Localization and Protein Expression in All Lung Samples. 4D-A101 Genome Localization Was Limited or Not Present in Other Tissues

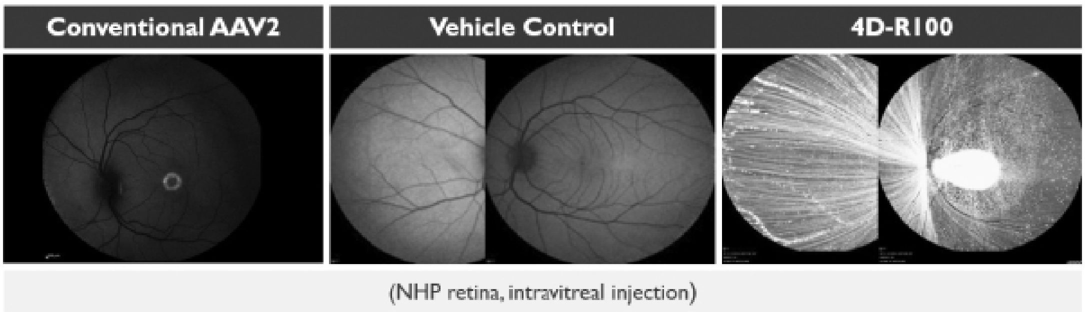


The Y axis is “viral genome copies per ug of DNA”—this refers to the number of viral genomes (a direct measurement of the number of virus particles) that can be quantified per quantity of DNA isolated from each tissue sample. The X axis is the tissue (e.g., lung, heart, liver) from which the samples were obtained.

In a fourth example of targeted delivery in NHP *in vivo*, our investigational, proprietary AAV for the retina, 4D-R100, was designed for intravitreal administration; we believe intravitreal injection is the optimal route of administration for the retina, as evidenced by approved biologics for the treatment of Wet AMD. Conventional AAVs such as AAV2 are not able to reach retinal cells effectively following intravitreal injection due to the inner-limiting membrane barrier between the vitreous and target retinal cells. In NHPs, whose ocular anatomy and physiology closely mirrors that of humans, we have observed that 4D-R100 administered by intravitreal injection covered the area of the retinal surface, and it transduced a high percentage of cells in all layers of the retina, including photoreceptors and retinal pigment epithelial (RPE) cells.

The Images Below Show Retinal Transduction and Protein Expression Patterns following Intravitreal Injection of 4D-R100 and Conventional 1st Generation AAV in NHP (in-life EGFP Expression Captured by Heidelberg Spectralis Camera). The Left Panel Illustrates that Typical Transduction and Protein Expression with Conventional AAV2 was Limited to a Ring of Cells Around the Fovea.

The Right Panel Illustrates Transduction and Protein Expression Pattern Following Intravitreal Dosing with 4D-R100 4D-R100 Exhibited Widespread Transgene Expression Across the Retinal Surface Area in NHP (in Life Images at 6-month Post-Injection)



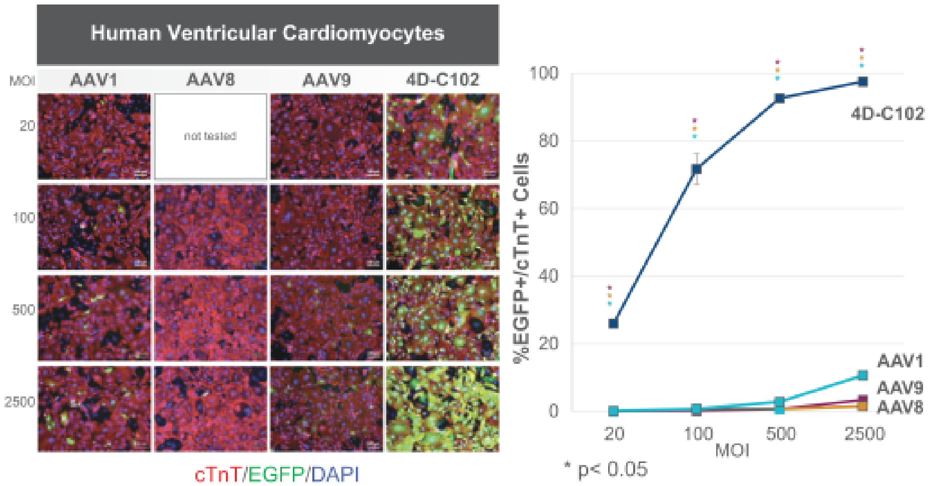
EGFP = enhanced green fluorescent protein

Improved Transduction of Target Human Cell Types and Tissues

We select AAVs for specific diseases that are designed to generate higher levels of gene expression than conventional AAV vectors in an effort to improve long-term efficacy and reduce vector doses required.

For example, our investigational novel AAV, 4D-C102, is designed to efficiently target human cardiomyocytes. Targeting is especially important when addressing diseases that impact cardiac cells, such as Fabry disease. Conventional AAVs 1, 8 and 9 have been used by competitors to target these cells; however, we believe the limited transduction with these AAVs may limit efficacy and lead to high dose requirements that present safety challenges. In preclinical studies, 4D-C102 exhibited significantly improved transduction of human cardiomyocytes (ventricular phenotype) compared to conventional AAVs across a wide range of concentrations, as shown below.

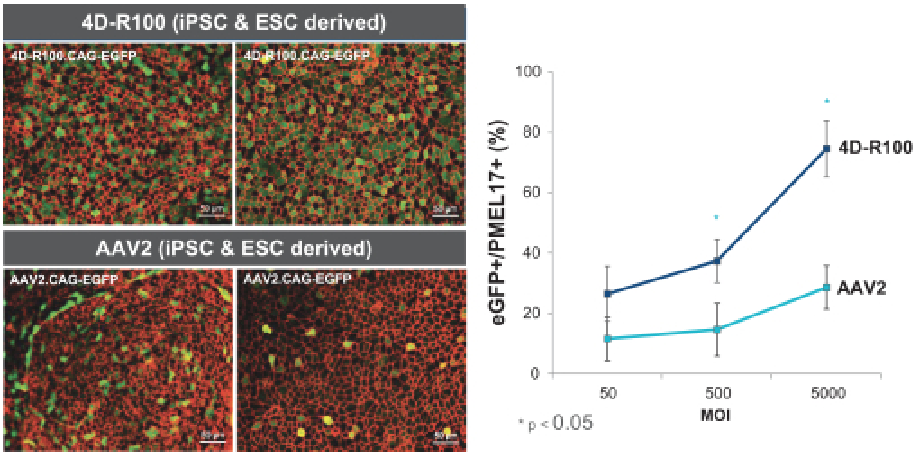
4D-C102 Exhibited Significantly Higher Transduction in Vitro Relative to Conventional AAV1, 8 and 9, in Human Cardiomyocytes of Ventricular Phenotype



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
vg = viral genome, a quantification of the viral particles present
%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

In a second example, we have observed that our intravitreal retina vector, 4D-R100, was significantly more efficient at transducing human retina cells *in vitro*, such as RPE cells below, than conventional AAV2, which is commonly used for retina treatment.

4D-R100 Exhibited Greater Transduction of Human Retinal Cells in Vitro Compared to Conventional AAV2



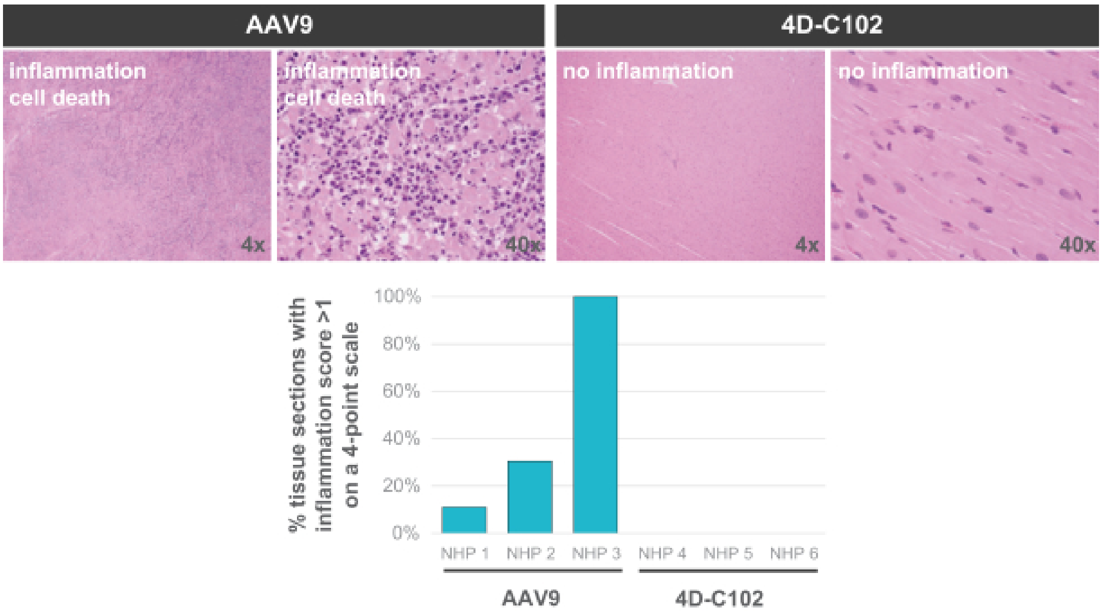
CAG = ubiquitous promoter comprised of CMV enhancer, chicken beta actin promoter and intron, and rabbit beta globin intron element
iPSC = induced pluripotent stem cell
ESC = embryonic stem cell
PMEL17 = premelanosome protein, a marker of retinal pigmented epithelial cell identity
%EGFP+/PMEL17+ Cells = 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

Potentially Lower Toxicity With Reduced Inflammation

We select AAVs that are designed to target specific diseased cells while avoiding non-target cells. We believe that vectors selected in this way have the potential to result in less inflammation, require lower doses and lead to a lower toxicity versus conventional AAVs such as AAV9.

As illustrated below, relative to conventional AAV9, our 4D-C102 vector was associated with lower inflammation and toxicities in NHP heart tissues after IV administration. The two vectors carried the same CAG promoter and EGFP transgene.

NHP Cardiac Muscle Exhibited Reduced Inflammation After Treatment with 4D-C102 Versus AAV9 (IV Administration of Vectors Carrying the EGFP Transgene)

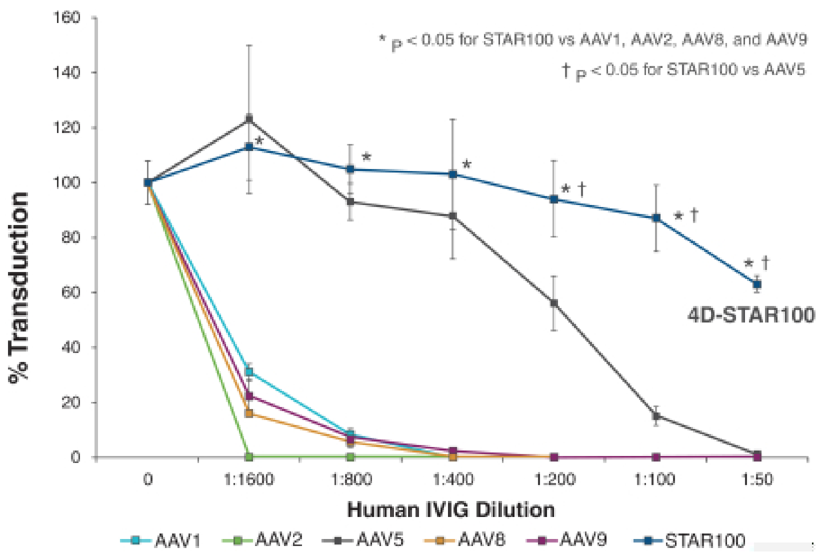


Ability to Avoid Neutralization by Pre-Existing Antibodies in Humans

We can select AAVs designed for resistance to neutralization by pre-existing antibodies in the human population, which we believe may broaden our potential target patient population compared to conventional AAVs. We believe 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 when desirable by developing product candidates with different proprietary vectors that target the same tissues; this approach would utilize a proprietary AAV first whose antibodies do not cross-react with the second vector.

For example, our proprietary AAV 4D-STAR100, which was designed for IV administration, has shown improved antibody resistance when compared to conventional AAV1, 2, 5, 8 and 9 as demonstrated below.

4D-STAR100 Showed Improved Transduction In Vitro in the Presence of Human Antibodies (IVIG) Compared with Conventional AAV Vectors



IVIG = intravenous immune globulin, a human blood-derived product that contains antibodies (including antibodies against AAV)

Our Proprietary Therapeutic Vector Evolution Platform

Our proprietary Therapeutic Vector Evolution platform is based on directed evolution. Directed evolution is a high-throughput discovery and optimization approach harnessing the power of evolution in an effort to create biologics with new and desirable characteristics. The first step involves the generation of diverse libraries of biological variants. In the second step, these libraries can be screened to identify improved variants with the desired 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 performed by academic investigators; these investigators have no relationship to us.

Our co-founder, Dr. Schaffer, pioneered the use of directed evolution to create improved AAV capsids for use as gene therapy vectors at U.C. Berkeley over 15 years ago. Over the past five years, we have developed our Therapeutic Vector Evolution platform, inspired by Dr. Schaffer's work on AAV directed evolution, to produce improved AAV capsid vectors designed for use in human therapeutic products. Since in-licensing six libraries from UC Regents, we have created 31 new AAV capsid libraries as of August 1, 2019. In addition, we have developed significant experience in performing discovery in NHPs, with over 10 different discovery efforts to date. We believe the investment in our proprietary platform provides us with the largest and most diverse AAV vector library and vector sequences in the field of gene therapy.

Proprietary AAV Vector Libraries

We have 37 distinct libraries as of August 1, 2019, with an estimated over one billion vector sequences. Each library is defined by its starting material (AAV capsid gene sequences) and genetic diversification methodologies, such as mutagenesis, random peptide sequence insertions and shuffling technologies. 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 optimized vectors from those libraries.

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

Disease First Approach—Target Vector Profile

We employ a rigorous approach to AAV vector selection based on what we consider an optimal product profile, which we term target vector profile (TVP). For any target disease, or set of diseases that affect the same tissues, this profile includes 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 antibody resistance.

We use our Therapeutic Vector Evolution platform to identify the unique vector variant in our libraries that best matches our TVP. We achieve this through serial rounds of “selection”, or discovery, with each round of selection filtering down to fewer and fewer capsids from the original library. This funneling process is achieved by applying selective pressures—forcing competition—among all capsid variants in the library to achieve delivery to the target cells as defined in the TVP. Each round is performed in a primate *in vivo*, sometimes in the presence of human IVIG (pooled human antibody preparation). While none of our product candidates have begun clinical trials, we believe this deliberate approach to selection in NHPs and human tissues should lead to identification of vectors with a higher likelihood of success in humans.

By the end of a typical discovery process, we will have identified approximately two to four lead capsids, or hits, based on their frequency in the final pool of capsid sequences, in addition to numerous sequences present at lower frequencies. We then file patent applications disclosing all identified gene sequences from the discovery program.

Discovery Results to Date

To date, we have completed more than 10 unique vector discovery programs or “selection processes” for specific AAV capsids with specific TVPs. We have utilized four different routes of administration, including intravitreal, intrathecal, aerosol, and intravenous administrations. We have completed discovery programs targeting multiple tissue types including various retinal cell types, heart and skeletal muscle tissues, brain, dorsal root ganglia, different lung cell types, liver, and synovial joints. We have identified and filed patent applications on over 300 unique capsid sequences.

Characterization of Novel Vector Variant “Hits”

Vector hits are typically characterized in three major areas: manufacturing, human cell and 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 EGFPs.

Development Platform: Human Cell and Disease Modeling

With the goal of optimizing our product development programs prior to entering the clinic, we have developed a robust human cell and disease modeling platform. We evaluate vector transduction, transgene expression and function in target cells of interest in these human models. These cells can be derived from both normal donors or from patients with specific genetic diseases of interest. This approach allows us to perform head-to-head comparisons between different AAV capsids, promoter elements, and transgene payloads. We believe this approach better characterizes and informs the behavior of our vector products in the human body and their potential for clinical success.

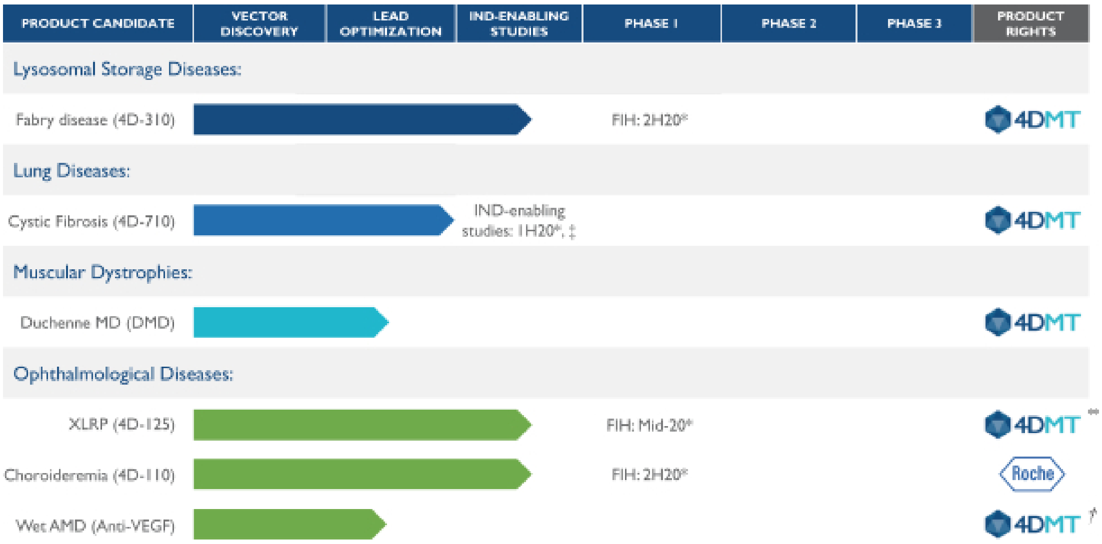
Therapeutic Areas, Lead Vectors and Product Candidates

Our proprietary platform has enabled broad and diverse AAV programs that we are translating into product candidates with the goal of transformative patient benefit. We currently have a product pipeline that includes product candidates in four therapeutic areas: lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological diseases.

For each of these therapeutic areas we have customized proprietary targeted lead vectors that were discovered using our proprietary technology platform. These lead vectors are designed for delivery by optimal clinical routes. We believe that these proprietary vectors will allow us to develop product candidate portfolios within each of these therapeutic areas.

	Cardiac and Skeletal Muscle		Lung	Retina
Lead Vector	**4D-C102**	**4D-STAR100**	**4D-A101**	**4D-R100**
Tissue and Cell Types Targeted	Diffuse Regions throughout Heart and Skeletal Muscle	Diffuse Regions throughout Heart and Skeletal Muscle	Diffuse Regions throughout Lung	Multiple Layers of Retina
4DMT Product Candidate	**4D-310**	**Lead Optimization**	**4D-710**	**4D-125 / 4D-110**
Route of Administration	Intravenous	Intravenous	Aerosolized	Intravitreal
Selected for Resistance to Pre-existing Antibodies to Naturally-Occurring AAV Vectors	Yes	Yes	Yes	N/A (eye is generally immune-privileged)
Conventional AAV Typically Used for Tissue Target	AAV1, AAV8, AAVrh74, AAV9	AAV1, AAV8, AAVrh74, AAV9	AAV5, AAV6	AAV2

Our initial focus is on developing a broad pipeline of transformative gene therapy product candidates designed to treat patients suffering from lysosomal storage diseases, lung diseases, muscular dystrophies and ophthalmological diseases. We are developing a diverse pipeline of wholly-owned and partnered programs for both rare and large market diseases. We believe our AAV products are modular, in that a single vector can be armed with different transgene payloads in order to treat multiple diseases within the same tissue types or therapeutic areas. Our pipeline is represented in the diagram below.



*	*Expected timing of milestone. FIH refers to first-in-human, Phase 1 or Phase 1/2, clinical studies.*
**	*We are responsible for development of this product candidate and Roche has an exclusive option to assume development and commercialization at its sole cost and expense. Such option may be exercised at any time prior to pivotal trial initiation.*
†	*We are independently optimizing lead assets in this field. If we elect to declare product candidates in the field specified in our collaboration and license agreement with Roche, Roche could exercise the option to license, further develop and commercialize this product candidate at any time prior to pivotal trial initiation. See the section title "Business—Strategic Collaborations—Collaboration and License Agreement with F. Hoffman Ltd. and Hoffman-La Roche Inc." for further information.*
‡	*Proof of concept studies for 4D-710 were conducted in a pig model of Cystic Fibrosis and utilized a species-specific (i.e., pig-specific) vector rather than the primate-specific 4D-A101 vector, which is the vector for Cystic Fibrosis product candidate 4D-710.*

4D-310 for the Treatment of Fabry Disease

Target Product Profile

4D-310 is our wholly-owned product candidate for the treatment of Fabry disease. 4D-310 is comprised of our proprietary vector 4D-C102, carrying a codon-optimized *GLA* transgene. The product candidate is designed for efficient, single low dose intravenous delivery to cardiac tissue, kidney, liver and skeletal muscle tissues. The intended result is for alpha-galactosidase A (AGA) enzyme expression within cardiac tissues for cardiac disease correction, in addition to expression and secretion from other tissues within the body, such as liver and kidney. We believe 4D-310 has the potential to treat "classic" (early onset) Fabry disease, as well as late onset Fabry disease, both of which are often associated with cardiomyopathy. To that end, 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.

We anticipate completing IND-enabling toxicology and biodistribution studies with 4D-310 in early 2020, and we expect 4D-310 to enter clinical trials in the second half of 2020. We expect initial human data by .

Disease Background, Unmet Medical Need and Target Patient Population

Fabry disease is a rare genetic disorder that results in the body's inability to produce an enzyme called AGA, causing the accumulation of globotriaosylceramide-3 (Gb3) in critical organs, including the heart and kidney. Such substrate accumulation can lead to life-threatening heart failure, arrhythmias, vascular blockages, and various degrees of kidney dysfunction. Fabry disease is progressive and fatal, with an average life expectancy of approximately 50 years and cardiac complications being the leading cause of death. Progression of the disease causes significant reduction in the quality of life and significant economic burden associated with greater patient needs for supportive care. It is estimated that at least 5,000 people in the United States are diagnosed with Fabry disease, but studies have suggested that a large number of patients may be undiagnosed.

Fabry disease is currently treated by regular infusions, approximately every two weeks, of replacement AGA enzyme, a class of therapies broadly referred to as ERTs. Two of these approved ERT products are Fabrazyme from Sanofi and Replagal from Takeda, both of which are administered to patients every two weeks. In addition to high burdens of therapy, patients on these ERTs may be exposed to sub-therapeutic levels of AGA for a period of time between infusions, potentially leading to recurrences of disease symptoms and complications. Furthermore, ERTs reportedly lack efficient uptake by cardiac muscle cells; hence the patients remain at risk of cardiac complications, including death. Specifically, a medical officer's review of Fabrazyme which was conducted during the U.S. Food and Drug Administration (FDA)'s evaluation of this drug candidate indicates that consistent increases in Gb3 levels were measured in cardiomyocytes (as opposed to decreases measured in vascular endothelium). Therefore, we believe cardiac-specific treatment of Fabry disease is still an unmet medical need. Despite these shortcomings, ERT for Fabry disease does provide significant benefit for patients.

Competition and Differentiation—Viral Vector Gene Therapy including AAV for Fabry Disease

A number of biotechnology companies are pursuing gene therapy solutions, including with conventional AAV vectors, to treat Fabry disease. In addition to being in early stages of development, these developmental AAV gene therapies are specifically designed to target transduction to the liver only, with liver-specific promoters, which therefore would prevent expression in cardiac muscle cells. When administered as ERT, the AGA protein does not efficiently enter cardiomyocytes; it is therefore unclear whether production of AGA from the liver would result in effective cardiac muscle cell treatment. As a result, 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 that a gene therapy that is specifically targeted to transduce cardiac muscles with high efficiency has the potential to significantly improve patient outcome through the synthesis of AGA directly within the heart tissues, including cardiomyocytes. Our 4D-310 program, for which we expect to initiate clinical trials in the second half of 2020, is designed to take advantage of our proprietary 4D-C102 vector for delivery of transgenes to cardiac muscle cells and other relevant tissues within the body.

Finally, to our knowledge, conventional AAV gene therapy programs in development are limited to treatment of the "classic" (early onset) patient population at this time. In contrast, 4D-310 is designed for the treatment of all patient subpopulations with Fabry disease, including "late onset" patients with cardiomyopathy. The late onset sub-population is substantially larger than the early onset population.

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As we achieve proof-of-concept with the 4D-C102 vector, we intend to advance additional programs for lysosomal storage diseases using the same vector.

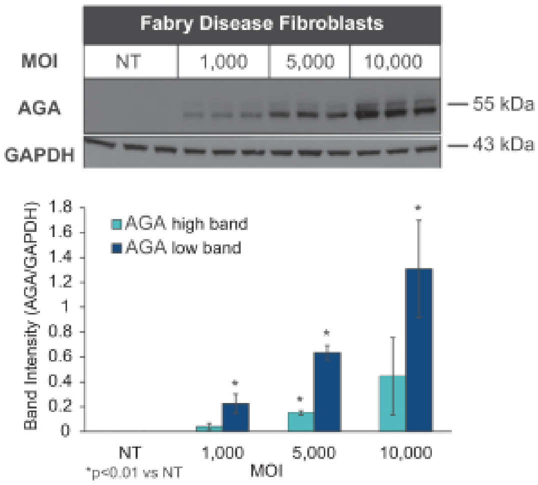
Pharmacology and Toxicology Program

In the second quarter of 2019 we initiated a GLP toxicology and biodistribution study of 4D-310 in normal mice. We also received feedback from the FDA on our preclinical study plans in connection with a pre-IND interaction. Pharmacology studies have been performed in Fabry patient-derived cells. We plan to complete IND-enabling preclinical pharmacology and toxicology studies by the first quarter of 2020, and to file an IND for 4D-310 in the second half of 2020.

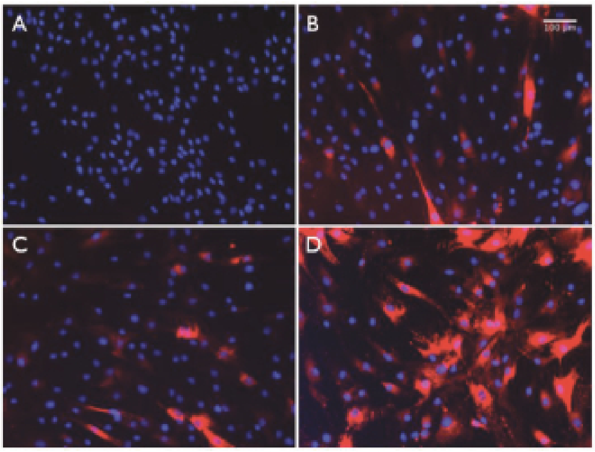
In *in vitro* studies with 4D-310 in Fabry patient-derived fibroblasts and cardiomyocytes we observed dose-related AGA expression and function as shown below.

4D-310 Transduced Fibroblasts Derived from Fabry Patients. These 4D-310-Transduced Fibroblasts Expressed AGA in a Dose-Dependent Manner

Panel A: Fabry-derived fibroblasts expressed AGA after treatment with 4D-310 as measured by western blot.



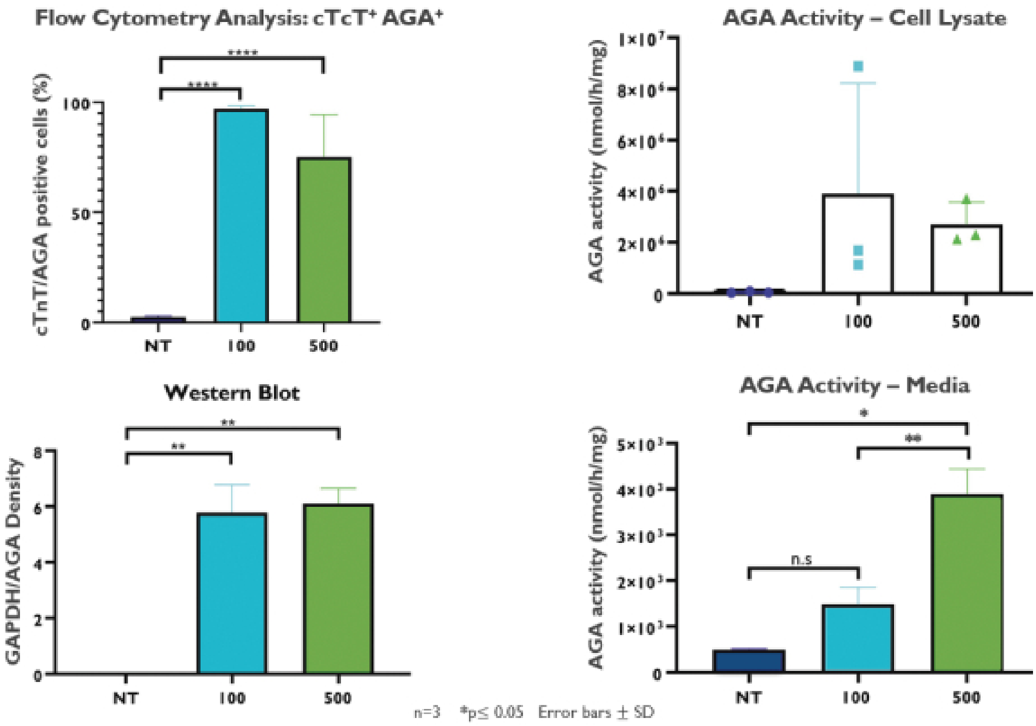
Panel B: Fabry Patient-Derived fibroblasts expressed AGA after treatment with 4D-310 as measured by IHC. AGA is visible in red, cell nuclei are shown in blue.A) vehicle control, B) 4D-310 low dose (MOI 1000), C) 4D-310 medium dose (MOI 5000), and D)4D-310 high dose (MOI 10,000)



Transduced Fabry fibroblasts were stained for AGA and DAPI/Nucleus. Vehicle, MOI 1000, MOI 5000, and MOI 10,000 (A-D, respectively) are shown. Scale bar = 100 µm

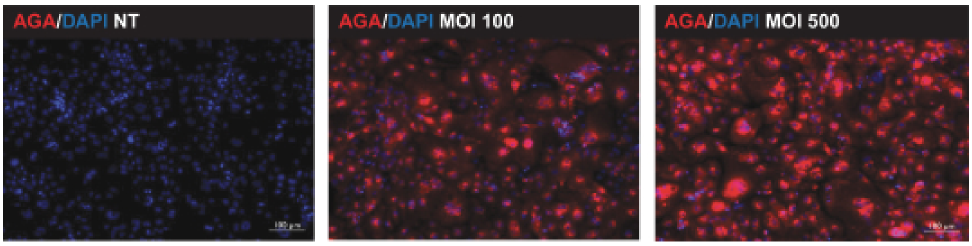
AGA Enzyme Expressed in Fabry Patient-Derived Cardiomyocytes After Treatment with 4D-310 Exhibited Enzymatic Activity.

Panel A: Cardiomyocytes that were differentiated from Fabry patient-derived fibroblasts expressed functional AGA after treatment with 4D-310, as measured by western blot and flow cytometry.



%/cTnT+/AGA+ Cells = the percentage of AGA-expressing cells within the cTnT-expressing cardiomyocyte population
nmol = nanomoles
GAPDH = Glyceraldehyde 3-phosphate dehydrogenase, used as a control to show equal amounts of sample are analyzed across conditions
AGA/GAPDH Density = a quantification of the amount of AGA protein expression normalized to the amount of control protein expressed by the same cells
IHC = immunohistochemistry

Panel B: Cardiomyocytes that were differentiated from Fabry patient-derived fibroblasts expressed AGA after treatment with 4D-310, as measured by IHC.



Clinical Development Plans—Patient Natural History Study

In the beginning of 2020 we expect to initiate a natural history study in approximately 20 patients with Fabry disease. Patients will be followed over time for changes in biomarkers of Fabry disease, including cardiac MRI (to assess substrate build up and cardiomyopathy), blood levels of AGA and the substrate Gb3, and organ function. We expect some of these patients will subsequently enroll in our planned Phase 1/2 clinical trial of 4D-310, which could accelerate enrollment in the clinical trial.

Clinical Development Plans—Phase 1/2 Trial Design

Our Phase 1/2 clinical trial initiation is targeted for the second half of 2020. We expect this will be a single dose escalation study carried out at multiple sites within the United States with an estimated 15 to 20 patients enrolled. We expect to treat both early-onset and late-onset patients, including those with cardiomyopathy. We anticipate the primary endpoint will be safety, plus the definition of the maximum-tolerated or -feasible dose. Pharmacodynamic assessments may include cardiac MRI, a well-established non-invasive diagnostic imaging technique that allows quantitative assessment of Gb3 substrate buildup in cardiac tissues. Additional pharmacodynamic endpoints may include changes in blood levels of Gb3 and AGA.

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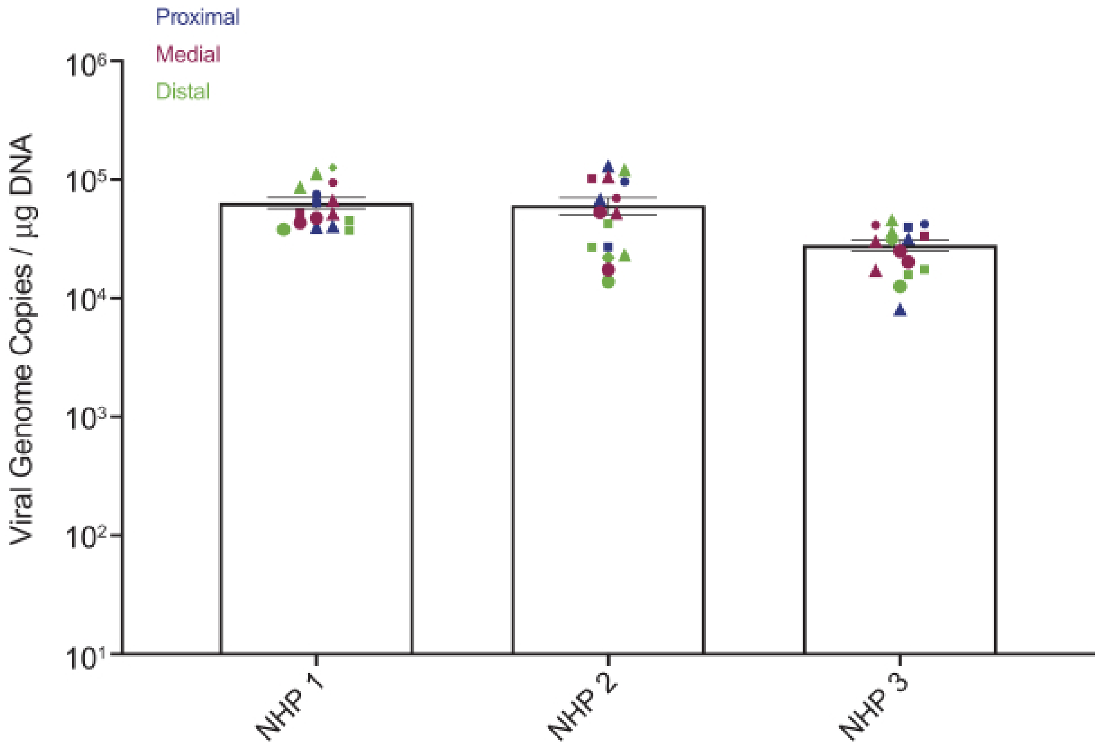
4D-710 for the Treatment of Cystic Fibrosis

Target Product Profile

4D-710 is our wholly-owned product candidate for the treatment of Cystic Fibrosis lung disease. 4D-710 is comprised of our proprietary vector 4D-A101, and designed for an efficient, single dose aerosol delivery to the lung airways with resistance to pre-existing antibodies. The intended result is for Cystic Fibrosis transmembrane conductance regulator (CFTR) expression within lung airway cells for lung disease correction. We believe 4D-710 has the potential to treat Cystic Fibrosis patients with a broad range of mutations. Due to the fact that the CFTR coding sequence is larger than can be packaged into AAV gene therapy vectors, we have focused our efforts on assessing codon-optimized versions of a synthetic *CFTR* transgene *deltaR-CFTR*, which we refer to as *microCFTR*, a well-characterized and truncated variant that has shown activity in a large animal model of Cystic Fibrosis. The vector will carry *microCFTR*, a construct that retains the most critical components of the full-size *CFTR* gene yet is small enough to fit within AAV packaging constraints.

While we present preclinical data for our cystic fibrosis product candidate 4D-710 below, we have yet to conduct IND-enabling studies with 4D-710. We expect to initiate IND-enabling studies with 4D-710 in the first half of 2020.

Aerosol Delivery with 4D-A101 in NHP Resulted in Genome Localization and Protein Expression in All Lung Samples



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 *CFTR* gene. Cystic Fibrosis is a multisystem disorder affecting primarily the pulmonary, gastro-intestinal tract, pancreas and reproductive organs. 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 an eventual end stage respiratory failure. There is no cure for Cystic Fibrosis and the median age of death for Cystic Fibrosis patients is 39 years. 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. Cystic Fibrosis patients 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, for patients with certain gene mutations, three therapies from Vertex have been approved for marketing in the United States and the European Union. Kalydeco (ivacaftor—a CFTR potentiator), Orkambi (ivacaftor plus lumacaftor—a CFTR corrector), and Symdeko (ivacaftor plus tezacaftor—also a CFTR corrector) were all approved based on their ability to improve lung function in genetically defined subsets of Cystic Fibrosis patients. Additionally, an NDA was recently filed by Vertex for the triple combination of VX-445 plus Symdeko (ivacaftor plus tezacaftor), which Vertex management 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.

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.

Competition and Differentiation—Viral Vector Gene Therapy including AAV for Cystic Fibrosis

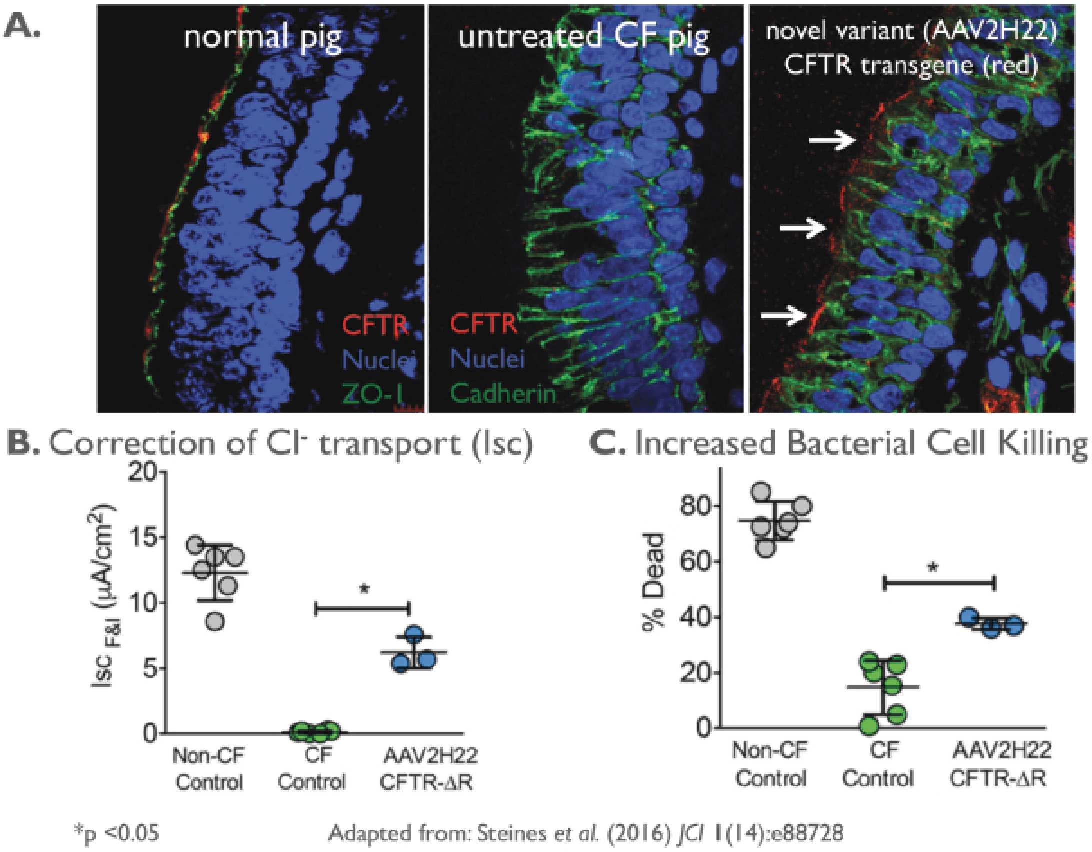
A number of biotechnology companies are pursuing gene therapy solutions to treat Cystic Fibrosis, including with conventional AAV vectors. In addition to being in early stages of development, these developmental AAV gene therapies are not, to our knowledge, comprised of AAV vectors evolved for aerosol delivery in NHP. In addition, these products were not designed for resistance to pre-existing antibodies to conventional AAVs. As a result, while we have not initiated any clinical trials for 4D-710, we believe it is the only AAV gene therapy product candidate designed specifically with a vector selected for aerosol delivery to NHP, and to have antibody-resistance.

Preclinical Proof-of-Concept Studies

Our co-founder Dr. Schaffer and his academic colleagues conducted preclinical proof-of-concept (POC) 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 POC studies, our product candidate 4D-710 will utilize a different vector (4D-A101), which has been designed to package the same *microCFTR* gene payload in a customized vector (4D-A101) that was identified through a directed evolution process for aerosol delivery in NHP. We expect to initiate IND-enabling studies with 4D-710 in the first half of 2020.

Dr. Schaffer and his colleagues first observed the potential to treat Cystic Fibrosis via aerosolized delivery of an evolved AAV variant (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 microCFTR using the *AAV2H22 vector* resulted in CFTR expression in diseased pig lungs with expression patterns that resembled those observed in normal pig lungs as well as in humans (Panel A). In addition to CFTR protein expression, *AAV2H22-CFTR* gene therapy also resulted in a significant increase in chloride ion transport (Isc) compared to untreated controls (Panel B) as well as a reduction in bacterial colonies within the lungs of treated animals (Panel C).

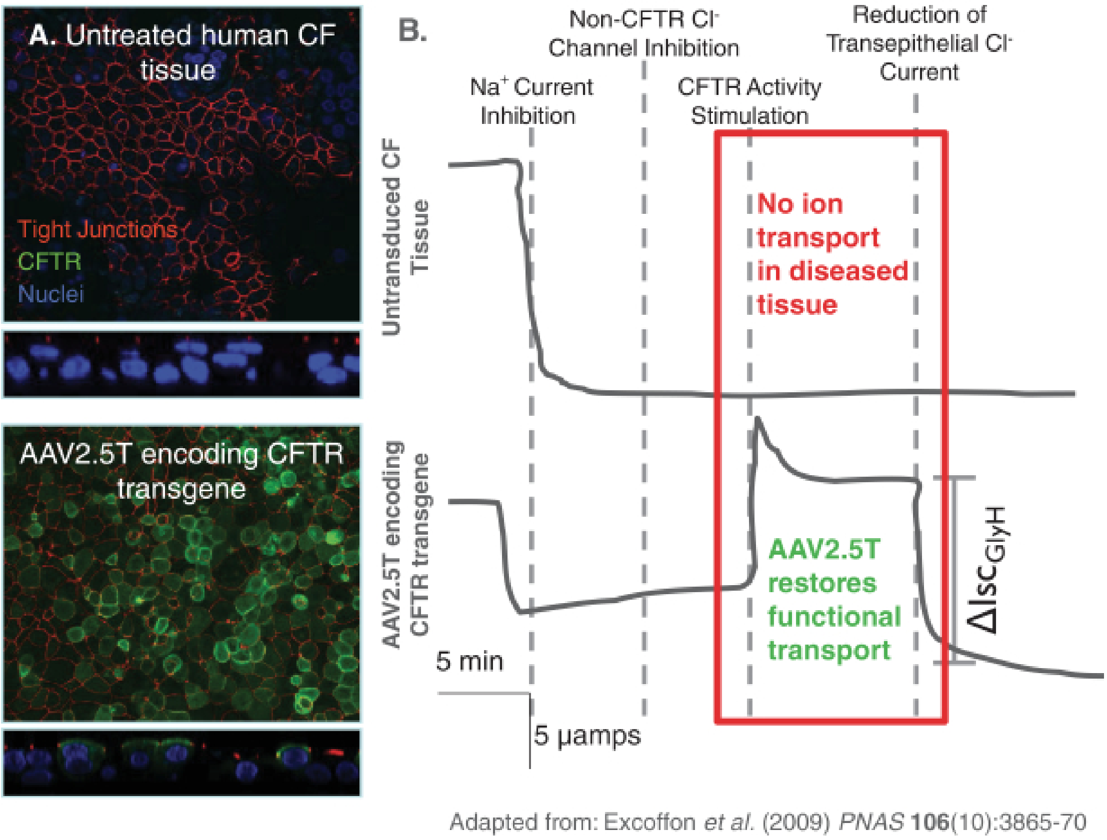
Illustrative Images in Panel (A) Below Exhibit the Pattern of CFTR Expression Observed by Steines et al. in Normal Pigs, Untreated CF Pigs and CF Pigs Treated with AAV2H22 Carrying the MicroCFTR Transgene Payload (Same Transgene Utilized in 4D-710, but Different AAV Vector). The Study Involved Six Healthy Pigs, Six Untreated CF Pigs and Three AAV2H22.MicroCFTR-Treated CF Pigs. These Animals Are Represented by the Dots in Each of the Graphs (B) and (C) which Illustrate the Range of Responses Between Animals, and the Significant Difference Between Treated and Untreated CF Pigs.



CFTRDR = 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
Isc = short circuit current, a measurement of Cl- movement through cell membranes
µA = microAmp
cm^2 = square centimeter.

In addition, Dr. Schaffer and colleagues used directed evolution in an *in vitro* human organotypic air-liquid interface model of Cystic Fibrosis lung epithelium to select AAV2.5T, which we in-licensed and termed 4D-A100. In preclinical studies, AAV2.5T carrying microCFTR transduced human lung epithelial tissue and resulted in expression of functional protein as suggested by increased chloride ion (Cl-) transport (Isc) as compared to untreated control (Panel B).

Excoffon et al. Previously Observed Restoration of CFTR Expression and Chloride Transport in Cystic Fibrosis Patient-Derived Airway Epithelium with AAV2.5T Vector Carrying MicroCFTR Payload (Same Payload, but Different Proprietary AAV Vector, Utilized in 4D-710).



CF = Cystic Fibrosis
Na+ = sodium ion
IscGlyH = short circuit current, a measurement of Cl- movement through cell membranes
µamps = microAmp
min = minute

We believe that these results provide evidence suggesting that the directed evolution platform enabled isolation of viral vectors that could penetrate the mucus layer of diseased Cystic Fibrosis lungs and deliver functional CFTR protein in a well-validated large animal model of the disease.

Pharmacology and Toxicology Studies

We plan to expand on these results and to conduct dose-ranging and durability studies with 4D-710, and to carry out planned GLP toxicology and biodistribution studies to enable an IND filing and clinical trials in patients. We plan to initiate IND-enabling toxicology and biodistribution studies in first half of 2020.

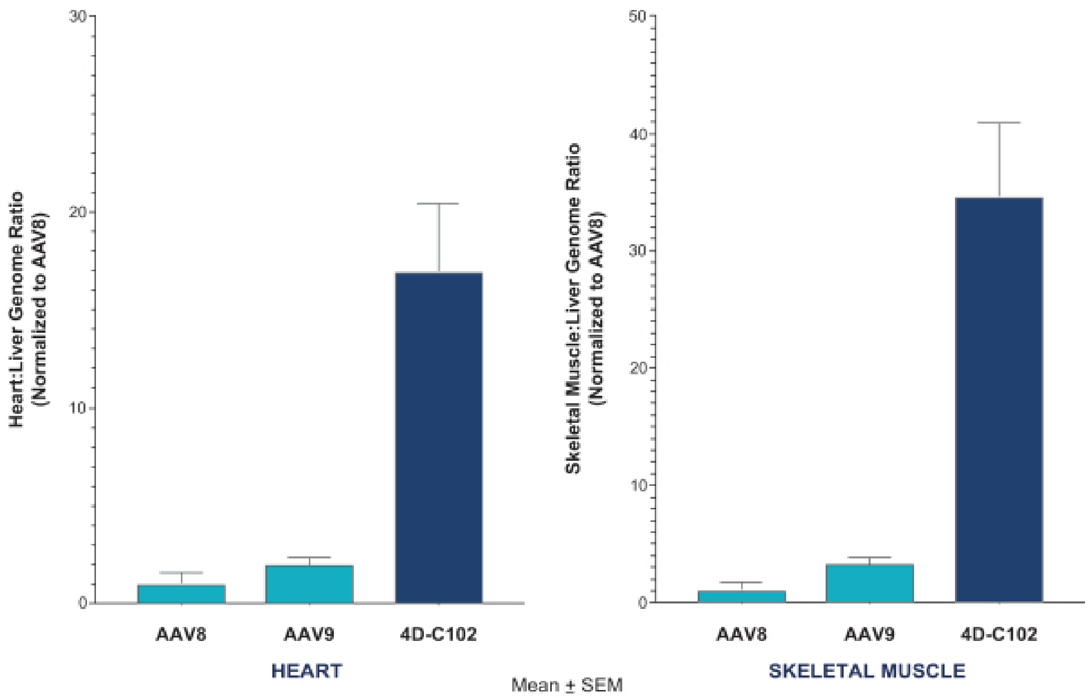
Product Candidates in Lead Optimization for the Treatment of Duchenne Muscular Dystrophy

Target Product Profiles

We wholly-own our product candidates that are in lead optimization for muscular dystrophies, including for DMD. These product candidates are designed to treat different patient populations within DMD. We are currently in lead optimization for product candidates using our proprietary 4D-C102 vector, which is designed for efficient, low dose intravenous delivery to cardiac and skeletal muscle tissues, to have minimal toxicities, and potential resistance to pre-existing antibodies to conventional AAVs in the human population. A second product candidate in lead optimization has been selected from our proprietary 4D-STAR100 vector, which is designed for resistance to pre-existing antibodies to conventional AAVs in humans. Thus, this product candidate is designed for the treatment of patients who have either been excluded from receiving AAV gene therapy treatments due to their antibody titers, or who have received prior treatment with another AAV gene therapy and we believe would potentially benefit from re-dosing. The promoter used in these product candidates has been observed to be active in both cardiac and skeletal muscle cells. We are evaluating several mini-dystrophin transgene payloads that have preclinical or clinical proof-of-concept.

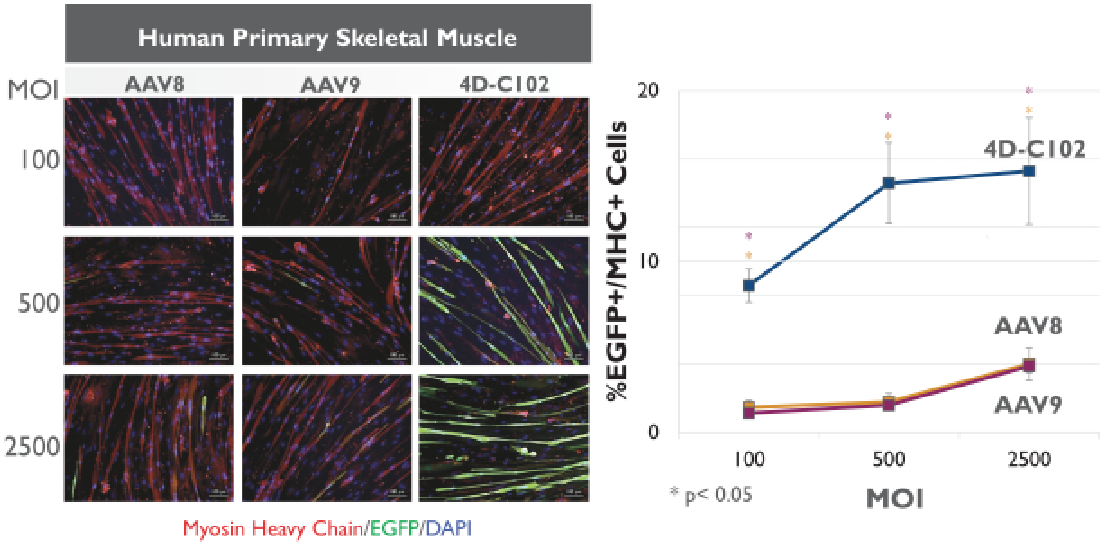
Additionally, in preclinical studies 4D-C102 improved delivery to muscle cells, and in doing so, did not increase delivery to the liver. 4D-C102 was observed to be significantly more selective for muscle tissue versus liver tissue when compared to both AAV8 and AAV9 as demonstrated below.

4D-C102 Intravenous Targeting to NHP
Skeletal Muscle and Cardiac Tissue Versus Liver Tissue was Superior to AAV8 and AAV9



Moreover, 4D-C102 transduced human skeletal muscle with EGFP more efficiently than did AAV8 or AAV9 *in vitro* as demonstrated below.

4D-C102 Exhibited Superior Transduction of Human Primary Skeletal Muscle in Vitro when Compared to Conventional AAV8 and AAV9 Vectors



MHC = myosin heavy chain, a marker of skeletal muscle cell identity
%EGFP+/MHC+ Cells = the percentage of EGFP-expressing cells within the MHC-expressing skeletal muscle cell population, a quantification of the transduction efficiency of the capsid for the target cell type.

Disease Background, Unmet Medical Need and Target Patient Population

DMD is a progressive and fatal muscular-wasting disease, and one of the most prevalent rare genetic diseases, with an estimated prevalence of 10,000 to 15,000 cases in the United States. DMD is caused by inadequate production of functional dystrophin, a protein necessary for muscle function, as a result of mutations in the dystrophin gene. Early indicators of disease due to muscle weakness include difficulty walking or jumping, frequent falling over and becoming fatigued more easily. By approximately 12 years of age, most DMD patients will need to use a wheelchair on a regular basis. In the later stages of disease progression, life-threatening heart and respiratory conditions become common. Cardiomyopathy, heart disease due to weakened cardiac muscles, which may result in death of patients in their twenties.

Competition and Differentiation—Viral Vector Gene Therapy with Conventional AAV for DMD

Sarepta is commercializing Exondys 51 for patients who have a confirmed mutation of the *DMD* gene amenable to exon 51 skipping, which affects about 13% of the population with DMD. Currently, Pfizer, Sarepta and Solid Biosciences are developing AAV therapy treatments for DMD. All three are in early clinical trials in boys with DMD with products utilizing conventional AAV vectors administered by IV infusion.

Preclinical proof-of-concept has been observed in a dog model of DMD in which a truncated version of the dystrophin gene, microdystrophin, was delivered using conventional AAV leading to stable expression and prevention of dystrophic damage in skeletal muscles; long-term effects on heart function were not reported. The AAV vectors used in clinical-stage products to date are naturally-occurring conventional AAV capsids AAVrh74 (similar to AAV8) and AAV9 and therefore are not specifically targeted to human cardiac or skeletal muscle tissue. AAV gene therapy in DMD patients treated intravenously by Nationwide Children's Hospital and Sarepta has resulted in transgene expression within skeletal muscle biopsies and a decrease in serum markers of muscle inflammation including creatine kinase. Sarepta has also reported anecdotal improvements in boys' functional performance without signs of adverse effects after nine months. AAV gene therapies for DMD utilizing these conventional vectors have been subject to inflammation-related toxicity issues and manufacturing challenges.

In addition to requiring high doses, patients have been excluded from clinical trials due to significant pre-existing neutralizing antibody titers to AAVrh74 and AAV9. This antibody-based exclusion from treatment limitation increases in frequency with patient age. Finally, as patients grow and develop more muscle mass following AAV treatment, re-dosing with AAV gene therapy would likely be beneficial. AAV vectors that are not neutralized by antibodies to AAVrh74 and AAV9 would therefore be highly desirable for subsequent treatment. We believe our proprietary vectors that were selected for resistance to antibodies to conventional AAVs have potential in this clinical situation.

Pharmacology and Toxicology Programs

We expect to complete lead optimization and to identify our lead research product candidate in 2020.

Ophthalmological Diseases

We have a broad partnership with Roche in ophthalmology, excluding ddRNAi delivery. Roche is a leader in ophthalmology biotherapeutics development and commercialization. In the ophthalmology field, we and Roche both have the right to declare product candidates. Roche has an option to acquire rights to product candidates declared by us prior to initiation of a pivotal clinical trial by paying an option fee as well as milestone and royalty payments that are higher than for Roche-declared product candidates. If exercised, Roche will assume all commercial and development-related costs.

Approximately 200 rare genetic diseases of the eye have been described, in addition to large market indications such as macular degeneration, diabetic retinopathy and glaucoma. The retina is an attractive tissue to target using gene therapy for the following reasons:

- Therapeutics can be easily administered locally (with intravitreal delivered vectors only)
- The small volume of retinal tissue requires minimal doses
- The eye is a relatively immune-privileged organ
- A number of clinically-validated endpoints, with rapid readouts, have been defined

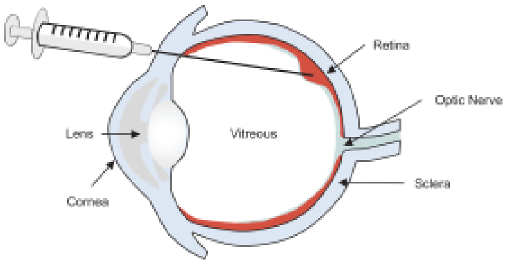
Initial AAV gene therapy products for the eye have displayed limitations associated with conventional AAVs. The eye is a complex organ composed of multiple types of cells and tissues such as retina, optic nerve, cornea and the iris. We believe gene therapies are effective only when target cells and tissues receive and express the proper transgene in a widespread fashion. Naturally-occurring conventional AAV vectors such as AAV2 do not transduce the primate retina efficiently after intravitreal injection, likely due to the inner-limiting membrane acting as a barrier to AAV.

As a result, the majority of conventional AAV product candidates studied in humans, including the marketed product Luxturna (voretigene neparvovec-rzyl) from Spark Therapeutics, are administered by subretinal injection surgery, a complex procedure performed in an operating room by highly-specialized retinal surgeons. This route of administration, typically using AAV2, generally results in a minority of retina area being transduced. Investigators have reported transduction of less than 10% of the retina in primates and humans. Therefore, in most patients, the majority of retinal tissue is left untreated. In addition, retinal detachment can occur, and cataracts routinely result after subretinal injections. Finally, ophthalmic surgeons must be specially trained for this operator-dependent surgical technique, thus limiting the number of sites and ophthalmologists who can perform the surgery.

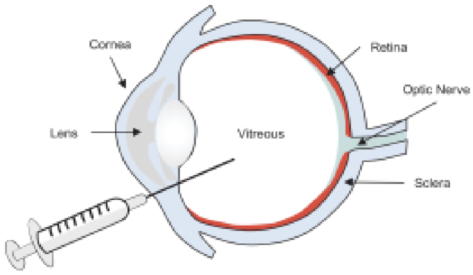
We are developing a product to be administered by intravitreal injection, which includes a vector that tranduces the entire retinal surface area. Intravitreal injection is performed routinely thousands of times every day in the United States and European Union for administration of anti-VEGF protein therapeutics for Wet AMD. Procedure-related complications are uncommon, and the procedure can be carried out in the majority of out-patient eye clinics in the United States.

Key Aspects of the Intravitreal and Subretinal Ocular Injection Routes Which We Considered when Designing Our Target Product Profile Are Listed Below

subretinal



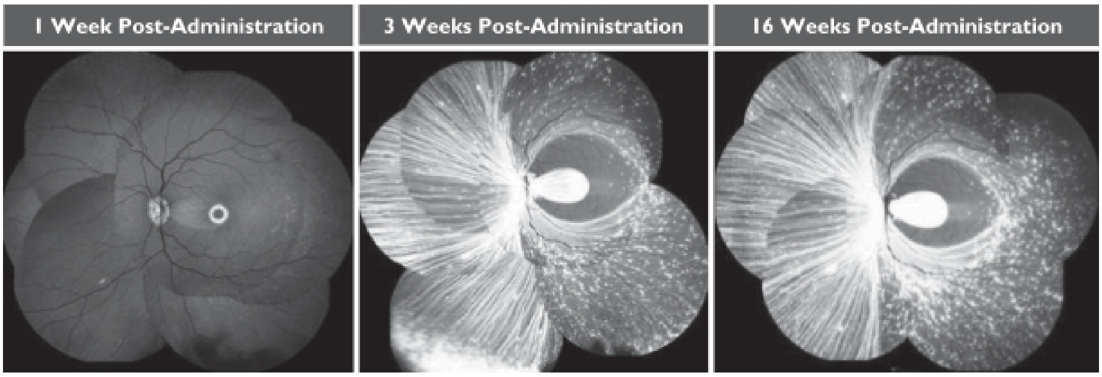
intravitreal



	subretinal	intravitreal
Retinal coverage	Bleb area only (estimated <10% of total retina surface area)	Up to 100% of total retina surface area
Simultaneous Bilateral injection possible	No	Yes
# Injection procedures performed in U.S. (daily)	Not used in routine clinical practice	Estimated >5,000 per day
Operating room required	Yes	No
Routine out-patient procedure	No	Yes
Cataract development risk due to associated vitrectomy	~80%	N/A

We utilized our Therapeutic Vector Evolution platform to create and discover proprietary vectors we believed to be suitable for intravitreal injection and transduction of the retina. Assuming our preclinical results are substantiated by our planned clinical trials, we believe the use of intravitreal injection will result both in a more accessible mode of administration and a higher percentage of retinal cells that express our proprietary vectors.

Widespread, Robust Retinal Transduction of NHP Retina Observed Following Administration of 4D-R100 Over Time (Heidelberg Spectralis Images, in Life. EGFP Represented in White)



4D-125 for the Treatment of XLRP

Target Product Profile

We are developing 4D-125 for the treatment of XLRP. This product candidate is comprised of our proprietary intravitreal vector 4D-R100 carrying a codon-optimized *RPGR* and designed to address all stages of XLRP. In non-human primate models, we have observed widespread transduction and transgene expression across the entire retinal surface, in contrast to localized results with subretinal injection of AAV vectors. IND-enabling studies with 4D-125 are expected to be completed in 2019, and 4D-125 is expected to enter clinical trials in mid-2020.

Disease Background, Unmet Medical Need and Target Patient Population

XLRP is a rare inherited X-linked recessive genetic disorder, which causes progressive vision loss and blindness in boys and young men. It is characterized by dysfunction and degeneration of photoreceptors in the retina. Seventy percent of cases are caused by mutations in the *retinitis pigmentosa GTPase regulator* (RPGR) gene. Loss of RPGR function in retinal cells causes the progressive loss of rod and cone photoreceptors, leading to the loss of vision experienced by patients. Symptoms of XLRP are initially characterized by night blindness, followed by loss of peripheral visual field, decreasing visual acuity and eventually blindness. Males are usually the most affected with symptoms starting in the early years of life. The estimated worldwide prevalence of XLRP due to RPGR variants is approximately one in 40,000 people, which represents approximately 20,000 patients in the United States and European Union.

Competition and Differentiation—Viral Vector Gene Therapy including AAV for XLRP

Conventional AAV gene therapy approaches are being developed to treat XLRP by delivering a functional copy of the *RPGR* gene by subretinal injection. Similar to treatment of other rare retinal diseases with AAV gene therapy, these XLRP therapies require delivery by subretinal injections; thus, only a small fraction of the retina is transduced and treated directly. Nightstar Therapeutics, recently acquired by Biogen, is developing NSR-RPGR for XLRP. Investigators reported interim Phase 1 clinical trial data in September 2018. Investigators concluded that microperimetry endpoints, which measure visual field function, improved in a subset of patients; they stated that "clinical proof-of-concept" was achieved with this data on visual improvement. AGTC and MeiraGTx are developing AAV gene therapy product candidates for XLRP to be administered by subretinal injection.

While 4D-125 also expresses the *RPGR* transgene, in contrast it is designed for intravitreal delivery. In addition, we believe intravitreal dosing may allow for treatment of patients earlier in their disease course, prior to loss of visual field than those who are typically included in subretinal injection trials. In this patient population, our goal will be to prevent vision loss.

Pharmacology and Toxicology Studies

In 2019, we initiated and expect to complete 4D-125 IND-enabling toxicology and biodistribution studies in NHP. We utilized the same GLP toxicology study design as what we submitted in the IND application for 4D-110. We plan to complete pharmacology studies in XLRP patient-derived cells.

Clinical Development Plans- Phase 1/2 Clinical Trial Design

We are targeting initiation of our planned 4D-125 Phase 1/2 clinical trial in mid-2020. We expect the Phase 1/2 clinical trial will be a single ascending dose trial of intravitreal injection with 4D-125 in patients with clinically-significant XLRP due to *RPGR* gene mutation. We anticipate the primary endpoint will be safety through six months after treatment, and definition of the maximum-tolerated or -feasible dose. We plan to assess efficacy based on functional visual field of the retina (e.g. with microperimetry) within three to six months after treatment. In addition, changes in retina field area over time will be measured by optical coherence tomography (OCT). Additional efficacy endpoints may include changes in functional endpoints including visual acuity. We expect that the earliest biomarker readouts from the Phase 1/2 clinical trial could be obtained by .

4D-110 for the treatment of Choroideremia

Target Product Profile

We are developing 4D-110, based on our proprietary intravitreal vector 4D-R100, for the treatment of the rare blinding disease, Choroideremia. 4D-110 is designed to deliver the *CHM* transgene, the dysfunctional gene in Choroideremia, to RPE cells. We have partnered this program with Roche. We are responsible for filing and maintaining the IND, and for conducting the Phase 1/2 clinical trial(s). We filed an IND application for 4D-110 in 2019. The FDA did not identify any hold issue and the IND was allowed to proceed. Roche will be responsible for conducting any pivotal clinical trials and commercialization, if approved. Our Choroideremia program is also supported by the Choroideremia Research Foundation. We plan to initiate a Phase 1/2 clinical trial in Choroideremia patients in the second half of 2020.

Disease Background, Unmet Medical Need and Target Patient Population

Choroideremia is an X-linked, slowly-progressive, degenerative disease of the retina and choroid of the eye caused exclusively by mutations in the *CHM* gene which codes for the protein, REP1. It is estimated approximately 10,000 individuals in the United States and the European Union have Choroideremia, with similar prevalence rates globally. While Choroideremia primarily affects men, some heterozygous females also suffer variable visual loss from the condition. No products are approved currently for the treatment of this disease in the United States or European Union.

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. Many Choroideremia patients are blind by the middle decades of life. 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.

Competition and Differentiation—Viral Vector Gene Therapy including AAV for Choroideremia

Conventional AAV gene therapy approaches are being developed to treat Choroideremia. Similar to treatment of other rare retinal diseases with AAV gene therapy, these Choroideremia therapies require delivery by subretinal injection; thus, only a small fraction of the retina is transduced and treated directly. Nightstar Therapeutics, recently acquired by Biogen, is developing a 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, with 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 trial is enrolling patients with advanced disease with decreased visual acuity.

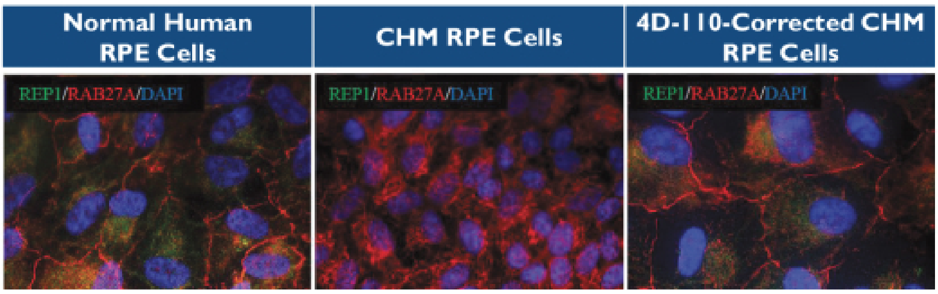
4D-110, which has not yet begun clinical trials, also expresses the *CHM* transgene. We believe the product candidate's intravitreal delivery data, which showed widespread transduction of the retina in NHPs, suggests that intravitreal treatment of Choroideremia patients with 4D-110 may result in better outcomes than can be achieved with subretinal approaches utilizing conventional AAV vectors. In addition, we believe intravitreal dosing may allow for treatment of earlier stage patients than is typical with subretinal injection trials.

Pharmacology and Toxicology Program

In 2018, we completed an IND-enabling toxicology and biodistribution study in NHP with 4D-110 administered by intravitreal injection. No meaningful toxicities were reported, and retinal transduction and transgene expression was observed across the retinal surface.

In these preclinical studies involving 50 NHPs, 4D-110 delivered the *CHM* gene resulting in REP1 protein expression as shown in green in the right panel below. Moreover, this expressed REP1 protein functionally corrected RAB27A trafficking from the cytoplasm to the cell membrane. When compared to normal RPE cells in the leftmost panel below, CHM cells in the rightmost panel which were treated with 4D-110 had RAB27A protein associated with their cell membranes as shown in red in both panels. By contrast, untreated diseased CHM cells in the center panel did not exhibit a pattern of cell membrane-associated RAB27A. In these cells, RAB27A was instead seen diffusely throughout the cytoplasm.

4D-110-Transduced RPE Cells Expressed Functional REP1 and Exhibited Corrected Trafficking of RAB27A
Left Panel: Healthy Human RPE Cells Exhibited Normal REP1 Expression in Green and Trafficking of RAB27A to the Cell Membrane in Red
Center Panel: Un-transduced CHM Patient-Derived RPE Cells Exhibited No Visible REP1 (i.e. No Visible Green Staining) and Un-trafficked RAB17A Diffusely Throughout the Cell in Red.
Right Panel: 4D-110-Transduced RPE Cells Exhibited Clear REP1 Expression in Green as well as Corrected RAB17A Trafficking to the Cell Membrane in Red.



Widespread retinal GFP-induced fluorescence was detected in the animals through study termination at six months. Onset of expression was detected by two-weeks following injection and increased up to 12 weeks, appearing to plateau thereafter until study completion. Fluorescence was widespread at this highest dose by direct EGFP fluorescence imaging (including periphery, macula and fovea). Histological analysis shows transduction was even more widespread and diffuse than the fluorescence pattern shown here. Following terminal sacrifice at days 22, 29 or 58, dose-dependent EGFP expression was also observed in the Cynomolgus monkey retina. 4D-R100 mediated broad transduction of retinal pigmented epithelia, photoreceptors, and retinal ganglion cells across central, macula and peripheral regions of the retina.

Clinical Development Plans—Natural History Patient "Run-In" Study

We have fully enrolled a natural history trial of approximately 50 patients with CHM to document the rate of visual and anatomical decline, and to identify candidates who are most likely to benefit from participation in our planned Phase 1/2 clinical trial. We expect that some of these subjects will enroll in our planned Phase 1/2 clinical trial or other future trials we may conduct.

Clinical Development Plans—Phase 1/2 Trial Design

We plan to initiate a Phase 1/2 clinical trial for 4D-110 in the second half of 2020. The trial will be a single ascending dose trial of intravitreal injection with 4D-110 in patients with clinically-significant CHM due to *CHM* gene mutation. The primary endpoints will be safety through six months after treatment, and definition of the maximum-tolerated or -feasible dose. Efficacy will be assessed by measuring changes over time in both best corrected visual acuity as well as OCT endpoints.

Research Candidates for the Treatment of Wet AMD

Target Product Profiles

In addition to rare ophthalmic diseases, we are also evaluating AAV gene therapy candidates for large market diseases. We have constructed product candidates in lead optimization, using the 4D-R100 vector, designed to deliver various *anti-VEGF* transgene candidates to treat Wet AMD and other related disorders. We believe these *anti-VEGF* transgene candidates express proteins that have a high degree of similarity to approved anti-VEGF protein therapeutics, which we believe may increase the likelihood of technical success with these product candidates.

Disease Background, Unmet Medical Need and Target Patient Population

Wet AMD is a type of macular degeneration where abnormal blood vessels (choroidal neovascularization) grow into the macula of the retina. As a consequence, retina swelling (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 incidences of Wet AMD in the United States alone. Wet AMD accounts for 10% of all diagnosed cases of AMD, but it results in 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.

The current treatment paradigm for Wet AMD is intravitreal injection of patients with anti-VEGF proteins which inhibit the proliferation of new blood vessels, reducing edema and bleeding and some visual acuity to be recovered. Most anti-VEGF therapies require repeated intravitreal injections every few months to obtain full efficacy. However, 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 patient compliance.

We believe Wet AMD is an ideal candidate application for gene therapy. There are multiple products on the market that validate the anti-vascular endothelial growth factor or anti-VEGF therapeutic approach. Delivering intravitreal gene therapies to the eye is straightforward, and there is an advantage for a single dose therapy that can provide long-term efficacy in patients for whom compliance, or treatment resistance, is a problem.

Competition and Differentiation—Viral Vector Gene Therapy including AAV for Wet AMD

Conventional AAV gene therapy approaches are being developed to treat Wet AMD by delivering a functional copy of an *anti-VEGF* gene by either subretinal injection or intravitreal administration. To our knowledge, these assets are in Phase 1 or Phase 1/2 clinical trials.

Pharmacology and Toxicology Program

To date, we have identified at least four research candidates with potential for anti-VEGF activity. Our *in vitro* experiments have shown expression of the therapeutic transgenes from RPE cells, which resulted in VEGF binding and neutralization. We expect to complete pilot toxicology studies for research candidates utilizing 4D-R100 in NHP in 2020.

Promoter Discovery Platform: Directed Evolution

We are generating next-generation optimized promoter elements through directed evolution. 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 safety and/or efficacy, as well as any necessary size constraints. Under a Sponsored Research Agreement with UC Regents, we are working with our co-founder Dr. Schaffer to create customized and proprietary promoters for use in our products. Libraries of novel and diverse synthetic promoters have been engineered, currently comprising approximately five million unique sequences, and promoter selections will be applied to identify the best promoters within the libraries for any Target Promoter Profile.

Human Cell and Disease Modeling

In order to fulfill our strategy to extensively characterize our vectors and products prior to treatment in patients, we have designed and developed a robust in-house human cell and disease modeling platform. Our group of scientists is experienced in the use of induced pluripotent stem (iPS) cell and embryonic stem (ES) cell techniques to generate and characterize human cell models to evaluate vector transduction, transgene expression and transgene product function. This core resource allows us to perform detailed *in vitro* pharmacology and toxicology evaluations together with head-to-head comparisons between different AAV capsids, promoter elements and transgene payloads. We have differentiated and characterized the following human cell types:

Cell Cultures:

- Ventricular phenotype cardiomyocytes (cardiac muscle cells)
- Skeletal muscle myofibers
- Lung epithelial cells
- Retinal cells: RPE, photoreceptors and ganglion cells
- Hepatocytes (liver cells)
- Neural cells
- Endothelial cells

Tissue Cultures and Organotypic Tissues:

- Lung Air Liquid Interface
- Optic vesicles

Of note, these cells and models can be derived from both normal human donors and from patients with specific genetic diseases of interest. Patient-derived cells used in our preclinical pharmacology studies include RPE cells from Choroideremia patients, retinal cells from patients with XLRP and cardiomyocytes, fibroblasts and endothelial cells from patients with Fabry disease.

Manufacturing

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 a robust in-house manufacturing platform. Some companies in the field in-license clinical trial material or manufacturing technologies from other companies or academic manufacturing centers. In contrast, our manufacturing processes have been developed internally in our own process development labs. Our current in-house manufacturing capabilities allow us to supply clinical trial materials for early stage clinical trials. We intend to further scale these capabilities to support later stage programs and indications requiring higher doses. In addition to our internal activities, we also work with CMOs, with work currently ongoing at Paragon and WuXi.

Process and Capabilities

We use robust and scalable manufacturing unit operations throughout the vector characterization process and product development. 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 columns used in our process are from stable sources including General Electric.

Our team has extensive experience with the manufacturing and analytical testing of numerous unique AAV capsids. To date, our team has internally manufactured approximately 50 unique AAV vector capsids, including both proprietary evolved 4DMT capsid variants and naturally-occurring capsids. Our team has manufactured over 100 total lots of AAV vectors. This total includes 9 lots of material for GLP toxicology and biodistribution studies. We plan to initiate our first in-house manufacturing run for clinical trial material for use in patients, according to cGMP, in 2019.

Facilities

Our manufacturing facilities are on site at company headquarters in Emeryville, California and include a process development lab, an analytical development lab, and a larger-scale manufacturing facility. Our manufacturing facility is approximately 800 square feet, and we intend to build a second cGMP facility that is approximately 8,000 square feet. In this new facility, we expect to utilize large-scale bioreactors that are designed to enable higher titer clinical trial material lots for clinical trials. These manufacturing facilities are also designed for production of material for GLP toxicology and biodistribution studies.

Team

Our team of twenty highly-trained individuals is led by our Chief Technical Officer, Dr. Kamal; 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 with manufacturing multiple AAV 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 AVXS-101 or Zolgensma (Novartis).

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.

Our solely owned patent portfolio includes one pending U.S. non-provisional application, thirty-one pending foreign applications, one of which has been allowed, one granted foreign patent and two pending international applications. We expect that United States and European patents and the patent applications in this portfolio, if issued, would expire between May 12, 2037 and November 26, 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.

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, Thailand, United Arab Emirates, Ukraine, Vietnam and South Africa), the patent applications 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, where applicable, are expected to expire between May 12, 2037 and November 26, 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.

Our in-licensed patent portfolio includes four granted U.S. patents and six granted foreign patents; each of these patents is expected to expire between June 28, 2024. and June 13, 2029. Our in-licensed patent portfolio also includes three pending U.S. non-provisional patent applications, five pending foreign patent applications and one pending international patent application.

In other jurisdictions (currently, Canada, China, France, Germany, Great Britain, Hong Kong, Japan and Italy), the term and patent applications 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, where applicable, are expected to expire between June 29, 2024 and June 28, 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, sublicenseable, 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. Upon the achievement of specified development milestones in connection with the licensed products, Roche will be required to pay us up to $223.0 million. In addition, Roche is required to pay us up to $123 million in the event it reaches specified worldwide calendar year net sales thresholds in connection with the 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-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.

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 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 Option Agreement with AstraZeneca (previously MedImmune).

In December 2017, we entered into a Collaboration and Option Agreement (the MedImmune Agreement), with MedImmune, LLC (MedImmune). Under the MedImmune Agreement, we and MedImmune will collaborate to optimize AAV capsid variants for the delivery of certain genes to the lung for the treatment of chronic lung disease (the MedImmune Field), using our AAV technology. We are primarily responsible for the initial optimization and MedImmune has an option to select up to 3 capsid variants. Upon MedImmune's exercise of its option, and subject to its payment of the applicable option exercise fee, we will automatically grant MedImmune an exclusive, sublicenseable, worldwide license under certain of our intellectual property rights to make, use, sell, import, export or otherwise utilize the selected capsid variants and products containing such selected capsid variants and certain genes in the MedImmune Field. Following the exercise of its option, MedImmune will be responsible for the development and commercialization of the licensed products and has agreed to certain diligence obligations.

We received an upfront payment from MedImmune of $1.5 million. Upon MedImmune's exercise of its option, it will be required to pay us a one-time option exercise fee of $2 million. Upon the achievement of specified development milestones, MedImmune will be required to pay us up to $45.0 million on a licensed product-by-licensed product basis. MedImmune will be required to pay us tiered royalties on worldwide annual net sales of licensed products between low-single digit and mid-single digit percentage rates, subject to certain specified reductions. These 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 licensed product in such country and the expiration of the last-to-expire licensed patent right covering such licensed product (the MedImmune Royalty Term).

The MedImmune Agreement will expire on a product-by-product basis on the earlier of the expiration of the option period if the option for such product is unexercised by MedImmune or the MedImmune Royalty Term for the product. Either party may terminate the agreement in its entirety if the other party fails to cure its material breach within 90 days of receiving notice, subject to additional cure period in accordance with the terms of the agreement. Prior to its option exercise, MedImmune may terminate the agreement upon 30 days' prior written notice. Following its option exercise, MedImmune may terminate the agreement in its entirety or on a licensed product-by-licensed product basis upon 90 days' prior written notice.

If we terminate the agreement for MedImmune's material breach or if MedImmune terminates the agreement for convenience, our rights to the licensed products generally revert back to us. If MedImmune terminates the agreement for our material breach, MedImmune may retain its rights under the license that we grant to MedImmune under our intellectual property rights and MedImmune'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, sublicenseable, worldwide license under certain of our intellectual property 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 the New Variants (uniQure New Variants), and compounds and products containing the uniQure New Variants, that affect the uniQure Targets (Licensed Products). We granted uniQure an exclusive, sublicenseable, worldwide license under certain of our intellectual property rights to research, develop, make, use, and commercialize the Licensed Products. We retain all rights to the uniQure New Variants in the uniQure Field that affect targets other than the uniQure Targets (4DMT Targets). We also retain all rights to the New Variants that are not uniQure New Variants (4DMT New Variants), and compounds and products containing 4DMT New 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 later 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, 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 sublicensing to third parties our intellectual property rights licensed under the Amended and Restated uniQure Agreement or the Second uniQure Agreement at a percentage ranging from the mid-single digits to mid-twenties, depending on the stage of development at which the sublicense is granted.

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 uniQure 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 uniQuire a non-exclusive right for uniQure to develop and commercialize certain licensed products using the 4DMT New Variants in the uniQure Field to deliver transgene constructs that affect 4DMT 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 licensing party will also be required to pay the other party a portion of the amounts that it may receive for 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.

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. Each party may terminate either agreement for the other party's insolvency or bankruptcy. Each party may also terminate either agreement in its entirety 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 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). Under both UC Agreements, the UC Regents granted us an exclusive, sublicenseable 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 (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.

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

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 studies. 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, 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.

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.

Once a BLA has been submitted, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. 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. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter 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 Complete Response Letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response Letter, 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. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

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 drugs and 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. 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. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious disease or condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

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 if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

In addition, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA designates a product as a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation.

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

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 many 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 Chroideremia, 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

Any products manufactured or distributed by us pursuant to FDA approvals 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 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 governmental 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 (HITECH), and their respective implementing regulations, 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. Additionally, HITECH created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce HIPAA and seek attorneys’ fees and costs associated with pursuing federal civil actions. 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 takes effect on January 1, 2020 and has been dubbed the first “GDPR-like” law in the United States (referring to the EU’s General Data Protection Regulation, described below). The CCPA gives California residents expanded rights regarding their personal information. Although CCPA contains a HIPAA exemption, 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 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, repealing its predecessor directive and increasing responsibility and liability of pharmaceutical companies in relation to the processing of personal data of European Union data subjects. The GDPR, together with national legislation, regulations and guidelines of the European Union 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 European Economic Area (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. 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 manufactures 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. While the Texas U.S. District Court Judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect, and on December 30, 2018 the Texas District Court Judge issued an order staying the judgment pending appeal, it is unclear how this decision, subsequent appeals, and other efforts to repeal and 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 2027 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. At the federal level, the Trump administration’s budget proposals for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation. Further, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. 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

As of June 30, 2019, we had 57 full-time employees. Of these employees, 46 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.

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.

Legal Proceedings

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

MANAGEMENT

Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors as of June 30, 2019:

Name	Age	Position(s)
Executive Officers and Employee Directors		
David Kirn, M.D.	57	Chairman and Chief Executive Officer
August Moretti	68	Chief Financial Officer
Theresa Janke	44	Chief Operating Officer
Peter Francis, M.D., Ph.D.	50	Chief Medical Officer
Fred Kamal, Ph.D.	56	Chief Technical Officer, Head of Regulatory and Quality
Non-Employee Directors		
David Schaffer, Ph.D.	48	Director, Chief Scientific Advisor
Bill Burkoth, MBA	42	Director
Jacob Chacko, M.D., MBA	41	Director
Charles Theuer, M.D., Ph.D.	55	Director
Tony Yao, M.D., Ph.D.	47	Director

(1) Member of compensation committee.
(2) Member of audit committee.
(3) Member of nominating and corporate governance committee.

Executive Officers and Employee Directors

David Kirn, M.D., is our co-founder and has served as our Chief Executive Officer and Chairman of our board of directors since our inception in 2013. Dr. Kirn is an Adjunct Professor of Bioengineering at U.C. Berkeley. He currently serves as Executive Chairman of the board of the following privately held company: Ignite Immunotherapy Inc., where he is a co-founder. Dr. Kirn held senior development positions at Onyx Pharmaceuticals and Celgene, and he was a senior advisor on viral vector gene therapeutics and cancer immunotherapy for over 10 years with numerous companies, including Biogen Idec, Novartis, Cell Genesys, Pfizer and Bayer. Dr. Kirn received a B.A. in Physiology (Departmental Citation; Phi Beta Kappa) from U.C. Berkeley in 1985, an M.D. (Alpha Omega Alpha) from U.C. San Francisco Medical School in 1989 and completed internal medicine residency training at Harvard Medical School, Brigham and Women's Hospital (including a term as Chief Medical Resident at affiliated VA hospital). He has also completed hematology-oncology and clinical research fellowships at U.C. San Francisco and completed a certificate of business excellence from the Haas Business School at U.C. Berkeley. In 2013, he was awarded the Johnson & Johnson Entrepreneur Innovator award from the J&J Innovation Center. We believe that Dr. Kirn is qualified to serve as a member of our board of directors based on his perspective and the experience he brings as one of our founders and Chief Executive Officer, and because of his extensive experience at other life science companies.

August Moretti has served as our Chief Financial Officer since January 2019. Mr. Moretti previously served as Chief Financial Officer at Assertio Therapeutics (formerly Depomed, Inc.), a publicly held specialty pharmaceuticals company focused in pain and neurology, from January 2012 until August 2018. Mr. Moretti received his B.A. in Economics from Princeton University in 1972. He received his J.D. from Harvard Law School in 1975.

Theresa Janke is a co-founder and has served in positions of increasing responsibility since our inception. She has served as our Chief Operating Officer since April 2018. Ms. Janke previously served in various consulting roles in 2013-2014 including: Senior Director of Corporate Projects & Alliance Management at SillaJen, Inc. (formerly Jennerex Biotherapeutics Inc.), a biotech company focused on engineering and developing oncolytic immunotherapeutics, and Director, Clinical Research & Development—Strategy and Alliances at Celgene Corporation, a global biopharmaceutical company. Prior to that, she served in positions of increasing responsibility, including Director of Clinical Operations, at Jennerex Biotherapeutics Inc., an oncolytic immunotherapy biotech company, from 2007 through 2013. She is a co-founder and currently serves on the board of directors of Ignite Immunotherapy Inc., a private biotech company focused on oncolytic cancer vaccine discovery and development. Ms. Janke received a B.S. in Biopsychology from the U.C. Santa Barbara in 1996.

Peter Francis, M.D., Ph.D., has served as our Chief Medical Officer since January 2019. Dr. Francis previously served as our Senior Vice President, Clinical Translational R&D, and Retina Therapeutic Area Head from August 2018 to January 2019. Dr. Francis previously served as Chief Medical Officer at RetroSense Therapeutics from February 2012 until August 2016 when it was purchased by Allergan Inc. Dr. Francis practices as a physician at Orion Eye Center. Dr. Francis received his B.Sc. in Molecular Cell Biology from the University of Southampton, England in 1991. He earned his M.D. from the University of Southampton, England in 1992. He earned his Ph.D. in ophthalmic genetics from University College, London in 2000.

Fred Kamal, Ph.D., has served as our Chief Technical Officer since October 2018. Dr. Kamal previously served as Senior Vice President of Quality and Regulatory CMC for AveXis Inc., a gene therapy company, from May 2017 through August 2018. Prior to AveXis, Dr. Kamal served as the Vice President of Quality for Juno Therapeutics from May 2015 through April 2017 and prior to that Dr. Kamal served as the Vice President of Quality and Regulatory CMC for Intermune Inc. from January 2013 through March 2015. Dr. Kamal received his B.S. in Chemistry from San Jose State University in 1986. Dr. Kamal received his M.Sc. in Chemistry from The American University in 2000. He received his Ph.D. in Chemistry from The American University in 2003.

Non-Employee Directors

David Schaffer, Ph.D. is our co-founder and has served as our Chief Scientific Advisor and a member of our board of directors since our inception in 2013. Dr. Schaffer has served as a Professor of Chemical and Biomolecular Engineering, Bioengineering, Molecular and Cell Biology, and the Helen Wills Neuroscience Institute at the U.C. Berkeley since 1999 and has served as the Director of the Berkeley Stem Cell Center since 2011. He current serves on the board of directors of the following publicly-held company: uniQure NV since January 2014. Dr. Schaffer received a B.S. in Chemical Engineering from Stanford University in 1993. He earned his Ph.D. in Chemical Engineering from the Massachusetts Institute of Technology in 1998. We believe Dr. Schaffer is qualified to serve as a member of our board of directors based on his prospective and the experience he brings as one of our founders, and because of his scientific expertise and leading work in directed evolution.

Bill Burkoth, MBA, has served as a member of our board of directors since March 2019. Mr. Burkoth has served on the venture investments team of Pfizer Inc. since 2004 and currently serves as their executive director. Mr. Burkoth worked in business development at Galileo Pharmaceuticals, Inc. and at IntraBiotics Pharmaceuticals, Inc. from 2002 to 2004. Mr. Burkoth worked as an analyst at Bay City Capital, a life sciences venture capital firm, from 1999 to 2002. He previously served on the board of directors of the following publicly-held company: NovoCure Limited from July 2009 to May 2019. Mr. Burkoth received a B.A. in Chemistry from Whitman College in 1999 and an M.B.A. from Columbia Business School in 2011. We believe Mr. Burkoth is qualified to serve as a member of our board of directors based on his finance background and his extensive investment experience in the life science industry.

Jacob Chacko, M.D., MBA, has served as a member of our board of directors since March 2019. Dr. Chacko has served as Chief Executive Officer of ORIC Pharmaceuticals, Inc., a clinical-stage oncology company focused on discovery and development of novel therapies against treatment-resistant cancers, since May 2018. Prior to ORIC, Dr. Chacko served as Chief Financial Officer of Ignyta, Inc., a publicly traded precision oncology company, from May 2014 until February 2018 when Ignyta was acquired by Roche Holdings, Inc. Prior to Ignyta, Dr. Chacko was Vice President at TPG Capital from August 2008 until May 2014. From 2002 until 2003, Dr. Chacko was a consultant serving healthcare clients at McKinsey & Company. Dr. Chacko currently serves on the board of directors of Turning Point Therapeutics, Inc., a publicly-traded biotechnology company, from November 2018. Dr. Chacko served on the board of directors of RentPath Inc., a digital media company, from 2011 until 2014, Envision Pharmaceutical Services, LLC from 2013 until 2014, Bonti, Inc., a biotechnology company, from February 2018 until October 2018 and the Packard Children's Health Alliance at the Lucile Packard Children's Hospital Stanford from 2013 until June 2017. Dr. Chacko currently chairs the Western Regional Selection Committee for the Marshall Scholarship. Dr. Chacko concurrently received his M.D. from the U.C. Los Angeles and his M.B.A. from Harvard Business School. Dr. Chacko received a M.Sc. from Oxford University as a Marshall Scholar. We believe Dr. Chacko is qualified to serve as a member of our board of directors based on his medical and finance background, his experience in investing in life science companies and his service on the boards of public and private companies.

Charles Theuer, M.D., Ph.D., has served as a member of our board of directors since December 2015. Dr. Theuer has served as President and Chief Executive Officer at Tracon Pharmaceuticals, Inc., since June 2006. He previously served as Chief Medical Officer at TargeGen Pharmaceuticals, Inc. until June 2006. He current serves on the board of directors of the following publicly-held companies: Tracon Pharmaceuticals Inc., since June 2006 and Oncternal Therapeutics Inc. since May 2018, where he serves on the Science and Development and Nominating and Corporate Governance committees. Dr. Theuer received a B.S. in Life Sciences from the Massachusetts Institute of Technology in 1985. He received his M.D. from U.C. San Francisco in 1989. He received his Ph.D. in Environmental Health Science from U.C. Irvine in 2002. We believe that Dr. Theuer is qualified to serve as a member of our board of directors based on his medical and scientific background and because of his experience in leading and serving on the boards of public and private life science companies.

Tony Yao, M.D., Ph.D. has served as a member of our board of directors since August 2018. Dr. Yao has served as portfolio manager of life science strategy at ArrowMark Partners since April 2012. He previously served as an equity analyst at Janus Capital Group until March 2012. He currently serves on the board of directors of the following publicly-held company: Precision Biosciences since June 2018, where he serves on the compensation and audit committee. Dr. Yao received a B.S. in biochemistry from Brown University in 1994. He earned an M.D. and a Ph.D. in Immunology from Stanford University in 2002. We believe that Dr. Yao is qualified to serve as a member of our board of directors based on his scientific background and his extensive experience in investing in life science companies.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Board Composition

Director Independence

Our board of directors currently consists of six members. Our board of directors has determined that all of our directors, other than Dr. Kirn, qualify as "independent" directors in accordance with The

Nasdaq Global Market listing requirements. Dr. Kirn is not considered independent because he is an employee. The Nasdaq Global Market's independence definition includes a series of objective tests, such as that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his or her family members has engaged in various types of business dealings with us. In addition, as required by The Nasdaq Global Market rules, our board of directors has made a subjective determination as to each independent director that no relationships exists that, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified Board of Directors

In accordance with our amended and restated certificate of incorporation to be in effect immediately prior to the consummation of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the consummation of this offering, we expect that our directors will be divided among the three classes as follows:

- the Class I directors will be and , and their terms will expire at the annual meeting of stockholders to be held in 2020;
- the Class II directors will be and , and their terms will expire at the annual meeting of stockholders to be held in 2021; and
- the Class III directors will be and , and their terms will expire at the annual meeting of stockholders to be held in 2022.

Our amended and restated certificate of incorporation will provide that the authorized number of directors may be changed only by resolution of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our board of directors or a change in control.

Voting Arrangements

The election of the members of our board of directors is governed by the Second Amended and Restated Investors' Rights Agreement, dated as of August 27, 2018, that we entered into with certain holders of our common stock and certain holders of our redeemable convertible preferred stock (the Investors' Rights Agreement) and the related provisions of our amended and restated certificate of incorporation.

Pursuant to the Investors' Rights Agreement, the holders of our common stock and redeemable convertible preferred stock who are parties to the Investors' Rights Agreement are obligated to vote for the election of certain designees of our board of directors which are as follows:

- one member designated by Pfizer, for which Mr. Burkoth has been designated;
- one member designated by the holders of a majority of our Series B redeemable convertible preferred stock, voting exclusively and as a separate class, for which Dr. Yao has been designated; and

- two members designated by the holders of a majority of our common stock (other than any common stock issued or issuable upon the conversion of the redeemable convertible preferred stock), voting exclusively and together as a single class, for which Dr. Kirn and Dr. Shaffer have been designated; and
- three members, who are not otherwise affiliated with any of our investors, the first of whom shall be mutually agreed upon by a majority of the other members of our board of directors, which is currently vacant; the second of whom shall be proposed by our management subject to the approval of a majority of the members of our board of directors, for which Dr. Theuer has been designated; and the third of whom shall be an individual that satisfies the independence, financial literacy and financial expertise requirements to serve as an audit committee chairperson pursuant to relevant SEC and Nasdaq laws and regulations, and mutually acceptable to a majority of the other members of our board of directors, for which Jacob Chacko has been designated.

The above provisions of Investors’ Rights Agreement will terminate upon the consummation of this offering and our amended and restated certificate of incorporation will be amended and restated, after which there will be no further contractual obligations or charter provisions regarding the election of our directors. Our directors hold office until their successors have been elected and qualified or appointed, or the earlier of their death, resignation or removal.

Leadership Structure of our Board

Our amended and restated bylaws and corporate governance guidelines will provide our board of directors with flexibility to combine or separate the positions of Chairman of our board of directors and Chief Executive Officer and to implement a lead director in accordance with its determination that utilizing one or the other structure would be in our best interest. Dr. Kirn currently serves as the chairman of our board of directors. In that role, Dr. Kirn presides over the executive sessions of our board of directors and as a liaison between management and our board of directors.

Our board of directors has concluded that our current leadership structure is appropriate at this time. However, our board of directors will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Role of our Board in Risk Oversight Process

Risk assessment and oversight are an integral part of our governance and management processes. Our board of directors encourages management to promote a culture that incorporates risk management into our corporate strategy and day-to-day business operations. Management discusses strategic and operational risks at regular management meetings, and conducts specific strategic planning and review sessions during the year that include a focused discussion and analysis of the risks facing us. Throughout the year, senior management reviews these risks with our board of directors at regular board meetings as part of management presentations that focus on particular business functions, operations or strategies, and presents the steps taken by management to mitigate or eliminate such risks.

Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. While our board of directors is responsible for monitoring and assessing strategic risk exposure, our audit committee is responsible for overseeing our major financial risk exposures and the steps our management has taken to monitor and control these exposures. The audit committee also monitors compliance with legal and regulatory requirements and considers and approves or disapproves any related person transactions. Our nominating and corporate governance committee monitors the effectiveness of our corporate governance guidelines. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Board Committees

Our board of directors has the following standing committees: an audit committee, a compensation committee and a nominating and corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business. The composition and functions of each committee are described below.

Audit Committee

Our audit committee oversees our corporate accounting and financial reporting process. Among other matters, the audit committee:

- appoints our independent registered public accounting firm;
- evaluates the independent registered public accounting firm's qualifications, independence and performance;
- determines the engagement of the independent registered public accounting firm;
- reviews and approves the scope of the annual audit and pre-approves the audit and non-audit fees and services;
- reviews and approves all related party transactions on an ongoing basis;
- establishes procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls or auditing matters
- discusses with management and the independent registered public accounting firm the results of the annual audit and the review of our quarterly financial statements;
- approves the retention of the independent registered public accounting firm to perform any proposed permissible non-audit services;
- monitors the rotation of partners of the independent registered public accounting firm on our engagement team in accordance with requirements established by the SEC;
- discusses on a periodic basis, or as appropriate, with management our policies and procedures with respect to risk assessment and risk management;
- is responsible for reviewing our financial statements and our management's discussion and analysis of financial condition and results of operations to be included in our annual and quarterly reports to be filed with the SEC;
- annually reviews and assesses internal controls and treasury functions including cash management procedures;
- investigates any reports received through the ethics helpline and report to our board of directors periodically with respect to the information received through the ethics helpline and any related investigations;
- reviews our critical accounting policies and estimates; and
- reviews the audit committee charter and the committee's performance at least annually.

Effective upon the consummation of this offering, the members of our audit committee will be , and . will serve as the chairperson of the committee. All members of our audit committee will meet the requirements for financial literacy under the applicable rules and regulations of the SEC and The Nasdaq Global Market. Our board of directors will have determined that is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of The Nasdaq Global Market. Under the rules of the SEC, members of the audit committee must also meet heightened independence standards. Our board of directors will have determined that each of , and are independent under the applicable rules of the SEC and The Nasdaq Global Market. The audit committee will operate under a written charter that satisfies the applicable standards of the SEC and The Nasdaq Global Market.

Compensation Committee

Our compensation committee oversees policies relating to compensation and benefits of our officers and employees. The compensation committee reviews and approves or recommends corporate goals and objectives relevant to compensation of our executive officers (other than our Chief Executive Officer), evaluates the performance of these officers in light of those goals and objectives and approves the compensation of these officers based on such evaluations. The compensation committee also reviews and approves or makes recommendations to our board of directors regarding the issuance of stock options and other awards under our stock plans to our executive officers (other than our Chief Executive Officer). The compensation committee reviews the performance of our Chief Executive Officer and makes recommendations to our board of directors with respect to his compensation and our board of directors retains the authority to make compensation decisions relative to our Chief Executive Officer. The compensation committee will review and evaluate, at least annually, the performance of the compensation committee and its members, including compliance by the compensation committee with its charter.

Effective upon the consummation of this offering, the members of our compensation committee will be , and . will serve as the chairman of the committee. Each of the members of our compensation committee will be independent under the applicable rules and regulations of The Nasdaq Global Market, will be a “non-employee director” as defined in Rule 16b-3 promulgated under the Exchange Act and will be an “outside director” as that term is defined in Section 162(m) of the U.S. Internal Revenue Code of 1986, as amended (Section 162(m)). The compensation committee will operate under a written charter that satisfies the applicable standards of the SEC and The Nasdaq Global Market.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee is responsible for making recommendations to our board of directors regarding candidates for directorships and the size and composition of our board of directors. In addition, the nominating and corporate governance committee is responsible for overseeing our corporate governance policies and reporting and making recommendations to our board of directors concerning governance matters.

Effective upon the consummation of this offering, the members of our nominating and corporate governance committee will be , and . will serve as the chairman of the committee. Each of the members of our nominating and corporate governance committee will be an independent director under the applicable rules and regulations of The Nasdaq Global Market relating to nominating and corporate governance committee independence. The nominating and corporate governance committee will operate under a written charter that satisfies the applicable standards of the SEC and The Nasdaq Global Market.

Compensation Committee Interlocks and Insider Participation

During the year ended December 31, 2018, our compensation committee consisted of Dr. Margi McLoughlin, who resigned from our board of directors on March 20, 2019, Dr. Huh, who resigned from our board of directors on December 31, 2018 and Dr. Theuer. None of the members of our compensation committee during 2018 nor any of the current members of our compensation committee has at any time been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of our board of directors or compensation committee of any entity that has one or more executive officers on our board of directors or compensation committee.

Board Diversity

Upon consummation of this offering, our nominating and corporate governance committee will be responsible for reviewing with our board of directors, on an annual basis, the appropriate characteristics, skills and experience required for our board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and our board of directors, in approving (and, in the case of vacancies, appointing) such candidates, may take into account many factors, including but not limited to the following:

- personal and professional integrity;
- ethics and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly held company;
- experience in the industries in which we compete;
- experience as a board member or executive officer of another publicly held company;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- conflicts of interest; and
- practical and mature business judgment.

Currently, our board of directors evaluates, and following the consummation of this offering will evaluate, each individual in the context of our board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of Business Conduct and Ethics

Prior to the consummation of this offering, we will adopt a code of business conduct and ethics that will apply to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the consummation of this offering, the code of business conduct and ethics will be available on our website. We expect that any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately prior to the consummation of this offering, will contain 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, which will become effective immediately prior to the consummation of this offering, will 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 will 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.

Director Compensation

Historically, we have not had a formalized non-employee director compensation program. However, we have generally adopted a practice of paying director fees of $35,000 per year and issuing options to purchase shares of our common stock targeted at certain percentages of our fully diluted capitalization to our independent directors. We paid director fees in the amount of $35,000 to both of our independent directors, Dr. Theuer and Dr. Huh, for their board service in fiscal year 2018. In addition, during April 2018, we issued to Dr. Theuer two options to purchase 13,684 shares of our common stock each, with per share exercise prices of $3.19, one of which was vested as to 100% of its shares at time of grant, and the other of which vested as to 100% of its shares in March 2019, subject to Dr. Theuer's continued service to us through such date. In addition, during April 2018, we issued to Dr. Huh two options to purchase 13,684 shares of our common stock each, with per share exercise prices of $3.19, one of which was vested as to 100% of its shares in at time of grant, and the other of which vested as to 100% of its shares in March 2019, subject to Dr. Huh's continued service to us through such date. All unvested options accelerate in full on a change in control. We did not make any other equity grants to our non-employee directors in 2018. In addition, we paid consulting fees in the amount of $50,000 to Dr. Schaffer for research services he provided to us in addition to his service as a member of the board of directors. We also provide reimbursement to our non-employee directors for their reasonable expenses incurred in attending meetings of our board of directors and committees of our board of directors.

We intend to approve and implement a compensation policy for our non-employee directors, or the Director Compensation Program, to be effective in connection with the consummation of this offering.

The following table summarizes the total compensation earned during the year ended December 31, 2018 for our non-employee directors.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	All Other Compensation ($)(2)	Total ($)
David Schaffer, Ph.D.	0	0	50,000	50,000
Charles Theuer, M.D., Ph.D.	35,000	60,757	0	95,757
Jacob Chacko, M.D.	0	0	0	0
Hoyoung Huh, M.D., Ph.D.	35,000	60,757	0	95,757
Tony Yao, M.D., Ph.D.	0	0	0	0
Bill Burkoth	0	0	0	0

(1) Amounts shown represent the grant date fair value of options granted during fiscal year 2018 as calculated in accordance with ASC Topic 718. See Note 12 of the financial statements included in this prospectus for the assumptions used in calculating this amount. As of December 31, 2018, Dr. Theuer held options to purchase 23,017 shares of our common stock, Dr. Huh held options to purchase 101,351 shares of our common stock and no other non-employee directors held any outstanding options or other equity awards.

(2) Amount represents $50,000 consulting payments paid to Dr. Schaffer in consideration for research services provided us in 2018.

EXECUTIVE COMPENSATION

The following is a discussion and analysis of compensation arrangements of our named executive officers (NEOs). This discussion contains forward looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt may differ materially from currently planned programs as summarized in this discussion. As an "emerging growth company" as defined in the JOBS Act, we are not required to include a Compensation Discussion and Analysis section and have elected to comply with the scaled disclosure requirements applicable to emerging growth companies.

We seek to ensure that the total compensation paid to our executive officers is reasonable and competitive. Compensation of our executives is structured around the achievement of individual performance and near-term corporate targets as well as long-term business objectives.

Our NEOs for fiscal year 2018 were as follows:

- David Kirn, M.D., our Chief Executive Officer;
- Peter Francis, M.D., Ph.D., our Chief Medical Officer (and formerly our Senior Vice President, Clinical Translational R&D Program Leader, Retina Therapeutic Area for the entirety of fiscal year 2018); and
- Fred Kamal, Ph.D., our Chief Technical Officer.

2018 Summary Compensation Table

The following table sets forth information concerning the compensation of our NEOs for the year ended December 31, 2018.

Name and Principal Position	Year	Salary ($)(1)	Bonus ($)(7)	Option Awards ($)(2)	Non-Equity Incentive Plan Compensation ($)(3)	All Other Compensation ($)(4)	Total ($)
David Kirn, M.D. *Chief Executive Officer*	2018	396,445	0	0	137,700	12,250	546,395
Peter Francis, M.D., Ph.D. *Chief Medical Officer(5)*	2018	270,000	24,300	200,024	65,610	46,204	606,138
Fred Kamal, Ph.D. *Chief Technical Officer(6)*	2018	70,303	9,552	1,855,340	19,931	9,439	1,964,565

(1) Amounts represent (i) for Dr. Kirn, $382,500 base salary earned in 2018 and $13,945 paid to him in 2018 in consideration for accrued vacation benefits lost as a result of a decrease in the maximum amount of vacation benefits that employees are able to accrue; (ii) for Dr. Francis, $157,500 consulting fee for services performed in 2018 prior to Dr. Francis' hire as a full-time employee in August 2018 and $112,500 base salary earned by Dr. Francis in 2018 as a full-time employee; and (iii) for Dr. Kamal, $70,303 base salary earned in 2018.

(2) Amounts shown represents the grant date fair value of options granted during fiscal year 2018 as calculated in accordance with ASC Topic 718. See Note 12 of the financial statements included in this registration statement for the assumptions used in calculating this amount.

(3) Amounts represent the annual performance-based cash bonuses earned by our NEOs based on the achievement of certain corporate performance objectives during 2018. These amounts were paid to the NEOs in early 2019. Please see the descriptions of the annual performance bonuses paid to our named executive officers under "2018 Bonuses" below.

(4) Amounts represent: (i) for Dr. Kirn, $12,250 for matching contributions made by us under our 401(k) plan; (ii) for Dr. Francis, $43,069 for reimbursements of travel expenses and $3,135 for matching contributions made by us under our 401(k) plan; and (iii) for Dr. Kamal, $9,439 for relocation expenses.

(5) Dr. Francis commenced employment with us in August 2018, and prior to such time served as a consultant to us.
(6) Dr. Kamal commenced employment with us in October 2018.
(7) Amounts represents discretionary, one-time cash bonuses paid to Drs. Francis and Kamal in late 2018 and early 2019 for their performance during 2018.

Outstanding Equity Awards at 2018 Fiscal Year End

The following table lists all outstanding equity awards held by our NEOs as of December 31, 2018. Dr. Kirn does not hold any outstanding equity awards as of December 31, 2018.

		Option Awards			
Name	Vesting Commencement Date(1)	Number of Securities Underlying Unexercised Options Exercisable (#)	Number Of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)	Option Expiration Date
Peter Francis, M.D., Ph.D.	9/30/2016(2)	37,830	37,170	3.19	4/19/2028
Fred Kamal, Ph.D.	10/11/2018	0	214,887	8.27	10/11/2028
	10/11/2018	0	71,930	8.27	12/19/2028

(1) Except as otherwise noted, options vest as to 25% of the shares on the one year anniversary of the vesting commencement date and vest as to 1/48th of the shares monthly thereafter, such that all awards will be vested on the four year anniversary of the vesting commencement date, subject to the holder continuing to provide services to us through such vesting date.
(2) The options vested as to 11,280 of the shares on the one year anniversary of the vesting commencement date and vest as to 1,770 of the remaining shares monthly thereafter, subject to the holder continuing to provide services through such vesting date.

Narrative to Summary Compensation Table

2018 Salaries

Our NEOs each receive a base salary to compensate them for services rendered to our company. The base salary payable to each NEO is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities.

For fiscal year 2018, Dr. Kirn's annual base salary was $375,000 from January 1, 2018 to March 31, 2018, and $385,000 from April 1, 2018 to December 31, 2018. Drs. Francis' and Kamal's base salaries were prorated for their start dates in August 2018 and October 2018, respectively.

2018 Bonuses

We maintain an annual performance-based cash bonus program in which each of our NEOs participated in 2018. Each NEO's target bonus is expressed as a percentage of base salary which can be achieved by meeting company goals at target level. The 2018 annual bonuses for Drs. Kirn, Francis and Kamal were targeted at 40%, 30% and 35%, respectively, of their respective base salaries. Our board of directors has historically reviewed these target percentages to ensure they are adequate, but does not follow a formula. Instead, our board of directors set these rates based on each NEO's experience in their role with us and the level of responsibility held by the NEO, which we believe directly correlates to their ability to influence corporate results.

For determining performance bonus amounts, our board of directors set certain corporate performance goals after receiving input from our Chief Executive Officer. The performance goals generally relate to product development and other goals relating to our business.

Following its review and determinations of corporate performance for 2018, our board of directors determined an achievement level of 90% for each NEO. The actual amount of the cash bonuses awarded to each NEO for 2018 performance are set forth above in the Summary Compensation Table in the column titled "Non-Equity Incentive Plan Compensation."

In addition, in late 2018 and early 2019, we awarded to Drs. Francis and Kamal discretionary bonuses, in consideration for their services to us through 2018. No other NEO received any discretionary bonus for their service in 2018. The one-time cash bonuses awarded to Drs. Francis and Kamal are set forth above in the Summary Compensation Table in the column titled "Bonus."

Equity-Based Compensation

In October and December 2018, we granted to Dr. Kamal options to purchase an aggregate of 286,817 shares of our common stock. Each option vests and becomes exercisable as to 25% of the shares on the one year anniversary of October 11, 2018 and vest as to 1/48th of the shares monthly thereafter, subject to his continued service through the applicable vesting date. The exercise price per share for each option was $8.27, which was the fair market value of our common stock as of the date of grant. In April 2018, we granted to Dr. Francis options to purchase an aggregate of 75,000 shares of our common stock. The option vests and becomes exercisable as to 11,280 of the shares on the one year anniversary of September 30, 2016 and vest as to 1,770 of the remaining shares monthly thereafter, subject to his continued service through the applicable vesting date. The exercise price per share for each option was $3.19, which was the fair market value of our common stock as of the date of grant.

We intend to adopt the 2019 Plan, in order to facilitate the grant of cash and equity incentives to directors, employees (including our NEOs) and consultants of our company and certain of its affiliates and to enable us to obtain and retain services of these individuals, which is essential to our long-term success. We expect that the 2019 Plan will be effective on the date on which it is adopted by our board of directors, subject to approval of such plan by our stockholders. For additional information about the 2019 Plan, please see the section titled "Equity Compensation Plans" below.

Other Elements of Compensation

Retirement Savings and Health and Welfare Benefits

We currently maintain a 401(k) retirement savings plan for our employees, including our NEOs, who satisfy certain eligibility requirements. Our NEOs are eligible to participate in the 401(k) plan on the same terms as other full-time employees. We make matching contributions equal to 50% of employee contributions of the first ten percent of compensation. Matching contributions will vest annually over 4 years. We believe that providing a vehicle for tax-deferred retirement savings though our 401(k) plan adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our NEOs, in accordance with our compensation policies.

All of our full-time employees, including our NEOs, are eligible to participate in our health and welfare plans, including medical, dental and vision benefits; medical and dependent care flexible spending accounts; short-term and long-term disability insurance; and life and AD&D insurance.

Perquisites and Other Personal Benefits

We provide limited perquisites to our NEOs, such as the reimbursement of Dr. Kamal's relocation expenses and Dr. Francis' travel reimbursements, when our compensation committee determines that such perquisites are necessary or advisable to fairly compensate or incentivize our employees. We reimbursed Dr. Kamal in the amount of $9,439 in 2018 for expenses he incurred in connection with his relocation to California related to his commencement of employment. In addition, we reimbursed Dr. Francis in the amount of $43,069 in 2018 for travel-related expenses incurred in connection with his travel between his home office in Oregon and our headquarters in California.

Executive Compensation Arrangements

Employment Agreements

As of December 31, 2018, we were party to offer letters with each of our NEOs, which set forth their initial base salary, annual bonus opportunity, initial stock option grant, benefit plans participation and the other benefits noted below for each NEO.

David Kirn, M.D. In addition to the above, Dr. Kirn is eligible to receive certain severance benefits upon qualifying terminations under the offer letter. In the event we terminate Dr. Kirn other than for cause or Dr. Kirn resigns for good reason, then (i) he will receive a lump sum payment equal to 12 months of his base salary, (ii) a lump sum cash payment equal to his prorated annual target bonus for the year in which the termination occurs and (iii) reimbursement of COBRA premiums for up to 12 months. The severance benefits set forth above are subject to his timely execution and non-revocation of a general release of claims against us. In addition, effective as of late 2018, the board approved that Dr. Kirn is also eligible for 100% accelerated vesting of any of his outstanding equity awards upon a change in control, subject to his continued employment through such date.

Peter Francis, M.D., Ph.D. In addition to the above, effective as of Dr. Francis' promotion in early 2019, Dr. Francis is eligible to receive certain severance benefits upon qualifying terminations under the offer letter. In the event we terminate Dr. Francis other than for cause or Dr. Francis resigns for good reason, then (i) he will receive a lump sum payment equal to 9 months of his base salary and (ii) reimbursement of COBRA premiums for up to 9 months. In addition to the severance benefits above, in the event we undergo a change in control, he will receive accelerated vesting of 100% of the then-unvested equity awards held by him. The severance benefits set forth above are subject to his timely execution and non-revocation of a general release of claims against us.

Prior to Dr. Francis becoming an employee in August 2018, he was party to a consulting agreement. The consulting agreement provided for Dr. Francis to provide research and advisory services on our internal retinal program. In consideration for these services, Dr. Francis was entitled to a fixed fee of $22,500 per month, as well as a discretionary performance bonus, the payment and amount of which was subject to approval by our board of directors. The consulting agreement was superseded in full by his offer letter when he became an employee.

Fred Kamal, Ph.D. In addition to the above, Dr. Kamal is eligible to receive certain severance benefits upon qualifying terminations under the offer letter. In the event we terminate Dr. Kamal other than for cause or Dr. Kamal resigns for good reason, in any case, outside of 1 month prior to, or 12 months following a change in control (as defined in the 2015 Plan), then he will receive (i) a lump sum payment equal to 9 months of his base salary and (ii) reimbursement of COBRA premiums for up to 9 months. In the event we terminate Dr. Kamal other than for cause or Dr. Kamal resigns for good reason, in any case, within the 1 month prior to or the 12 months following a change in control, then, in addition to the benefits in (i) and (ii) above, he will receive accelerated vesting of 100% of the then-unvested equity awards held by him. The severance benefits set forth above are subject to his timely execution and non-revocation of a general release of claims against us and continued compliance with the Confidential Information and Invention Assignment Agreement.

For the purposes of Drs. Kirn's and Francis' offer letters, "cause" is defined as (i) their material failure to perform their principally assigned duties or responsibilities as an employee, director or consultant (other than a failure resulting from disability (as defined under Section 22(e)(3) of the Code); provided that, the failure to achieve certain results, such as the our business plan, in and of itself, would not constitute “cause”; (ii) their engaging in any act of dishonesty, fraud or material misrepresentation; (iii) their violation of any federal or state law or regulation applicable to our business that results in or could reasonably be expected to result in harm or creates material risk, as determined by the board of directors; (iv) their breach of any confidentiality agreement or invention assignment agreement, or any other material contract made between us and them or violation of any of our written policies; or (v) their being convicted of, or entering a plea of nolo contendere to, any crime or committing any act of moral turpitude. In the case of (i) above, we shall not terminate Drs. Kirn or Francis without first providing them with written notice of the acts or omissions constituting the grounds for such termination and expiration of a reasonable cure period not to exceed thirty 30 days following the date of such notice if we reasonably judge that such failure may be cured within 30 days.

For the purposes of Dr. Kamal’s offer letter, “cause” is defined as (i) his material failure to perform his principally assigned duties or responsibilities as an employee, director or consultant (other than a failure resulting from disability (as defined under Section 22(e)(3) of the Code); provided that, the failure to achieve certain results, such as our business plan, in and of itself, would not constitute “cause”; (ii) his engaging in any act of dishonesty, fraud or material misrepresentation; (iii) his violation of any federal or state law or regulation applicable to our business that results in or could reasonably be expected to result in harm, or creates material risk, as determined by the board of directors; (iv) his breach of any confidentiality agreement or invention assignment agreement, or any other material contract between him and us or his violation of any of our written policies (or any of our affiliates); (v) his being convicted of, or entering a plea of nolo contendere to, any crime or committing any act of moral turpitude; or (vi) his commission of any act or involvement in any situation, or occurrence, which brings him into widespread public disrepute, contempt, scandal or ridicule, or which justifiably shocks, insults or offends a significant portion of the community, or his being subject to publicity for any such conduct or involvement in such conduct. In the case of (i) above, we shall not terminate Dr. Kamal without first providing him with written notice of the acts or omissions constituting the grounds for such termination and expiration of a reasonable cure period not to exceed thirty 30 days following the date of such notice if we reasonably judge that such failure may be cured within 30 days.

For the purposes of Dr. Kamal’s offer letter, “good reason” is defined as (i) a material diminution in his salary except for across-the-board salary reductions similarly affecting all or substantially all similarly situated employees, (ii) a material diminution in his authority, duties or responsibilities or (iii) a change of more than 50 miles in the geographic location at which he provides services, provided, however, that in the event of the occurrence of a good reason condition listed above, he must provide notice to us within 30 days of the initial occurrence of such condition and allow us 30 days in which to cure such condition. Additionally, in the event we fail to cure the condition within the cure period provided, he must terminate employment with us within sixty (60) days of the end of the cure period.

For the purposes of Dr. Francis’ offer letter, “good reason” is defined as the occurrence, without his written consent, of (i) a material diminution in his salary except for across-the-board salary reductions similarly affecting all or substantially all similarly situated employees, (ii) any material and adverse change, including any material diminution in his title, duties, authority or responsibilities, but excluding any such changes in the event of a change of control; provided his remaining duties and responsibilities are consistent with industry norms for the title, (iii) a change of more than 50 miles in the geographic location of our offices, (iv) assignment of duties materially inconsistent with his position, or (v) any material breach by us of the offer letter; provided, however, that in the event of the occurrence of a good reason condition listed above, he must provide written notice to us within 20 days of the initial occurrence of such condition and allow us 30 days in which to cure such condition. His termination will be effective once the 30 day period has lapsed and we have failed to materially cure such acts, failures or failures to act that gave rise to the good reason. We may, in our sole election, waive any cure period such that his termination will be effective on such earlier date determined by our board of directors.

For the purposes of Dr. Kirn's offer letter, "good reason" is defined as (i) a change of more than 50 miles in the geographic location of our offices; (ii) his removal from the our board of directors or (iii) any material and adverse change, including any material diminution in his title, duties, authority or responsibilities, but excluding any such changes or changes in reporting relationships in the event of a Change of Control; provided his remaining duties and responsibilities are consistent with industry norms for the title.

For the purposes of Drs. Kirn's offer letter, a "change in control" occurs when any "person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) is or becomes the "beneficial owner" (as defined in Rule 13d-3 under the Securities Exchange Act of 1934), directly or indirectly, of our securities representing more than 50% of the total voting power or (ii) on the date of the consummation of a merger or consolidation with any other corporation that has been approved by our stockholders, other than a merger or consolidation which would result in our voting securities outstanding immediately prior to the merger or consolidation continuing to represent at least 50% of the total voting power represented by our voting securities or the voting securities such surviving entity or its parent outstanding immediately after such merger or consolidation; or (iii) the date of the consummation of the sale or disposition by us of all or substantially all the our assets. A transaction will not be deemed a change in control under Dr. Kirn's offer letter unless the transaction qualifies as a "change in control event" within the meaning of Section 409A of the Code.

Equity Compensation Plans

The following summarizes the material terms of the long-term incentive compensation plan in which our NEOs will be eligible to participate following the consummation of this offering and our 2015 Equity Incentive Plan, referred to as the 2015 Plan, under which we have previously made periodic grants of equity and equity-based awards to our NEOs and other key employees. We intend to file with the SEC a registration statement on Form S-8 covering the shares of our common stock issuable under the 2019 Plan, the 2015 Plan and the ESPP.

2019 Incentive Award Plan

We intend to adopt the 2019 Plan, which we expect will become effective on the date on which it is adopted by our board of directors, subject to approval of such plan by our stockholders. The principal purpose of the 2019 Plan is to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards and cash-based performance bonus awards. The material terms of the 2019 Plan, as it is currently contemplated, are summarized below.

Share reserve. Under the 2019 Plan, shares of our common stock will be initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, stock appreciation rights (SARs) restricted stock awards, restricted stock unit awards and other stock-based awards. The number of shares initially reserved for issuance or transfer pursuant to awards under the 2019 Plan will be increased by an annual increase on the first day of each fiscal year beginning in 2020 and ending in 2029, equal to the lesser of (i) % of the shares of stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (ii) such smaller number of shares of stock as determined by our board of directors; provided, however, that no more than shares of stock may be issued upon the exercise of incentive stock options.

The following counting provisions will be in effect for the share reserve under the 2019 Plan:

- to the extent that an award terminates, expires or lapses for any reason or an award is settled in cash without the delivery of shares, any shares subject to the award at such time will be available for future grants under the 2019 Plan;
- to the extent shares are tendered or withheld to satisfy the grant, exercise price or tax withholding obligation with respect to any award under the 2019 Plan, such tendered or withheld shares will be available for future grants under the 2019 Plan;
- to the extent shares subject to SARs are not issued in connection with the stock settlement of SARs on exercise thereof, such shares will be available for future grants under the 2019 Plan;
- to the extent that shares of our common stock are repurchased by us prior to vesting so that shares are returned to us, such shares will be available for future grants under the 2019 Plan;
- the payment of dividend equivalents in cash in conjunction with any outstanding awards will not be counted against the shares available for issuance under the 2019 Plan; and
- to the extent permitted by applicable law or any exchange rule, shares issued in assumption of, or in substitution for, any outstanding awards of any entity acquired in any form of combination by us or any of our subsidiaries will not be counted against the shares available for issuance under the 2019 Plan.

Administration. The compensation committee of our board of directors is expected to administer the 2019 Plan unless our board of directors assumes authority for administration. The compensation committee must consist of at least three members of our board of directors, each of whom is intended to qualify as a “non-employee director” for purposes of Rule 16b-3 under the Exchange Act and an “independent director” within the meaning of the rules of the applicable stock exchange, or other principal securities market on which shares of our common stock are traded. The 2019 Plan provides that the board or compensation committee may delegate its authority to grant awards to employees other than executive officers and certain senior executives to a committee consisting of one or more members of our board of directors or one or more of our officers, other than awards made to our non-employee directors, which must be approved by our full board of directors.

Subject to the terms and conditions of the 2019 Plan, the administrator has the authority to select the persons to whom awards are to be made, to determine the number of shares to be subject to awards and the terms and conditions of awards, and to make all other determinations and to take all other actions necessary or advisable for the administration of the 2019 Plan. The administrator is also authorized to adopt, amend or rescind rules relating to administration of the 2019 Plan. Our board of directors may at any time remove the compensation committee as the administrator and revest in itself the authority to administer the 2019 Plan. The full board of directors will administer the 2019 Plan with respect to awards to non-employee directors.

Eligibility. Options, SARs, restricted stock and all other stock-based and cash-based awards under the 2019 Plan may be granted to individuals who are then our officers, employees or consultants or are the officers, employees or consultants of certain of our subsidiaries. Such awards also may be granted to our directors. Only employees of our company or certain of our subsidiaries may be granted incentive stock options (ISOs).

Awards. The 2019 Plan provides that the administrator may grant or issue stock options, SARs, restricted stock, restricted stock units, other stock- or cash-based awards and dividend equivalents or any combination thereof. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- *Nonstatutory stock options*. Nonstatutory Stock Options (NSOs) will provide for the right to purchase shares of our common stock at a specified price which may not be less than fair market value on the date of grant, and usually will become exercisable (at the discretion of the administrator) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of corporate performance targets and individual performance targets established by the administrator. NSOs may be granted for any term specified by the administrator that does not exceed ten years.

- *Incentive stock options*. ISOs will be designed in a manner intended to comply with the provisions of Section 422 of the Code and will be subject to specified restrictions contained in the Code. Among such restrictions, ISOs must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees and must not be exercisable after a period of ten years measured from the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) at least 10% of the total combined voting power of all classes of our capital stock, the 2019 Plan provides that the exercise price must be at least 110% of the fair market value of a share of common stock on the date of grant and the ISO must not be exercisable after a period of five years measured from the date of grant.
- *Restricted stock*. Restricted stock may be granted to any eligible individual and made subject to such restrictions as may be determined by the administrator. Restricted stock, typically, may be forfeited for no consideration or repurchased by us at the original purchase price if the conditions or restrictions on vesting are not met. In general, restricted stock may not be sold or otherwise transferred until restrictions are removed or expire. Purchasers of restricted stock, unlike recipients of options, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse, however, extraordinary dividends will generally be placed in escrow, and will not be released until restrictions are removed or expire.
- *Restricted stock units*. Restricted stock units may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Like restricted stock, restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.
- *Stock appreciation rights*. SARs may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The exercise price of any SAR granted under the 2019 Plan must be at least 100% of the fair market value of a share of our common stock on the date of grant. SARs under the 2019 Plan will be settled in cash or shares of our common stock, or in a combination of both, at the election of the administrator.
- *Other stock or cash based awards*. Other stock or cash based awards are awards of cash, fully vested shares of our common stock and other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock. Other stock or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of base salary, bonus, fees or other cash compensation otherwise payable to any individual who is eligible to receive awards. The plan administrator will determine the terms and conditions of other stock or cash based awards, which may include vesting conditions based on continued service, performance and/or other conditions.
- *Dividend equivalents*. Dividend equivalents represent the right to receive the equivalent value of dividends paid on shares of our common stock and may be granted alone or in tandem with

awards other than stock options or SARs. Dividend equivalents are credited as of dividend payments dates during the period between a specified date and the date such award terminates or expires, as determined by the plan administrator. In addition, dividend equivalents with respect to shares covered by a performance award will only be paid to the participant at the same time or times and to the same extent that the vesting conditions, if any, are subsequently satisfied and the performance award vests with respect to such shares.

Any award may be granted as a performance award, meaning that the award will be subject to vesting and/or payment based on the attainment of specified performance goals.

Change in control. In the event of a change in control, unless the plan administrator elects to terminate an award in exchange for cash, rights or other property, or cause an award to accelerate in full prior to the change in control, such award will continue in effect or be assumed or substituted by the acquirer, provided that any performance-based portion of the award will be subject to the terms and conditions of the applicable award agreement. In the event the acquirer refuses to assume or replace awards granted, prior to the consummation of such transaction, awards issued under the 2019 Plan will be subject to accelerated vesting such that 100% of such awards will become vested and exercisable or payable, as applicable. The administrator may also make appropriate adjustments to awards under the 2019 Plan and is authorized to provide for the acceleration, cash-out, termination, assumption, substitution or conversion of such awards in the event of a change in control or certain other unusual or nonrecurring events or transactions.

Adjustments of awards. In the event of any stock dividend or other distribution, stock split, reverse stock split, reorganization, combination or exchange of shares, merger, consolidation, split-up, spin-off, recapitalization, repurchase or any other corporate event affecting the number of outstanding shares of our common stock or the share price of our common stock that would require adjustments to the 2019 Plan or any awards under the 2019 Plan in order to prevent the dilution or enlargement of the potential benefits intended to be made available thereunder, the administrator will make appropriate, proportionate adjustments to: (i) the aggregate number and type of shares subject to the 2019 Plan; (ii) the number and kind of shares subject to outstanding awards and terms and conditions of outstanding awards (including, without limitation, any applicable performance targets or criteria with respect to such awards); and (iii) the grant or exercise price per share of any outstanding awards under the 2019 Plan.

Amendment and termination. The administrator may terminate, amend or modify the 2019 Plan at any time and from time to time. However, we must generally obtain stockholder approval to the extent required by applicable law, rule or regulation (including any applicable stock exchange rule). Notwithstanding the foregoing, an option may be amended to reduce the per share exercise price below the per share exercise price of such option on the grant date and options may be granted in exchange for, or in connection with, the cancellation or surrender of options having a higher per share exercise price without receiving additional stockholder approval.

No incentive stock options may be granted pursuant to the 2019 Plan after the tenth anniversary of the effective date of the 2019 Plan, and no additional annual share increases to the 2019 Plan's aggregate share limit will occur from and after such anniversary. Any award that is outstanding on the termination date of the 2019 Plan will remain in force according to the terms of the 2019 Plan and the applicable award agreement.

2015 Equity Incentive Plan

On March 20, 2015, our board of directors adopted, and our stockholders approved, the 2015 Plan. Following the offering, and in connection with the effectiveness of our 2019 Plan, the 2015 Plan will terminate, and no further awards will be granted under the 2015 Plan. However, all outstanding awards will continue to be governed by their existing terms.

Administration. Our board of directors, or a committee thereof appointed by our board of directors, has the authority to administer the 2015 Plan and the awards granted under it. The plan administrator has broad authority to make determinations and interpretations under, prescribe forms for use with and adopt rules for the administration of, the 2015 Plan, subject to its express terms and conditions. The plan administrator also sets the terms and conditions of all awards under the 2015 Plan, including any vesting and acceleration conditions.

Limitation on awards and shares available. The aggregate number of shares of our common stock that is authorized pursuant to the 2015 Plan is 2,694,528, which shares may be authorized but unissued shares, reacquired common stock or represent shares underlying forfeited awards. Shares tendered or withheld to satisfy grant or exercise price or tax withholding obligations associated with an award granted under the 2015 Plan and shares issued pursuant to awards of restricted stock or restricted stock units that are repurchased by us or are forfeited due to the failure to vest may be used again for new grants under the 2015 Plan.

Awards. The 2015 Plan provides that the administrator may grant or issue ISOs, NSOs, SARs, restricted stock and restricted stock units to our employees, directors and consultants, provided that only employees may be granted ISOs. Awards under the 2015 Plan are set forth in award agreements, which detail the terms and conditions of the awards, including any applicable vesting and payment terms and post-termination exercise limitations. Awards are generally settled in shares of our common stock.

- *Stock Options*. Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other Internal Revenue Code requirements are satisfied. The exercise price of a stock option may not be less than 100% of the fair market value of the underlying share on the date of grant (or 110% in the case of ISOs granted to certain significant shareholders), except with respect to certain substitute options granted in connection with a corporate transaction. The term of a stock option may not be longer than ten years (or five years in the case of ISOs granted to certain significant shareholders). Vesting conditions determined by the plan administrator may apply to stock options and may include continued service, performance and/or other conditions. A stock option may provide for “early exercise” prior to vesting in exchange for shares of restricted shares that vest on the option’s vesting schedule.
- *Stock appreciation rights.* SARs may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The exercise price of any SAR granted under the 2015 Plan must be at least 100% of the fair market value of a share of our common stock on the date of grant. SARs under the 2015 Plan will be settled in cash or shares of our common stock, or in a combination of both, as set forth in the applicable award agreement.
- *Restricted stock*. Restricted stock may be granted to any eligible individual and made subject to such restrictions as may be determined by the administrator. Restricted stock, typically, may be forfeited for no consideration or repurchased by us at the original purchase price if the conditions or restrictions on vesting are not met. In general, restricted stock may not be sold or otherwise transferred until restrictions are removed or expire. Purchasers of restricted stock, unlike recipients of options, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse.

- *Restricted stock units*. Restricted stock units may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions continuing service with us or our affiliates, the attainment of performance goals and/or such other conditions as the plan administrator may determine. Like restricted stock, restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.

Certain transactions. The plan administrator has broad discretion to equitably adjust the provisions of the 2015 Plan, as well as the terms and conditions of existing and future awards, to prevent the diminution or enlargement of intended benefits and facilitate necessary or desirable changes in the event of certain transactions and events affecting our common stock, such as a dividend or other distribution (whether in the form of cash, Shares, other securities or other property), recapitalization, reincorporation, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, reclassification, repurchase or exchange of our shares or our other securities, or other change in our corporate structure. In the event of a merger with or into another corporation or other entity or a change in control (as defined in the 2015 Plan), the plan administrator may provide, in any combination hereof, subject to the applicable award agreement and without the participant's consent, that (i) the surviving entity assume outstanding awards or substitute economically equivalent awards for such outstanding awards; (ii) that the participant's awards will terminate upon or immediately prior to the consummation of the merger or change in control; (iii) outstanding awards will vest and become exercisable, realizable or payable, or restrictions applicable to an award will lapse, in whole or in part prior to or upon consummation of such merger or change in control; and (iv) the termination of an award in exchange for any combination of cash, property or other rights, if any, selected by the administrator in its sole discretion, equal in value to the cash or other property that would have been attained upon the exercise of such award or realization of the participant's rights as of the date of the occurrence of the transaction. The administrator may also make appropriate adjustments to awards under the 2015 Plan and is authorized to provide for the acceleration, cash-out, termination, assumption, substitution or conversion of such awards in the event of a change in control or certain other unusual or nonrecurring events or transactions.

Foreign participants, transferability and participant payments. The plan administrator may establish sub-plans under the 2015 Plan, subject to the share limits described above, containing such limitations and other terms and conditions that the plan administrator determines is necessary or desirable to satisfy blue sky, securities, tax or other laws of various jurisdictions in which we intend to grant awards or qualifying for favorable tax treatment under applicable foreign laws. With limited exceptions for gifts or executors of the participant's estate upon the participant's death, in connection with certain acquisitions or a change in control, and transfers to us, awards under the 2015 Plan are generally non-transferable prior to exercise or delivery and are exercisable only by the participant. With regard to tax withholding, exercise price and purchase price obligations arising in connection with awards under the 2015 Plan, as applicable, the plan administrator may, in its discretion, accept cash, check, promissory note, shares of our common stock that meet specified conditions, such other consideration and method of payment for the issuance of shares, to the extent permitted by applicable laws, by "net exercise," a "market sell order" or any combination thereof.

Amendment; termination. Our board of directors may amend or terminate the 2015 Plan at any time; however, (i) no amendment or termination may adversely affect an outstanding award without the affected participant's written consent and (ii) except in connection with certain changes in our capital structure, stockholder approval will be required for (A) any amendment that increases the number of shares available under the 2015 Plan or extends the term of the 2015 Plan, or (B) as required under applicable law. No award may be granted pursuant to the 2015 Plan after the ten year anniversary of the date the 2015 Plan, as amended or restated, was approved by our board of directors or our stockholders (whichever was earlier), however, we will cease granting awards under the 2015 Plan upon effectiveness of the 2019 Plan.

We intend to file with the SEC a registration statement on Form S-8 covering our shares of common stock issuable under the 2015 Plan.

2019 Employee Stock Purchase Plan

We intend to adopt and ask our stockholders to approve the ESPP, which will be effective upon the day prior to the effectiveness of the registration statement to which this prospectus relates. The ESPP is designed to allow our eligible employees to purchase shares of our common stock, at semi-annual intervals, with their accumulated payroll deductions. The ESPP is intended to qualify under Section 423 of the Code. The material terms of the ESPP, as it is currently contemplated, are summarized below.

Administration. Subject to the terms and conditions of the ESPP, our compensation committee will administer the ESPP. Our compensation committee can delegate administrative tasks under the ESPP to the services of an agent and/or employees to assist in the administration of the ESPP. The administrator will have the discretionary authority to administer and interpret the ESPP. Interpretations and constructions of the administrator of any provision of the ESPP or of any rights thereunder will be conclusive and binding on all persons. We will bear all expenses and liabilities incurred by the ESPP administrator.

Share reserve. The maximum number of shares of our common stock which will be authorized for sale under the ESPP is equal to the sum of (i)   shares of common stock and (ii) an annual increase on the first day of each year beginning in 2020 and ending in 2029, equal to the lesser of (A) 1% of the shares of common stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (B) such number of shares of common stock as determined by our board of directors; provided, however, no more than   shares of our common stock may be issued under the ESPP. The shares reserved for issuance under the ESPP may be authorized but unissued shares or reacquired shares.

Eligibility. Employees eligible to participate in the ESPP for a given offering period generally include employees who are employed by us or one of our subsidiaries on the first day of the offering period, or the enrollment date. Our employees (and, if applicable, any employees of our subsidiaries) who customarily work less than five months in a calendar year or are customarily scheduled to work less than 20 hours per week will not be eligible to participate in the ESPP. Finally, an employee who owns (or is deemed to own through attribution) 5% or more of the combined voting power or value of all our classes of stock or of one of our subsidiaries will not be allowed to participate in the ESPP.

Participation. Employees will enroll under the ESPP by completing a payroll deduction form permitting the deduction from their compensation of at least 1% of their compensation but not more than 15% of their compensation. Such payroll deductions may be expressed as either a whole number percentage or a fixed dollar amount, and the accumulated deductions will be applied to the purchase of shares on each purchase date. However, a participant may not purchase more than 30,000 shares in each offering period and may not subscribe for more than $25,000 in fair market value of shares of our common stock (determined at the time the option is granted) during any calendar year. The ESPP administrator has the authority to change these limitations for any subsequent offering period.

Offering. Under the ESPP, participants are offered the option to purchase shares of our common stock at a discount during a series of successive offering periods, the duration and timing of which will be determined by the ESPP administrator. However, in no event may an offering period be longer than 27 months in length.

The option purchase price will be the lower of 85% of the closing trading price per share of our common stock on the first trading date of an offering period in which a participant is enrolled or 85% of the closing trading price per share on the purchase date, which will occur on the last trading day of each offering period.

Unless a participant has previously canceled his or her participation in the ESPP before the purchase date, the participant will be deemed to have exercised his or her option in full as of each purchase date. Upon exercise, the participant will purchase the number of whole shares that his or her accumulated payroll deductions will buy at the option purchase price, subject to the participation limitations listed above.

A participant may cancel his or her payroll deduction authorization at any time prior to the end of the offering period. Upon cancellation, the participant will have the option to either (i) receive a refund of the participant's account balance in cash without interest or (ii) exercise the participant's option for the current offering period for the maximum number of shares of common stock on the applicable purchase date, with the remaining account balance refunded in cash without interest. Following at least one payroll deduction, a participant may also decrease (but not increase) his or her payroll deduction authorization once during any offering period. If a participant wants to increase or decrease the rate of payroll withholding, he or she may do so effective for the next offering period by submitting a new form before the offering period for which such change is to be effective.

A participant may not assign, transfer, pledge or otherwise dispose of (other than by will or the laws of descent and distribution) payroll deductions credited to a participant's account or any rights to exercise an option or to receive shares of our common stock under the ESPP, and during a participant's lifetime, options in the ESPP shall be exercisable only by such participant. Any such attempt at assignment, transfer, pledge or other disposition will not be given effect.

Adjustments upon changes in recapitalization, dissolution, liquidation, merger or asset sale. In the event of any increase or decrease in the number of issued shares of our common stock resulting from a stock split, reverse stock split, stock dividend, combination or reclassification of the common stock, or any other increase or decrease in the number of shares of common stock effected without receipt of consideration by us, we will proportionately adjust the aggregate number of shares of our common stock offered under the ESPP, the number and price of shares which any participant has elected to purchase under the ESPP and the maximum number of shares which a participant may elect to purchase in any single offering period. If there is a proposal to dissolve or liquidate us, then the ESPP will terminate immediately prior to the consummation of such proposed dissolution or liquidation, and any offering period then in progress will be shortened by setting a new purchase date to take place before the date of our dissolution or liquidation. We will notify each participant of such change in writing at least ten business days prior to the new exercise date. If we undergo a merger with or into another corporation or sell all or substantially all of our assets, each outstanding option will be assumed or an equivalent option substituted by the successor corporation or the parent or subsidiary of the successor corporation. If the successor corporation refuses to assume the outstanding options or substitute equivalent options, then any offering period then in progress will be shortened by setting a new purchase date to take place before the date of our proposed sale or merger. We will notify each participant of such change in writing at least ten business days prior to the new exercise date.

Amendment and termination. Our board of directors may amend, suspend or terminate the ESPP at any time. However, the board of directors may not amend the ESPP without obtaining stockholder approval within 12 months before or after such amendment to the extent required by applicable laws.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2016 to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or beneficial owners of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest.

Sales and Purchases of Securities

Series B Convertible Preferred Stock Financing

In August 2018, we issued an aggregate of 5,154,632 shares of our Series B convertible preferred stock at $17.46 per share for aggregate proceeds to us of approximately $90.0 million.

The table below sets forth the aggregate number of shares of Series B convertible preferred stock sold to our directors, executive officers or owners of more than 5% of a class of our capital stock, or an affiliate or immediate family member thereof:

Name	Number of Shares of Series B Convertible Preferred Stock	Aggregate Purchase Price ($)
Pfizer Inc.(1)	343,642	5,999,989.32

(1) Bill Burkoth, a member of our board of directors, is an Executive Director of Pfizer Ventures (US) LLC, which is an affiliate of Pfizer Inc. and its affiliated funds.

Director and Executive Officer Compensation

Please see the sections titled “Director Compensation” and “Executive Compensation” for information regarding the compensation of our directors and executive officers.

Employment Agreements

We have entered into employment agreements with our executive officers. For more information regarding these agreements, see the section titled “Executive Compensation—Narrative to Summary Compensation Table and Outstanding Equity Awards at 2018 Fiscal Year End.”

Indemnification Agreements and Directors’ and Officers’ Liability Insurance

We have entered into or intend to enter into indemnification agreements with each of our directors and executive officers. These agreements will require us to, among other things, indemnify each director and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys’ fees, judgments, penalties fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person’s services as a director or executive officer. We have obtained an insurance policy that insures our directors and officers against certain liabilities, including liabilities arising under applicable securities laws. For additional information see the section titled “Management—Limitation of Liability and Indemnification Matters.”

Investors’ Rights Agreement

We entered into an amended and restated investors’ rights agreement with the purchasers of our outstanding redeemable convertible preferred stock, including entities with which certain of our directors are affiliated. As of June 30, 2019, the holders of approximately 7.4 million shares of our common stock, including the shares of our common stock issuable upon the conversion of our Series A, Series A-1 and Series B redeemable convertible preferred stock, are entitled to rights with respect to the registration of their shares under the Securities Act. For a more detailed description of these registration rights, see the section titled “Description of Capital Stock—Registration Rights.” The investors’ rights agreement also provides for a right of first refusal in favor of certain holders of redeemable convertible preferred stock with regard to certain issuances of our capital stock. The rights of first refusal will not apply to, and will terminate upon the consummation of, this offering. The investors’ right agreement also provides for certain voting arrangements. For a description of these voting arrangements, see the section titled “Management—Board Composition—Voting Arrangements.”

Right of First Refusal and Co-Sale Agreement

We entered into an amended and restated right of first refusal and co-sale agreement with certain holders of our common stock and redeemable convertible preferred stock. This agreement provides for rights of first refusal and co-sale relating to the shares of our common stock held by the parties to the agreement. Upon the consummation of this offering, the amended and restated right of first refusal and co-sale agreement will terminate.

Other Transactions

In April 2019, we entered into two sponsored research agreements (SRAs) with The UC Regents to conduct research in a lab on the Berkeley campus that is under the direction of Dr. Schaffer. Pursuant to the SRAs, we have committed to pay the UC Regents a total of $1.5 million, of which $0.4 million was paid upon execution of the SRAs. The SRAs have a three year term ending in 2022. While the SRAs are between us and the UC Regents, the payments under the SRAs may be used to fund the lab under the direction of Dr. Schaffer.

Our former Chief Operating Officer, Anthony Davies, who was employed through November 2017, was the Executive Chairman of Dark Horse Consulting. During the year ended December 31, 2017, we paid $0.2 million to Dark Horse Consulting under a consulting agreement to design and implement pharmaceutical quality manufacturing of and controls for drug products. The consulting agreement terminated in December 2017.

In 2016, we entered into a consulting agreement with one our former directors, Hoyoung Huh, who resigned as a director in December 2018, to provide business development strategy services. In connection with this agreement, Dr. Huh was granted stock options. In the years ended December 31, 2018 and 2017, we recorded $219,500 and $14,700, respectively, of stock-based compensation expense related to such stock options.

In 2016, Dr. Kirn, our Chief Executive Officer and several other of our employees founded Ignite Immunotherapy (Ignite). Dr. Kirn also serves as the Chief Executive Officer and Executive Chairman of Ignite. Certain of our executives hold ownership interests in Ignite and are members of the board of directors of Ignite. Additionally, Pfizer, who is one of our related parties, holds a significant equity stake in Ignite. There have been no transactions between us and Ignite for the years ended December 31, 2018 and 2017.

Other than as described above, since January 1, 2016, we have not entered into any transactions, nor are there any currently proposed transactions, between us and a related party where the amount involved exceeds, or would exceed, $120,000, and in which any related person had or will have a direct or indirect material interest. We believe the terms of the transactions described above were comparable to terms we could have obtained in arms-length dealings with unrelated third parties.

Policies and Procedures for Related Party Transactions

Prior to the consummation of this offering, our board of directors will adopt a written related person transaction policy, to be effective upon the consummation of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including without limitation purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including but not limited to whether the transaction is on terms comparable to those that could be obtained in an arm’s length transaction with an unrelated third party and the extent of the related person’s interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information relating to the beneficial ownership of our common stock as of July 31, 2019, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of our common stock;
- each of our directors;
- each of our named executive officers; and
- all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days after July 31, 2019 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of our common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 12,516,975 shares of our common stock outstanding as of July 31, 2019, which reflects the automatic conversion of 7,375,631 shares of our outstanding shares of redeemable convertible preferred stock into an equivalent number of shares of our common stock. Shares of our common stock that a person has the right to acquire within 60 days after July 31, 2019 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o 4D Molecular Therapeutics, Inc., 5858 Horton Street #455, Emeryville, California 94608.

Name of Beneficial Owner	Number of Outstanding Shares Beneficially Owned	Number of Shares Exercisable Within 60 Days	Number of Shares Beneficially Owned	Number of Shares Owned After the Offering	Percentage of Beneficial Ownership	
					Before Offering	After Offering
5% and Greater Stockholders:						
Viking Global Opportunities Illiquid Investments Sub-Master LP(1)	2,004,581	0	2,004,581	2,004,581	16.0%	
Entities Affiliated with Pfizer(2)	1,474,992	0	1,474,992	1,474,992	11.8%	
Repleon, LLC(3)	909,312	0	909,312	909,312	7.3%	
Executive Officers and Directors:						
David Kirn, M.D.(4)	2,000,000	0	2,000,000	2,000,000	16.0%	
Fred Kamal, Ph.D.	0	0	0	0	—	
Peter Francis, M.D., Ph.D.(5)	0	78,206	78,206	78,206	*	
David Schaffer, Ph.D.(6)	2,000,000	0	2,000,000	2,000,000	16.0%	
Charles Theuer, M.D., Ph.D.(7)	32,351	23,017	55,368	55,368	*	
Jacob Chacko, M.D.	0	0	0	0	—	
Tony Yao, M.D., Ph.D.(8)	458,190	0	458,190	458,190	3.7%	
Bill Burkoth, MBA	0	0	0	0	—	
All executive officers and directors as a group (8 persons)	4,490,541	101,223	4,591,764	4,591,764	36.4%	

* Indicates beneficial ownership of less than 1% of our total outstanding common stock.

(1) Consists of 2,004,581 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock held by Viking Global Opportunities Illiquid Investments Sub-Master LP (Opportunities Fund). Opportunities Fund has the authority to dispose of and vote the shares directly owned by it, which power may be exercised by its general partner, Viking Global Opportunities Portfolio GP LLC (Opportunities GP), and by Viking Global Investors LP (VGI), which provides managerial services to Opportunities Fund. O. Andreas Halvorsen, David C. Ott and Rose Shabet, as Executive Committee members of Viking Global Partners LLC (the general partner of VGI) and Opportunities GP, have shared authority to direct the voting and disposition of investments beneficially owned by the Opportunities Fund and Opportunities GP. The business address of each of the entities is c/o Viking Global Investors LP, 55 Railroad Avenue, Greenwich, CT 06830.

(2) Consists of (i) 1,131,350 shares of our common stock issuable upon the conversion of our Series A-1 redeemable convertible preferred stock directly held by Pfizer Ventures (US) LLC and (ii) 343,642 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by Pfizer, Inc. Pfizer Inc. is the parent company to Pfizer Ventures (US) LLC and may be deemed to beneficially own the shares directly owned by Pfizer Ventures (US) LLC. Bill Burkoth, a member of our board of directors, is an Executive Director at Pfizer, Inc. The address for these entities is 230 East Grand, South San Francisco, CA 94080.

(3) Consists of 909,312 shares of our common stock issuable upon the conversion of our Series A redeemable convertible preferred stock. These shares are directly owned by Repleon, LLC. The address for Repleon, LLC is 235 East 42nd Street, New York, NY 10010.

(4) Consists of 2,000,000 shares of our common stock.

(5) Consists of 78,206 shares of our common stock that may be acquired pursuant to the exercise of stock options within 60 days of July 31, 2019.

(6) Consists of 2,000,000 shares of our common stock directly held by the Shaffer-Hinh Family Trust.

(7) Consists of (i) 32,351 shares of our common stock and (ii) 23,017 shares of our common stock that may be acquired pursuant to the exercise of stock options within 60 days of July 31, 2019.

(8) Consists of 2,864 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock held directly by Dr. Yao and, (i) 1,432 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by CF Ascent LLC, (ii) 50,830 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by Iron Horse Investments, LLC, (iii) 5,727 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by Lookfar Investments, LLC, (iv) 229,095 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by Meridian Small Cap Growth Fund, (v) 50,830 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by THB Iron Rose LLC, (vi) 2,864 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by THB Iron Rose LLC, Life Sciences Portfolio, (vii) 57,274 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by Arrowmark Fundamental Opportunity Fundl L.P., and (viii) 57,274 shares of our common stock issuable upon the conversion of our Series B redeemable convertible preferred stock directly held by Arrowmark Life Science Fund, LP, which are referred to collectively as the ArrowMark Funds. ArrowMark Colorado Holdings LLC (ArrowMark Colorado) is investment advisor to ArrowMark Funds. Dr. Yao, one of our directors, is employed as a portfolio manager for ArrowMark Colorado and has direct voting and dispositive control over the shares held by the ArrowMark Funds. Dr. Yao may be considered the beneficial owner of the shares held by ArrowMark Funds and disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The principal business address of the ArrowMark Funds is 100 Fillmore Street, Suite 325, Denver, Colorado 80206.

DESCRIPTION OF CAPITAL STOCK

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective immediately prior to the consummation of this offering, the amended and restated investors' rights agreement to which we and certain of our stockholders are parties and of 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, copies of which have been filed as exhibits to the registration statement of which this prospectus is part.

General

Immediately prior to the consummation of this offering, we will file our amended and restated certificate of incorporation that authorizes shares of common stock, $0.0001 par value per share, and shares of preferred stock, $0.0001 par value per share. As of June 30, 2019, there were outstanding:

- 12,516,975 shares of our common stock, on an as-converted basis, held by approximately 46 stockholders of record; and
- 2,192,230 shares of our common stock issuable upon exercise of outstanding stock options.

In connection with this offering, we expect to consummate a forward stock split of our outstanding common stock at a ratio to be determined.

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, and the shares of our common stock to be issued in this offering will be, fully paid and nonassessable.

Redeemable Convertible Preferred Stock

Immediately prior to the consummation of this offering, all outstanding shares of our redeemable convertible preferred stock will be converted into shares of our common stock. See Note 10 to our audited financial statements included elsewhere in this prospectus for a description of our currently outstanding redeemable convertible preferred stock. Immediately prior to the consummation of this offering, our amended and restated certificate of incorporation will be amended and restated to delete all references to such shares of redeemable convertible preferred stock. From and after the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to   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. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of June 30, 2019, we had outstanding options to purchase 2,192,230 shares of our common stock, with a per share weighted-average exercise price of $6.10, under our 2015 Equity Incentive Plan.

Warrants

As of June 30, 2019, we had warrants outstanding with the option to purchase 68,669 shares of our common stock, with a weighted-average exercise price of $1.85 per share.

Registration Rights

Under our amended and restated investors' rights agreement, based on the number of shares outstanding as of December 31, 2018, following the consummation of this offering, the holders of approximately 7.4 million shares of our common stock, or their transferees, have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, and the holders of approximately 7.4 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, 2018, after the consummation of this offering, the holders of approximately 7.4 million shares of our common stock (on an as-converted basis), or their transferees, will be entitled to certain demand registration rights. Beginning 180 days following the effectiveness of the registration statement of which this prospectus is a part, 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, 2018, after the consummation of this offering, 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 approximately 7.4 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, 2018, after the consummation of this offering, the holders of approximately 7.4 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 this 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 that will become effective immediately prior to the consummation of this offering 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 will 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 will 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.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation and our amended and restated bylaws will eliminate the right of stockholders to act by written consent without a meeting.

Classified Board; Election and Removal of Directors; Filling Vacancies

Effective upon the consummation of this offering, our board of directors will be 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 will provide 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. For more information on the classified board, see the section titled "Management—Board Composition." 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 our amended and restated bylaws will 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 and Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of fiduciary duty; (iii) 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; (iv) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; or (v) any action asserting a claim against us that is governed by the internal affairs doctrine. Although our amended and restated certificate of incorporation and amended and restated bylaws will 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. The choice of forum provision does not apply to any actions arising under the Securities Act or the Exchange Act.

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.

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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

For a discussion of liability and indemnification, see the section titled “Management—Limitation on Liability and Indemnification Matters.”

Listing

We intend to apply to have our common stock listed on The Nasdaq Global Market under the symbol “DDDD.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is   . The transfer agent and registrar’s address is   .

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after consummation of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

Based on the number of shares of our common stock outstanding as of June 30, 2019 and assuming an initial public offering price of $ per share, the midpoint of the estimated price range set forth on the cover of this prospectus, upon the consummation of this offering and assuming (i) the conversion of all shares of our outstanding Series A, Series A-1 and Series B redeemable convertible preferred stock as of June 30, 2019, (ii) no exercise of the underwriters' option to purchase additional shares of our common stock and (iii) no exercise of any of our outstanding options or warrants, we will have outstanding an aggregate of approximately shares of our common stock. Of these shares, all of the shares of our common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of our common stock held by existing stockholders immediately prior to the consummation of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on the number of shares of our common stock outstanding as of June 30, 2019 and assumptions (i)-(iii) described above, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market, subject (A) to any waivers by the underwriters and/or our board of directors under the respective lock-up agreements and (B) with respect to shares held by directors, executive officers and other affiliates, the volume limitations under Rule 144 under the Securities Act, are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
shares	180 days after the date of this prospectus upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-Up Agreements

In connection with this offering, we, our executive officers, our directors and substantially all of our other security holders have agreed, subject to certain exceptions, with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of our common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of Goldman Sachs & Co. LLC and Evercore Group L.L.C on behalf of the underwriters.

Prior to the completion of the offering, certain of our employees, including our executive officers, and/or directors may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Exchange Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our “affiliates” for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our “affiliates,” is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than “affiliates,” then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our “affiliates,” as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately shares of our common stock immediately after this offering (calculated as of June 30, 2019 on the basis of the assumptions (i)-(iii) described above); or
- the average weekly trading volume of our common stock on The Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our “affiliates” or persons selling shares on behalf of our “affiliates” are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our “affiliates,” as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our “affiliates” may resell those shares without compliance with Rule 144’s minimum holding period requirements (subject to the terms of the lock-up agreement referred to above).

Registration Rights

Based on the number of shares outstanding as of June 30, 2019, after the consummation of this offering, the holders of approximately 7.4 million shares of our common stock, or their transferees, will, subject to the lock-up agreements referred to above, be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. For a description of these registration rights, see the section titled “Description of Capital Stock—Registration Rights.” If the offer and sale of these shares are registered, they will be freely tradable without restriction under the Securities Act.

Stock Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of our common stock that we may issue upon exercise of outstanding options reserved for issuance under our 2015 Equity Incentive Plan and our 2019 Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the consummation of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the IRS in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a “capital asset” within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder’s particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- “controlled foreign corporations,” “passive foreign investment companies” and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- tax-qualified retirement plans; and
- “qualified foreign pension funds” as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE

PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "U.S. person" nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

an individual who is a citizen or resident of the United States;

a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;

an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

a trust that (i) is subject to the primary supervision of a U.S. court and all substantial decisions of which are subject to the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code), or (ii) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section titled "Dividend Policy," we do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "—Sale or Other Taxable Disposition."

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable tax treaties.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

Subject to the discussions below regarding backup withholding, a Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder’s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest (USRPI) by reason of our status as a U.S. real property holding corporation (USRPHC) for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by certain U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder will not be subject to U.S. federal income tax if our common stock is “regularly traded,” as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder’s holding period.

Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the Non-U.S. Holder certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives the certification described above or the Non-U.S. Holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker that does not have certain enumerated relationships with the United States generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act (FATCA)) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (i) the foreign financial institution undertakes certain diligence and reporting obligations, (ii) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (iii) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (i) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA would have applied also to payments of gross proceeds from the sale or other disposition of stock on or after January 1, 2019, recently proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

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UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC and Evercore Group L.L.C. are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman Sachs & Co. LLC	
Evercore Group L.L.C.	
William Blair & Company, L.L.C.	
Chardan Capital Markets LLC	
Total	

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional shares from us.

	No Exercise	Full Exercise
Per Share	$	$
Total	$	$

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $ per share from the initial public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We and our executive officers, directors, and holders of substantially all of our common stock and securities convertible into or exchangeable for our common stock have agreed or will agree with the underwriters, subject to certain exceptions, not to dispose of or hedge any of our or their common stock or securities convertible into or exchangeable for shares of our common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior written consent of Goldman Sachs & Co. LLC and Evercore Group L.L.C. This agreement does not apply to any existing employee benefit plans. See the section titled "Shares Eligible for Future Sale" for a discussion of certain transfer restrictions.

Prior to the offering, there has been no public market for the shares. The initial public offering price has been negotiated among us and the representatives. Among the factors to be considered in determining the initial public offering price of the shares, in addition to prevailing market conditions, will be the our historical performance, estimates of the business potential and earnings prospects, an assessment of our management and the consideration of the above factors in relation to market valuation of companies in related businesses.

We intend to apply to list our common stock on The Nasdaq Global Market under the symbol "DDDD."

In connection with the offering, the underwriters may purchase and sell shares of our common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our common stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of our common stock. As a result, the price of our common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $. We have agreed to reimburse the underwriters for certain of their expenses in an amount up to $.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities or instruments of the issuer (directly, as collateral securing other obligations or otherwise) or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

European Economic Area

In relation to each member state of the European Economic Area (each, a Member State), no securities have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of securities may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

- to any legal entity which is a qualified investor as defined in the Prospectus Regulation;
- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to any securities in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed at qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets

Act 2000, as amended (Financial Promotion), Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged in with relevant persons. Any person who is not a relevant person should not act or rely on this prospectus or any of its contents.

Canada

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The securities may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (Companies (Winding Up and Miscellaneous Provisions) Ordinance) or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (Securities and Futures Ordinance), or (ii) to “professional investors” as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the securities may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the SFA)) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (i) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (ii) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (iii) where no consideration is or will be given for the transfer, (iv) where the transfer is by operation of law, (v) as specified in Section 276(7) of the SFA, or (vi) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore (Regulation 32).

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (i) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (ii) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (iii) where no consideration is or will be given for the transfer, (iv) where the transfer is by operation of law, (v) as specified in Section 276(7) of the SFA, or (vi) as specified in Regulation 32.

Solely for the purposes of its obligations pursuant to Section 309B of the SFA, we have determined, and hereby notify all relevant persons (as defined in the CMP Regulations 2018), that the shares are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended) (the FIEA). The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission (ASIC), in relation to the offering. This offering document does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the Corporations Act), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the Exempt Investors) who are “sophisticated investors” (within the meaning of section 708(8) of the Corporations Act), “professional investors” (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This offering document contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this offering document is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Dubai International Financial Centre

This offering document relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority (DFSA). This offering document is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth in this prospectus and has no responsibility for the offering document. The securities to which this offering document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this offering document you should consult an authorized financial advisor.

Switzerland

We have not and will not register with the Swiss Financial Market Supervisory Authority (FINMA) as a foreign collective investment scheme pursuant to Article 119 of the Federal Act on Collective Investment Scheme of 23 June 2006, as amended (CISA), and accordingly the securities being offered pursuant to this prospectus have not and will not be approved, and may not be licenseable, with FINMA. Therefore, the securities have not been authorized for distribution by FINMA as a foreign collective investment scheme pursuant to Article 119 CISA and the securities offered hereby may not be offered to the public (as this term is defined in Article 3 CISA) in or from Switzerland. The securities may solely be offered to “qualified investors,” as this term is defined in Article 10 CISA, and in the circumstances set out in Article 3 of the Ordinance on Collective Investment Scheme of 22 November 2006, as amended (CISO), such that there is no public offer. Investors, however, do not benefit from protection under CISA or CISO or supervision by FINMA. This prospectus and any other materials relating to the securities are strictly personal and confidential to each offeree and do not constitute an offer to any other person. This prospectus may only be used by those qualified investors to whom it has been handed out in connection with the offer described in this prospectus and may neither directly or indirectly be distributed or made available to any person or entity other than its recipients. It may not be used in connection with any other offer and shall in particular not be copied and/or distributed to the public in Switzerland or from Switzerland. This prospectus does not constitute an issue prospectus as that term is understood pursuant to Article 652a and/or 1156 of the Swiss Federal Code of Obligations. We have not applied for a listing of the securities on the SIX Swiss Exchange or any other regulated securities market in Switzerland, and consequently, the information presented in this prospectus does not necessarily comply with the information standards set out in the listing rules of the SIX Swiss Exchange and corresponding prospectus schemes annexed to the listing rules of the SIX Swiss Exchange.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Latham & Watkins LLP, Menlo Park, California. Cooley LLP, San Francisco, California, is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The financial statements as of December 31, 2017 and December 31, 2018 and for the years then ended included in this Prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to 4D Molecular Therapeutics, Inc. and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. The SEC maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at www.4dmoleculartherapeutics.com. Upon completion of this offering, you may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

4D Molecular Therapeutics, Inc.

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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, 2018 and 2017, and the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders’ 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, 2018 and 2017, 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 and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud.

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
August 2, 2019

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, 2017	As of December 31, 2018	As of June 30, 2019 (Unaudited)	Pro Forma As of June 30, 2019 (Unaudited)
Assets				
Current assets				
Cash and cash equivalents	$ 23,850	$ 91,761	$ 72,869	
Accounts receivable	321	1,124	1,161	
Prepaid expenses and other current assets (includes $0, $0 and $373 (unaudited), at December 31, 2017, December 31, 2018 and June 30, 2019, respectively, attributable to related parties)	328	1,183	1,415	
Total current assets	24,499	94,068	75,445	
Property and equipment, net	2,716	2,472	4,026	
Other assets	105	429	1,029	
Total assets	$ 27,320	$ 96,969	$ 80,500	
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' (Deficit) Equity				
Current liabilities				
Accounts payable	$ 460	$ 954	$ 1,115	
Accrued and other current liabilities	1,066	2,193	3,242	
Deferred revenue (includes $28, $0 and $0 (unaudited), at December 31, 2017, December 31, 2018 and June 30, 2019, respectively, attributable to related parties)	4,382	4,907	4,246	
Total current liabilities	5,908	8,054	8,603	
Deferred revenue, net of current portion (includes $5,000, $0 and $0 (unaudited), at December 31, 2017, December 31, 2018 and June 30, 2019, respectively, attributable to related parties)	22,188	13,076	10,777	
Derivative liability	78	64	70	
Other liabilities	228	382	374	
Total liabilities	28,402	21,576	19,824	
Commitments and contingencies (Note 8)				
Redeemable convertible preferred stock, $0.0001 par value; 2,309,312 shares authorized; 2,220,999 shares issued and outstanding at December 31, 2017. 7,375,638 shares authorized; 7,375,631 shares issued and outstanding at December 31, 2018 and June 30, 2019 (unaudited). Liquidation value of $18,596 at December 31, 2017 and $108,596 at December 31, 2018 and June 30, 2019 (unaudited). No shares authorized, issued or outstanding, pro forma (unaudited).	18,508	102,980	102,980	
Stockholders' (deficit) equity				
Common stock, $0.0001 par value; 50,000,000 shares authorized as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited); 5,063,303, 5,126,344 and 5,141,344 shares issued and outstanding at December 31, 2017, December 31, 2018, and June 30, 2019 (unaudited), respectively; shares authorized and shares issued and outstanding, pro forma (unaudited)	1	1	1	
Additional paid-in-capital	884	2,438	3,930	
Accumulated deficit	(20,475)	(30,026)	(46,235)	
Total stockholders' (deficit) equity	(19,590)	(27,587)	(42,304)	
Total liabilities, redeemable convertible preferred stock and stockholders' (deficit) equity	$ 27,320	$ 96,969	$ 80,500	

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,		Six Months Ended June 30,	
	2017	2018	2018	2019
			(Unaudited)	
Revenue:				
Collaboration and research revenue, related parties	$ 3,176	$ 5,143	$ 143	$ 26
Collaboration and research revenue	2,614	8,987	4,926	4,390
Total revenue	5,790	14,130	5,069	4,416
Operating expenses:				
Research and development (includes $2,881 and $160 for the years ended December 31, 2017 and 2018 and $135 (unaudited) and $99 (unaudited) for the six months ended June 30, 2018 and 2019, respectively, attributable to related parties)	13,573	18,362	8,208	16,985
General and administrative (includes $15 and $220 for the years ended December 31, 2017 and 2018 and $61 (unaudited) and $0 (unaudited) for the six months ended June 30, 2018 and 2019, respectively, attributable to related parties)	3,489	6,167	2,198	4,884
Total operating expenses	17,062	24,529	10,406	21,869
Loss from operations	(11,272)	(10,399)	(5,337)	(17,453)
Other income (expense):				
Interest income	89	850	147	945
Other income (expense), net	(40)	(2)	4	(8)
Total other income (expense)	49	848	151	937
Net loss and comprehensive loss	$ (11,223)	$ (9,551)	$ (5,186)	$ (16,516)
Net loss per share attributable to common stockholders, basic and diluted	(2.27)	(1.89)	(1.03)	(3.22)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	4,953,419	5,049,203	5,021,003	5,132,714
Pro forma net loss per share, basic and diluted (unaudited)				
Weighted-average shares outstanding used in computing pro forma net loss per share, basic and diluted (unaudited)				

The accompanying notes are an integral part of these financial statements

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4D Molecular Therapeutics, Inc.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balances at December 31, 2016	2,220,999	$ 18,508	5,048,932	$ 1	$ 612	$ (9,252)	$ (8,639)
Exercise of common stock options	—	—	14,371	—	16	—	16
Stock-based compensation	—	—	—	—	256	—	256
Net loss	—	—	—	—	—	(11,223)	(11,223)
Balances at December 31, 2017	2,220,999	18,508	5,063,303	1	884	(20,475)	(19,590)
Issuance of redeemable convertible preferred stock, net of $5,528 of issuance cost	5,154,632	84,472	—	—	—	—	—
Exercise of common stock options	—	—	63,041	—	105	—	105
Issuance of common stock warrants	—	—	—	—	72	—	72
Stock-based compensation	—	—	—	—	1,377	—	1,377
Net loss	—	—	—	—	—	(9,551)	(9,551)
Balances at December 31, 2018	7,375,631	$102,980	5,126,344	$ 1	$ 2,438	$ (30,026)	$ (27,587)

The accompanying notes are an integral part of these financial statements

4D Molecular Therapeutics, Inc.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit – (Continued)
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balances at December 31, 2017	2,220,999	$ 18,508	5,063,303	$ 1	$ 884	$ (20,475)	$ (19,590)
Exercise of common stock options (unaudited)	—	—	19,753	—	20	—	20
Issuance of common stock warrants (unaudited)	—	—	—	—	59	—	59
Stock-based compensation	—	—	—	—	403	—	403
Net loss (unaudited)	—	—	—	—	—	(5,186)	(5,186)
Balances at June 30, 2018 (unaudited)	2,220,999	$ 18,508	5,083,056	$ 1	$ 1,366	$ (25,661)	$ (24,294)
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 (unaudited)	—	—	—	—	—	307	307
Exercise of common stock options (unaudited)	—	—	15,000	—	20	—	20
Stock-based compensation (unaudited)	—	—	—	—	1,472	—	1,472
Net loss (unaudited)	—	—	—	—	—	(16,516)	(16,516)
Balances at June 30, 2019 (unaudited)	7,375,631	$102,980	5,141,344	$ 1	$ 3,930	$ (46,235)	$ (42,304)

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,		Six Months Ended June 30,	
	2017	2018	2018	2019
			(Unaudited)	
Cash flows from operating activities				
Net loss	$(11,223)	$ (9,551)	$ (5,186)	$(16,516)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities				
Stock-based compensation expense	256	1,377	403	1,472
Change in fair value of warrant obligation	31	—	—	—
Change in fair value of derivative liability	—	(14)	(20)	6
Depreciation and amortization	626	697	341	406
Loss on disposition of property and equipment	8	16	16	—
Changes in operating assets and liabilities				
Accounts receivable	(320)	(803)	(1,415)	(37)
Prepaid expenses and other current assets	6	(855)	60	(232)
Other assets	—	(324)	(40)	(300)
Accounts payable	(114)	438	559	62
Accrued and other liabilities	(59)	1,354	202	624
Deferred revenue	19,026	(8,587)	(1,401)	(2,653)
Net cash provided by (used in) operating activities	8,237	(16,252)	(6,422)	(17,168)
Cash flows from investing activities				
Proceeds on sale of property and equipment	24	—	—	—
Acquisition of property and equipment	(573)	(414)	(33)	(1,662)
Proceeds from maturities of short-term investments	8,224	—	—	—
Net cash provided by (used in) investing activities	7,675	(414)	(33)	(1,662)
Cash flows from financing activities				
Issuance of redeemable convertible preferred stock, net of issuance costs	—	84,472	—	—
Issuance of common stock	16	105	20	20
Deferred offering costs	—	—	—	(82)
Net cash provided by (used in) financing activities	16	84,577	20	(62)
Net increase (decrease) in cash and cash equivalents	15,928	67,911	(6,435)	(18,892)
Cash and cash equivalents, beginning of period	7,922	23,850	23,850	91,761
Cash and cash equivalents, end of period	$ 23,850	$ 91,761	$17,415	$ 72,869
Supplemental disclosures of non-cash investing and financing information				
Purchases of property and equipment in accounts payable and accrued and other liabilities	$ —	$ 56	$ —	$ 298
Unpaid deferred offering costs	$ —	$ —	$ —	$ 308
Issuance of common stock warrants in return for services	$ —	$ 72	$ 59	$ —

The accompanying notes are an integral part of these financial statements

4D Molecular Therapeutics, Inc.

Notes to Financial Statements

1. Organization and Nature of the Business

Organization and Business

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 development stage precision gene therapy company dedicated to the development of targeted therapies based on its adeno-associated viruses ("AAV") vectors discovered through its proprietary Therapeutic Vector Evolution platform.

Liquidity

The Company experienced negative operating cash flows of $16.3 million for the year ended December 31, 2018 and $17.3 million (unaudited) for the six months ended June 30, 2019. The Company had an accumulated deficit of $30.0 million as of December 31, 2018 and $46.2 million (unaudited) as of June 30, 2019. Since its inception, the Company has funded its operations primarily with proceeds from sales of redeemable convertible preferred stock and to a lesser extent collaboration and licensing arrangements. In August 2018, the Company received $84.5 million net proceeds from issuance of Series B redeemable convertible preferred stock.

The Company expects to increase operating losses and negative operating cash flows for the foreseeable future as the Company advances its product candidates into clinical trials, conducts additional preclinical studies, and expands internal manufacturing capabilities. The Company is seeking to complete an initial public offering ("IPO") of its common stock. In the event the Company does not complete an IPO, the Company expects to seek additional funding through private equity financings, debt financings, or other capital sources, including collaborations with other companies, or other strategic transactions.

The Company may not be able to obtain funding on acceptable terms, or at all. If the expected inflows are delayed or not received, or available capital resources are consumed more rapidly than currently expected, the Company expects to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or investment in internal manufacturing capabilities, which could adversely affect its business prospects. The Company expects that its existing cash and cash equivalents will be sufficient to fund its operations through at least 12 months from the date these financial statements are available for issuance.

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").

Unaudited Interim Financial Information

The accompanying balance sheet as of June 30, 2019, the statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' deficit and of cash flows for the six months ended June 30, 2018 and June 30, 2019 are unaudited. In the opinion of management, the unaudited data reflects all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of June 30, 2019 and the results of its operations and comprehensive loss and its cash flows for the six months ended June 30, 2018 and June 30, 2019. The financial data and other information disclosed in these notes related to the six months ended June 30, 2018 and June 30, 2019 are also unaudited. The results for the six months ended June 30, 2019 are not necessarily indicative of results to be expected for the year ending December 31, 2019, any other interim periods, or any future year or period.

Unaudited Pro Forma Information

The unaudited pro forma basic and diluted net loss per share were computed to give effect to the conversion of all outstanding shares of redeemable convertible preferred stock on a one-for-one basis into shares of common stock immediately prior to the completion of the planned IPO as though the conversion had occurred as of the beginning of the period or the date of issuance, if later.

The unaudited pro forma redeemable convertible preferred stock and stockholders' deficit were computed to give effect to the conversion of all outstanding shares of redeemable convertible preferred stock on a one-for-one basis into shares of common stock immediately prior to the completion of the planned IPO. The unaudited pro forma information does not assume any proceeds from the planned IPO.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions 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 research periods of collaboration agreements, as well as estimates of the fair value of common stock, stock options and derivative instruments and income tax uncertainties. Actual results could differ from those estimates.

Segments

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 consolidated basis for purposes of allocating resources and assessing financial performance.

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, 2017	Year Ended December 31, 2018	Six Months Ended June 30, 2018 (Unaudited)	Six Months Ended June 30, 2019 (Unaudited)
Partner A	55%	*	*	*
Partner B	19%	*	*	*
Partner C	14%	53%	79%	86%
Partner D	*	35%	*	*
Partner E	*	*	10%	12%
Total	88%	88%	89%	98%

* Less than 10%

The Company's accounts receivable as of December 31, 2017 and 2018 and June 30, 2019 (unaudited) was comprised of one partner.

The Company's total revenues by geographic region, based on the location of the customer, are as follows (in thousands):

	Year Ended December 31, 2017	Year Ended December 31, 2018	Six Months Ended June 30, 2018 (Unaudited)	Six Months Ended June 30, 2019 (Unaudited)
Australia	$ 408	$ 200	$ 100	$ 7
Netherlands	3,176	143	143	26
Switzerland	839	7,460	4,027	3,816
United States	1,367	6,327	799	567
	$ 5,790	$ 14,130	$ 5,069	$ 4,416

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 and clinical trials and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel 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).

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, 2017, December 31, 2018 and June 30, 2019 (unaudited). The Company did not have any write-offs relating to uncollectible accounts receivable during the years ended December 31, 2017 and 2018 and six months ended June 30, 2018 and 2019 (unaudited).

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 length of the lease. 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 statement 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, 2017 and 2018 and six months ended June 30, 2018 and 2019 (unaudited).

Redeemable Convertible Preferred Stock

The Company records 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 is recorded outside of permanent equity because while it is 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 will become redeemable at the option of the majority of outstanding shareholders of such series of redeemable convertible preferred stock. The Company has not adjusted 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 is not considered probable. Subsequent adjustments to the carrying values to the liquidation preference will be made only when it becomes probable that such a deemed liquidation event will occur.

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 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 revenues are 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 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 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 relative to 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.

Prior to the adoption of ASC 606 on January 1, 2019, the Company recognized revenue when all of the following criteria were met: persuasive evidence of an arrangement exists; transfer of technology has been completed or services have been rendered; the price to the customer is fixed or determinable and collectability is reasonably assured.

In arrangements involving the delivery of more than one element, each required deliverable was evaluated to determine whether it qualified as a separate unit of accounting. The determination was based on whether the deliverable had "standalone value" to the customer. If a deliverable did not qualify as a separate unit of accounting, it was combined with the other applicable undelivered item(s) within the arrangement and these combined deliverables were treated as a single unit of accounting.

The arrangement's consideration that was fixed or determinable was allocated to each separate unit of accounting based on the relative selling price methodology in accordance with the selling price hierarchy, which included vendor-specific objective evidence (VSOE) of selling price, if available, or third-party evidence of selling price if VSOE was not available, or the best estimate of selling price, if neither VSOE nor third-party evidence was available.

Payments or reimbursements for our research and development efforts for the arrangements where such efforts were considered as deliverables were recognized as the services were performed and were presented on a gross basis. When upfront payments were received and if there was no discernible pattern of performance, the Company recognized revenue ratably over the associated period of performance.

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

The Company accounts for stock-based compensation 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 Company's 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.

The Company recognizes the fair value of stock options granted to nonemployees as stock-based compensation expense over the period in which the related services are received. Stock-based compensation expense related to stock options granted to nonemployees is recognized based on the vesting date fair value of awards as the stock options are earned. The Company believes that the estimated fair value of stock options is more readily measurable than the fair value of the services rendered. In addition, the Company estimates the service period for the awards based on the time that would be required to satisfy the service condition, assuming the service condition will be satisfied. Stock-based compensation expense is recognized over the estimated service period but is accelerated if the performance condition is 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 Therapeutics, Inc. ("CFFT"). 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.

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 and early exercised stock options 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.

Under the two-class method, basic net loss per share attributable to common stockholders is calculated by dividing the net loss by the weighted-average number of common shares 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 common shares and contingently issuable shares, and 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.

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly related to the Company's in-process equity financings, including the planned IPO, until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds received as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately within the Company's statements of operations and comprehensive loss. As of June 30, 2019, $0.4 million (unaudited) of costs were recorded as deferred offering costs on the balance sheet. There were no material deferred offering costs capitalized as of December 31, 2017 and 2018.

Recent Accounting Pronouncements

Recently Adopted Accounting Pronouncements

In May 2014, the 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. The main principle of ASC 606 is to recognize revenue when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. 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. The new guidance has been applied to the most current period presented with a cumulative effect adjustment of $0.3 million (unaudited) reflected as a decrease to the opening balance of accumulated deficit and a decrease to deferred revenue. See Note 6 for further discussion on research and collaboration arrangements.

The following tables summarize the amount by which each financial statement line item was affected by the impact of the cumulative adjustment and as compared with the guidance that was in effect prior to the adoption (in thousands):

Impact of ASC 606 Adoption on
Balance Sheet as of January 1, 2019 (Unaudited)

	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Deferred revenue, current portion	$ (6,202)	$ 1,295	$ (4,907)
Deferred revenue, noncurrent portion	$ (11,474)	$ (1,602)	$ (13,076)
Accumulated deficit	$ (29,719)	$ (307)	$ (30,026)

Impact of ASC 606 Adoption on
Balance Sheet as of June 30, 2019 (Unaudited)

	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Deferred revenue, current portion	$ (4,246)	$ 306	$ (3,940)
Deferred revenue, noncurrent portion	$ (10,777)	$ (382)	$ (11,159)
Accumulated deficit	$ (46,235)	$ (76)	$ (46,311)

Impact of ASC 606 Adoption on Statements of Operations and Comprehensive Loss
Six Month Ended June 30, 2019 (Unaudited)

	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Collaboration and research revenue	$ 4,416	$ 231	$ 4,647
Net loss	$ (16,516)	$ 231	$ (16,285)
Net loss per share—basic and diluted	$ (3.22)	$ 0.05	$ (3.17)

Impact of ASC 606 Adoption on Statements of Cash Flows for the
Six Month Ended June 30, 2019 (Unaudited)

	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Cash flows from operating activities:			
Net loss	$ (16,516)	$ 231	$ (16,285)
Changes in operating assets and liabilities:			
Deferred revenue	$ (2,653)	$ (231)	$ (2,884)

In May 2017, the FASB issued Accounting Standards Update ("ASU") 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting*. This ASU provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting. This ASU is effective for fiscal years beginning after December 15, 2017, and interim periods within those years. The Company adopted this standard on January 1, 2018 with no impact to the financial statements and related disclosures.

In November 2015, the FASB issued ASU 2015-17, *Balance Sheet Classification of Deferred Taxes*. This ASU amends existing guidance on income taxes to require the classification of all deferred tax assets and liabilities as non-current on the balance sheets. This ASU is effective for fiscal years beginning after December 15, 2016. Early adoption is permitted and the guidance may be applied either prospectively or retrospectively. The Company adopted this standard on January 1, 2017 with no impact to the financial statements and related disclosures.

New Accounting Pronouncements Not Yet Adopted

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, 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: 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; 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 is currently evaluating the impact the adoption of this standard will have on its financial statements and related disclosures.

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. Early adoption is permitted, but may take place no earlier than a company's adoption date of 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 July 2017, 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 is currently evaluating the impact the adoption of this standard will have on its financial statements and related disclosures.

In August 2016, the FASB issued ASU 2016-15*, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*. This ASU requires changes to how cash receipts and cash payments are presented and classified in the statement of cash flows. This ASU is effective for fiscal years beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. Early adoption is permitted. This ASU requires adoption on a retrospective basis. 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") requires 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. The new leasing standard is effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted. 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. In March 2019, the FASB issued ASU 2019-01, which provides clarification on implementation issues associated with adopting ASU 2016-02. The Company is currently evaluating the impact the adoption of this standard will have on its financial statements and related disclosures.

In January 2016, the FASB issued ASU 2016-01, *Financial Instruments—Overall: Recognition and Measurement of Financial Assets and Financial Liabilities*. This ASU enhances the reporting model for financial instruments, which includes amendments to address aspects of recognition, measurement, presentation and disclosure. This ASU is effective for fiscal years beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. In February 2018, the FASB issued ASU 2018-03, *Technical Corrections and Improvements to Financial Instruments—Overall (Subtopic 825-10)*. This ASU clarified certain aspects of the previously issued standard. This ASU is effective on the same effective date as ASU 2016-01. 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

As of December 31, 2017, the Company's fair value hierarchy for financial assets and financial liabilities measured at fair value are as follows (in thousands):

	Basis for Fair Value Measurements			Fair Value as of December 31, 2017
	(Level 1)	(Level 2)	(Level 3)	
Assets				
Money market funds	$23,150	$ —	$ —	$ 23,150
Total	$23,150	$ —	$ —	$ 23,150
Liabilities				
Common stock warrant obligation	$ —	$ —	$ 60	$ 60
Derivative liability	—	—	78	78
Total	$ —	$ —	$ 138	$ 138

As of December 31, 2018, the Company's fair value hierarchy for financial assets and financial liabilities measured at fair value are as follows (in thousands):

	Basis for Fair Value Measurements			Fair Value as of December 31, 2018
	(Level 1)	(Level 2)	(Level 3)	
Assets				
Money market funds	$91,761	$ —	$ —	$ 91,761
Total	$91,761	$ —	$ —	$ 91,761
Liabilities				
Derivative liability	$ —	$ —	$ 64	$ 64
Total	$ —	$ —	$ 64	$ 64

As of June 30, 2019 (unaudited), the Company's fair value hierarchy for financial assets and financial liabilities measured at fair value are as follows (in thousands):

	Basis for Fair Value Measurements			Fair Value as of
	(Level 1)	(Level 2)	(Level 3)	June 30, 2019
Assets				
Money market funds	$72,869	$ —	$ —	$ 72,869
Total	$72,869	$ —	$ —	$ 72,869
Liabilities				
Derivative liability	$ —	$ —	$ 70	$ 70
Total	$ —	$ —	$ 70	$ 70

Level 3 Inputs

The fair value of the warrant obligation 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 common stock warrant obligation was determined using the Black-Scholes option pricing model. In determining the fair value of the warrant obligation, the inputs impacting fair value include the expected term, expected volatility, risk-free interest rate and dividend yield. See Note 13 for further discussion on common stock warrant obligation.

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 CFFT, 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):

	Common Stock Warrant Obligation	Derivative Liability
Balance as of December 31, 2016	$ 29	$ —
Issuance of derivative liability	—	78
Change in fair value included in other income (expense), net	31	—
Balance as of December 31, 2017	$ 60	$ 78
Issuance of common stock warrants	(59)	—
Change in fair value included in other income (expense), net	(1)	(14)
Balance as of December 31, 2018	$ —	$ 64
Change in fair value included in other income (expense), net (unaudited)	—	6
Balance as of June 30, 2019 (unaudited)	$ —	$ 70

4. Property and Equipment, Net

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

	December 31, 2017	December 31, 2018	June 30, 2019 (Unaudited)
Machinery and equipment	$ 2,058	$ 2,433	$ 3,035
Leasehold improvements	1,349	1,349	1,362
Furniture and fixtures	182	182	188
Office equipment	63	74	74
Computer equipment and software	28	52	190
Construction in progress	—	34	1,235
Total Property and Equipment	3,680	4,124	6,084
Less: Accumulated depreciation and amortization	(964)	(1,652)	(2,058)
Property and equipment, net	$ 2,716	$ 2,472	$ 4,026

All property and equipment are maintained in the United States. Depreciation expense was $0.6 million and $0.7 million for the years ended December 31, 2017 and 2018 and $0.3 million (unaudited) and $0.4 million (unaudited) for the six months ended June 30, 2018 and 2019, respectively.

5. Accrued and Other Current Liabilities

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

	December 31, 2017	December 31, 2018	June 30, 2019 (Unaudited)
Payroll and related	$ 787	$ 1,313	$ 1,069
Accrued clinical and preclinical study costs	98	75	485
Consulting and professional	79	549	1,284
Accrued state taxes	51	93	181
Other accrued expenses	51	163	223
	$ 1,066	$ 2,193	$ 3,242

6. Research and Collaboration Arrangements

Collaboration and license revenue for each period was as follows (in thousands):

	Revenue			
	Year Ended December 31,		Six Months Ended June 30,	
	2017	2018	2018 (Unaudited)	2019 (Unaudited)
uniQure	$ 3,176	$ 143	$ 143	$ 26
Benitec	408	200	100	7
AGTC	1,082	272	272	—
CRF	166	—	—	—
Pfizer	—	5,000	—	—
Roche	839	7,460	4,027	3,816
CFFT	119	55	27	19
AstraZeneca	—	1,000	500	548
	$ 5,790	$ 14,130	$ 5,069	$ 4,416

Deferred revenue for each period was as follows (in thousands):

	Deferred Revenue		
	December 31, 2017	December 31, 2018	June 30, 2019 (Unaudited)
uniQure	$ 28	$ —	$ —
Benitec	383	183	—
AGTC	337	—	—
CRF	—	—	—
Pfizer	5,000	—	—
Roche	20,522	17,055	14,587
CFFT	300	245	436
AstraZeneca	—	500	—
	$ 26,570	$ 17,983	$ 15,023

The total amount of revenue in the six months ended June 30, 2019, which was included in deferred revenue at January 1, 2019, was $4.2 million (unaudited).

uniQure

In January 2014, the Company and uniQure biopharma B.V. ("uniQure") 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 diseases within the central nervous system and liver (the "uniQure Agreement").

The uniQure Agreement provides 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.

Pursuant to the uniQure Agreement, the Company received upfront payments of $0.2 million, and is 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 will also receive 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 are 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.

During the years ended December 31, 2017 and 2018, the Company recognized revenue of $3.2 million and $0.1 million under the uniQure Agreement, respectively. The revenue recognized in 2017 consisted of $2.7 million from the ratable recognition of the value of the options, $0.4 million for the reimbursement of research services and $0.1 million for the ratable recognition of the upfront payment. During the six months ended June 30, 2018 and 2019, the Company recognized revenue of $0.1 million (unaudited) and less than $0.1 million (unaudited), respectively. No adjustment was necessary upon adoption of ASC 606. As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the uniQure Agreement was less than $0.1 million, $0 and $0 (unaudited), respectively. There were no amounts due from uniQure under the uniQure Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited).

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 has the option of nominating up to three project variants as part of the Benitec Agreement.

The Benitec Agreement provides 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 is two years and is 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 has concluded, Benitec is 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 is being 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.

Under ASC 605, the payments of $1.0 million were recorded as deferred revenue and were being recognized on a ratable basis over the estimated performance period of five years. Payments and reimbursements for research costs, including pass-through and other out-of-pocket costs, were recognized on an as-incurred basis under ASC 605. Under ASC 606, the Company uses the input method to measure progress toward completion of the performance obligation and concluded that revenue will be recognized based on actual costs incurred as a percentage of total budgeted costs as the Company completes its performance obligation. Upon adoption of ASC 606 on January 1, 2019, the Company recorded an additional $0.2 million of revenue through a decrease in deferred revenue and decrease in beginning accumulated deficit, based on the difference between the input method used under ASC 606 and the ratable recognition previously used under ASC 605.

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 joint steering committee (“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 six months ended June 30, 2019, there was no change in the transaction price.

During the years ended December 31, 2017 and 2018, the Company recognized revenue of $0.4 million and $0.2 million under the Benitec Agreement, respectively. During the six months ended June 30, 2018 and 2019, the Company recognized revenue of $0.1 million (unaudited) and less than $0.1 million (unaudited), respectively. As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the Benitec Agreement was $0.4 million, $0.2 million and $0 (unaudited), respectively. There were no amounts due from Benitec under the Benitec Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited). Upon termination of the Benitec Agreement in March 2019, the Company had no further obligations impacting revenue recognition.

AGTC

In April 2015, the Company entered into a collaboration and option agreement with Applied Genetic Technologies Corporation (“AGTC”) to discover and develop optimized AAV vectors to treat specific ophthalmic disease indications with high unmet medical need (the “AGTC Agreement”). The AGTC Agreement included both a research funding component as well as a licensing component, wherein AGTC was granted the option to license up to three resulting project variants for up to six products for further development and commercialization. The AGTC Agreement expired in October 2018 when AGTC did not exercise their option to license during the option period.

In accordance with ASC 605 the Company identified the following deliverables at the inception of the AGTC Agreement: (i) the research license, (ii) research services, and (iii) participation in a joint research steering committee. The Company determined that neither the research license nor participation in the joint research steering committee has stand-alone value to AGTC due to the specialized nature of the research services to be provided by the Company, and accordingly, this deliverable was combined with the research services as a single unit of accounting. Further, at the inception of the AGTC Agreement, AGTC's options to obtain an exclusive development and commercialization license for each research project target did not represent deliverables because they are substantive options and do not contain a significant or incremental discount. No adjustment was necessary upon adoption of ASC 606. The Company elected to use the practical expedients permitted related to adoption, which do not require the Company to apply the revenue standard to contracts that are completed as of the date of initial application.

Pursuant to the AGTC Agreement, the Company received two upfront payments totaling $3.0 million as consideration. The upfront payments of $3.0 million were recorded as deferred revenue and were recognized on a ratable basis over the estimated performance period of three years.

Revenue was fully recognized on the AGTC Agreement in the year ended December 31, 2018. During the years ended December 31, 2017 and 2018, the Company recognized revenue of $1.1 million and $0.3 million, respectively. During the six months ended June 30, 2018, the Company recognized revenue of $0.3 million (unaudited). As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the AGTC Agreement was $0.3 million, $0 and $0 (unaudited), respectively. No amount was due from AGTC under the AGTC Agreement as of December 31, 2017, December 31, 2018, and June 30, 2019 (unaudited).

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.

Pursuant to the CRF Agreement, the Company received an initial upfront grant of $50,000 in 2015 followed by a second upfront grant of $0.5 million in 2016 as consideration for the services to be provided.

Revenue was fully recognized for this agreement in the year ended December 31, 2017. During the year ended December 31, 2017, the Company recognized revenue of $0.2 million. There was no deferred revenue relating to the CRF Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited). No amount was due from CRF under the CRF Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited).

No adjustment was necessary upon adoption of ASC 606. The Company elected to use the practical expedient permitted related to adoption, which does not require the Company to apply ASC 606 to contracts that are completed as of the date of initial application.

Pfizer

In December 2015, the Company signed a collaboration and license agreement with Pfizer, Inc. ("Pfizer"). Under the terms of the Agreement, the Company agreed to deploy its Therapeutic Vector Evolution platform to generate and validate up to three project variants for gene delivery to treat diseases in cardiac tissue (the "Pfizer Agreement"). Once the Company's research activities concluded, Pfizer would be solely responsible for the continued development, manufacturing and commercialization of the project variants as potential product candidates.

Pursuant to the Pfizer Agreement, the Company received a non-refundable upfront payment of $5.0 million as consideration. No revenue was recognized under the Pfizer Agreement until Pfizer terminated this agreement for convenience in December 2018. The entire upfront payment of $5.0 million was recognized as revenue in December 2018 as the Company had no further obligations impacting revenue recognition. As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the Pfizer Agreement was $5.0 million, $0 and $0 (unaudited), respectively. No amount was due from Pfizer under the Pfizer Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited).

No adjustment was necessary upon adoption of ASC 606. The Company elected to use the practical expedient permitted related to adoption, which does not require the Company to apply ASC 606 to contracts that are completed as of the date of initial application.

Roche

In February 2015, 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 optimized next-generation AAV vectors for indications focusing on various rare retinal diseases caused by gene defects (the "2015 Roche Agreement"). As part of the 2015 Roche Agreement, two agreements were executed: (i) a Research Funding and Option Agreement requiring the Company to provide certain early-stage research services to Roche which are dependent on the licensed technology and gives Roche the right to choose to license the resulting project variants for further development and commercialization and (ii) a License Agreement which goes into effect if Roche elects to license the project variants.

The initial research term was two years with the option of three six-month extensions. The research program was completed on schedule and Roche chose not to extend the term. Roche also did not exercise its option to obtain the exclusive development and commercialization license for any of the research project targets.

The upfront payments of $1.0 million were recorded as deferred revenue and initially recognized on a ratable basis over the estimated performance period of three and a half years. Once the extension notification date passed, the balance of the unamortized deferred revenue was recognized in Q1 2017.

During the year ended December 31, 2017, the Company recognized revenue of $0.1 million under the 2015 Roche Agreement. There was no deferred revenue balance related to the 2015 Roche Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019. No amount was due from Roche under the 2015 Roche Agreement as of December 31, 2017, December 31, 2018 and June 30, 2019.

No adjustment was necessary upon adoption of ASC 606 as it relates to the 2015 Roche Agreement. The Company elected to use the practical expedient permitted related to adoption, which does not require the Company to apply ASC 606 to contracts that are completed as of the date of initial application.

In November 2017, the Company entered into a new collaboration and license agreement (the “2017 Roche Agreement”) with Roche to discover and develop products containing optimized next generation AAV Vectors focused on ophthalmological diseases and disorders excluding select criteria. 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 prior to pivotal clinical studies, 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, $86 million of which relate 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 605, the upfront payment of $21.0 million was recorded as deferred revenue and was being recognized on a ratable basis over the estimated performance period of five and a half years. Under ASC 606, the Company uses 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. Upon adoption of ASC 606, the Company recognized an additional $0.4 million of revenue through a decrease to deferred revenue and a decrease in beginning accumulated deficit, based on the difference between the input method used under ASC 606 and the ratable recognition previously used under ASC 605.

Under ASC 606, the Company identified one 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 includes the $21.0 million non-refundable upfront fee and $15.0 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 six months ended June 30, 2019, an adjustment of $4.4 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 resulted in a $0.1 million decrease in revenue recognized in the six months ended June 30, 2019 related to performance obligations partially satisfied in periods prior to January 1, 2019.

During the years ended December 31, 2017 and 2018, the Company recognized revenue of $0.7 million and $7.5 million, respectively. During the six months ended June 30, 2018 and 2019, the Company recognized revenue of $4.0 million (unaudited) and $3.8 million (unaudited), respectively. As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the Roche Agreement was $20.5 million, $17.1 million, and $14.6 million (unaudited), respectively. Accounts receivable from Roche under this agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 was $0.3 million, $1.1 million and $1.2 million (unaudited), respectively. As of June 30, 2019, the aggregate amount of the transaction price allocated to the remaining performance obligation was $23.7 million (unaudited). Based on current timelines, the revenue is expected to be recognized over the next five to seven years as the Company continues to develop nominated products until the initiation of pivotal studies.

CFFT

In September 2016, the Company entered into an award agreement for the Optimized Adeno- Associated Virus for Lung Epithelia Gene Delivery Development Program with CFFT, a non-profit organization dedicated to finding a cure for Cystic Fibrosis (“CF”), an inherited disorder that causes disease in the pulmonary airways leading to morbidity and mortality. Under this agreement, CFFT 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 “CFFT Agreements”). The total amount of the award under the CFFT Agreements is $3.5 million. As of December 31, 2017, December 31, 2018 and June 30, 2019, the Company received $0.6 million under the CFFT Agreements. The remaining award amount will be paid by CFFT based on achievement of certain development milestones by the Company.

The Company expects to make payments to CFFT 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 CFFT 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 collaboration agreement. The CFFT Agreements also require the Company to pay to CFFT 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, CFFT will receive certain payments, depending on the timing of the change of control and the size of the transaction.

To date, the Company had not developed a commercial product in connection with this award agreement, and it had not licensed, sold or otherwise transferred to another party the product developed under the agreement or the underlying technology.

If at any time prior to the first commercial sale of a product developed as a result of the agreement, the Company ceases to use commercially reasonable efforts to develop or commercialize any product under this 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 CFFT 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 605, the Company recognizes revenue under this agreement on a ratable basis over the estimated performance period of all milestones. Under ASC 606, the Company uses 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. Upon adoption of ASC 606, the Company decreased revenue by $0.2 million through an increase to deferred revenue and an increase to beginning accumulated deficit, based on the difference between the input method under ASC 606 and the ratable recognition previously used under ASC 605.

Under ASC 606, the Company identified one performance obligation within the CFFT grant agreement for research activities. The transaction price related to the agreement includes the $0.6 million non-refundable upfront fees and milestones previously met under the initial grant agreement. The Company's contract with CFFT 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 will re-evaluate the transaction price and estimated period of performance at each reporting period. For the six months ended June 30, 2019 there were no adjustments made to the transaction price.

During each of the years ended December 31, 2017 and 2018, the Company recognized revenue of $0.1 million. During each of the six months ended June 30, 2018 and 2019, the Company recognized revenue of less than $0.1 million (unaudited). As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the CFFT Agreement was $0.3 million, $0.2 million and $0.4 million (unaudited), respectively. No amount was due from CFFT under this agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited). As of June 30, 2019, the aggregate amount of the transaction price allocated to the remaining performance obligation was $0.4 million (unaudited). Based on current timelines, the revenue is expected to be recognized over the next five years as the Company performs research services through the completion of IND-enabling studies.

The obligation to make payments to CFFT 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 December 31, 2017, December 31, 2018 and June 30, 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 have concluded, AstraZeneca is 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. In addition, the Company is entitled to contingent payments including (i) a non-refundable license option exercise fee of $2.0 million and (ii) milestones up to $45.0 million for each product. The AstraZeneca Agreement also includes provisions that entitle the Company to receive royalties in the single digit range on future sales of the potential product candidates.

The Company has identified one single combined performance obligations 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 the performance obligations 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, does 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 will re-evaluate 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 605, the $1.5 million upfront payment was recorded as deferred revenue and was being recognized as revenue on a ratable basis over the estimated performance period of one and a half years. 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. Upon adoption of ASC 606, the Company reduced revenue by $48,000 through an increase to deferred revenue and an increase to beginning accumulated deficit, based on the difference between the input method used under ASC 606 and the ratable recognition previously used under ASC 605.

In June 2019, the research phase concluded and the Company delivered their final report to AstraZeneca. The option term continues for twelve months after AstraZeneca's receipt of the final report where they may exercise the option to obtain the license of up to three project vector variants.

During the years ended December 31, 2017 and 2018, the Company recognized revenue of $0 and $1.0 million, respectively. During each of the six months ended June 30, 2018 and 2019, the Company recognized revenue of $0.5 million (unaudited). As of December 31, 2017, December 31, 2018 and June 30, 2019, deferred revenue relating to the AstraZeneca Agreement was $0, $0.5 million and $0 (unaudited), respectively. No amount was due from AstraZeneca under this agreement as of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited).

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 on 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 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 each of the years ended December 31, 2017 and 2018, the Company incurred expenses of $0.1 million under the provisions of the UC Agreements. During the six months ended June 30, 2018 and 2019, the Company incurred expenses of $0.1 million (unaudited) and $0.2 million (unaudited), 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 extends the lease to March 31, 2023. In October 2018, the Company executed a second amendment to extend the lease to end at the same time as the new lease discussed below. 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 March 2019. This lease agreement also provides for a tenant improvement allowance of $0.4 million.

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

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December 31, 2029. The Company does 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, 2017 and 2018 and six months ended June 30, 2018 and 2019 for these facilities was $0.5 million, $0.5 million, $0.2 million (unaudited) and $0.3 million (unaudited), respectively. Deferred rent as of December 31, 2017, December 31, 2018 and June 30, 2019 was $0.1 million, $0.4 million and $0.2 million (unaudited), respectively. In conjunction with the lease agreements and amendments, the Company paid total security deposits of $0.1 million, $0.3 million and $0.6 million (unaudited), which are included in other assets within the balance sheets as of December 31, 2017, December 31, 2018 and June 30, 2019, respectively. The following table summarizes the Company's future minimum commitments under lease contracts (in thousands):

December 31, 2018	
2019	$ 850
2020	1,728
2021	1,804
2022	1,855
2023	1,911
2024 and beyond	5,379
Total	$13,527

June 30, 2019 (unaudited)	
Remainder of 2019	$ 567
2020	2,750
2021	2,885
2022	2,968
2023	3,058
2024 and beyond	18,213
Total	$ 30,441

Common Stock Warrant Obligation

As of December 31, 2017, the Company had an obligation to issue a warrant for 23,669 shares of the Company's common stock to a service provider. The Company issued the warrant in May 2018. See Note 13 for further discussion on common stock warrant obligation.

Indemnification Agreements

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. 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. Management is currently not aware of any matters that could have a material adverse effect on the Company's financial position, results of operations or cash flows.

9. Income Taxes

The Company did not record any income tax expense during the years ended December 31, 2017 and 2018. 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:

	2017	2018
Federal statutory income tax rate	34.0%	21.0%
Research tax credit	4.4%	10.0%
Permanent differences	(0.5%)	(1.1%)
Valuation allowance	(15.6%)	(27.4%)
2017 Tax Act—Tax rate change	(22.3%)	0.0%
Section 382 limitation	0.0%	(2.5%)
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):

	2017	2018
Deferred Tax Assets		
Net operating loss carryforwards	$ 2,853	$ 1,990
Other accrued liabilities	171	103
Deferred revenue	1,152	3,598
Research tax credits	951	1,872
Stock compensation	31	212
Total deferred tax assets	$ 5,158	$ 7,775
Less: valuation allowance	(5,158)	(7,775)
Net deferred tax assets	$ —	$ —

ASC 740 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 $1.7 million and $2.6 million during the years ended December 31, 2017 and 2018, respectively.

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (the "Tax Act"). The Tax Act makes broad and complex changes to the U.S. tax code, including, but not limited to: (i) reducing the U.S. federal corporate tax rate from 35% to 21%; (ii) requiring companies to pay a one-time transition tax on certain unrepatriated earnings of foreign subsidiaries; (iii) generally eliminating U.S. federal income taxes on dividends from foreign subsidiaries; (iv) requiring a current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations; (v) eliminating the corporate alternative minimum tax ("AMT") and changing how existing AMT credits can be realized; (vi) creating the base erosion anti-abuse tax ("BEAT"), a new minimum tax; (vii) creating a new limitation on deductible interest expense; and (viii) changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017.

As of December 31, 2018, the Company has completed its analysis of the income tax effects of the Tax Act and there was no material impact to the Company's financial statements when the analysis was complete. As of December 31, 2017 and 2018, the Company had federal net operating loss carryforwards of $13.6 million and $9.5 million, respectively, available to reduce future taxable income, if any, for federal income tax purposes, respectively. The federal net operating loss carryforwards expire in 2037.

As of December 31, 2017 and 2018, the Company had federal research and development credit carryforwards of $0.7 million and $1.3 million and state research and development credit carryforwards of $0.8 million and $1.4 million 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 net operating loss 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 net operating losses 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 NOLs as of December 31, 2018. 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, 2016	$ 143
Additions for current year tax positions	209
Balance as of December 31, 2017	352
Additions for current year tax positions	333
Reductions of prior year positions	(26)
Balance as of December 31, 2018	$ 659

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized. During the years ended December 31, 2017 and 2018, 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. All tax returns from inception to December 31, 2018 remain subject to examination. The Company has no ongoing income tax examinations by tax authorities at this time.

10. Redeemable Convertible Preferred Stock

In August 2018, the Company issued 5,154,632 shares of Series B redeemable convertible preferred stock at $17.46 per share for gross proceeds of $90.0 million.

As of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited), the Company's certificate of incorporation authorized the Company to issue up to 2,309,312 shares and 7,375,638 and 7,375,638 shares of redeemable convertible preferred stock, respectively, at a par value of $0.0001 per share.

Redeemable convertible preferred stock consists of the following as of December 31, 2017 (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	1,400,000	$ 8.84	1,311,687	11,595	11,548
Total	2,309,312		2,220,999	$ 18,596	$ 18,508

Redeemable convertible preferred stock consists of the following as of December 31, 2018 (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

Redeemable convertible preferred stock consists of the following as of June 30, 2019 (unaudited) (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

The holders of redeemable convertible preferred stock have various rights and preferences including the following:

Liquidation Preference—In the event of a liquidation event, the holders of the Series B redeemable convertible preferred stock are 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 Original Series B issue price plus all declared but unpaid dividends and (ii) such amount per share payable had all shares of Series B redeemable convertible preferred stock been converted into common stock. After full payment to holders of the Series B redeemable convertible preferred stock, payment should 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 should 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 are insufficient to pay the holders of a given series of redeemable convertible preferred stock the full amount to which they are entitled, then the available assets shall be distributed to the holders of such preferred stock on pro rata, on an equal priority, pari passu basis, in proportion to the full preferential amount such holder is otherwise entitled to receive.

Notwithstanding the above, for purposes of determining the amount each holder of shares of redeemable convertible preferred stock is entitled to receive with respect to a Liquidation Event, each such holder of shares of a series of redeemable convertible preferred stock shall 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 shall be deemed to have converted shares of redeemable convertible preferred stock into common stock pursuant to this paragraph, then such holder shall not be entitled to receive any distribution that would otherwise be made to holders of redeemable convertible preferred stock that have not converted into shares of common stock.

Conversion—Shares of any series of redeemable convertible preferred stock can 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. If, after the issuance date of the redeemable convertible preferred stock, the Company issues or sells, or is deemed to have sold, additional shares of common stock at a price lower than the original issuance price, except for certain exceptions allowed, the conversion price of the redeemable convertible preferred stock would be adjusted. As of December 31, 2018 and June 30, 2019 (unaudited), the conversion price for the Series A, A-1 and B redeemable convertible preferred stock is $7.700 per share, $8.839 per share and $17.460 per share, respectively, and the conversion ratio is one-for-one.

As of December 31, 2018 and June 30, 2019, shares of redeemable convertible preferred stock shall 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 (a "Qualified IPO") 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.

Dividends—Holders of shares of redeemable convertible preferred stock shall be entitled to non-cumulative dividends prior to, and in preference to any declaration or payment of any dividend on common stock. The amount of such dividends payable per share of preferred stock is at least equal to the dividend payable per share of common stock. Through December 31, 2018 and June 30, 2019 (unaudited), no dividends had been declared. Given this dividend preference, the Company considers all series of redeemable convertible preferred stock to be participating securities.

Voting Rights—Each holder of redeemable convertible preferred stock shall 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. Holders of redeemable convertible preferred stock and common stock generally vote as a single class. So long as at least 916,380 of the Series B redeemable convertible preferred stock issued remain outstanding, the holders of a majority of the Series B redeemable convertible preferred stock will be entitled to designate one director. So long as Pfizer and its Affiliates continue to own at least 25% of the Series A-1 redeemable convertible preferred stock, Pfizer will be entitled to designate one director.

Redemption and Balance Sheet Classification—The redeemable convertible preferred stock is recorded in mezzanine equity because while it is not mandatorily redeemable, it will become redeemable at the option of the stockholders upon the occurrence of a deemed liquidation event that is considered not solely within the Company's control.

11. Common Stock

As of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited), the Company's certificate of incorporation authorized the Company to issue 50,000,000 shares of common stock 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, 2017, December 31, 2018 and June 30, 2019 (unaudited), no dividends on common stock had been declared by the board of directors.

The number of authorized shares of common stock may be increased or decreased (but not below the number of shares thereof then outstanding or reserved for issuance) by the affirmative vote of the holders of a majority (assuming the conversion of all redeemable convertible preferred stock) of the capital stock of the Company entitled to vote and without a separate class vote of the common stock.

As of December 31, 2017, December 31, 2018 and June 30, 2019 (unaudited), the Company has reserved common stock, on an as-converted basis, for future issuance as follows:

	December 31, 2017	December 31, 2018	June 30, 2019 (Unaudited)
Conversion of redeemable convertible preferred stock	2,220,999	7,375,631	7,375,631
Stock options available for future stock option grant	1,004,239	578,842	399,886
Options issued and outstanding	792,290	2,028,274	2,192,230
Common stock warrants	68,669	68,669	68,669
Total common stock reserved	4,086,197	10,051,416	10,036,416

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 lapse over time and fully expired in March 2019. As of December 31, 2017, December 31, 2018, and June 30, 2019, 73,964, 14,793 and 0 (unaudited) shares of restricted common stock remained subject to repurchase, respectively.

12. Stock-based Compensation

2015 Equity Incentive Plan

In March 2015, the Company adopted the 2015 Equity Incentive Plan (the “2015 Plan”) under which the board of directors is authorized to issue 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, 2018 and June 30, 2019 (unaudited), there were 2,694,528 shares authorized and reserved for issuance. Under the 2015 Plan, as of December 31, 2018 and June 30, 2019, 578,842 and 399,886 (unaudited) of these shares respectively were available for grant. 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.

Stock Options

The following table summarizes the stock options activity:

	Number of Shares Available for Grant	Options Outstanding: Number of Shares Underlying Outstanding Options	Options Outstanding: Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balances at December 31, 2016	975,785	835,115	$ 1.09	9.10	$ 421
Options granted	(163,000)	163,000	1.59		
Options exercised	—	(14,371)	1.10		30
Options expired	10,833	(10,833)	1.14		
Options forfeited	180,621	(180,621)	1.22		
Balances at December 31, 2017	1,004,239	792,290	$ 1.16	8.27	$ 1,609
Options authorized	873,628				
Options granted	(1,454,173)	1,454,173	6.56		
Options exercised	—	(63,041)	1.66		488
Options expired	111,401	(111,401)	1.13		
Options forfeited	43,747	(43,747)	1.95		
Balances at December 31, 2018	578,842	2,028,274	$ 5.00	8.97	$ 8,939
Options granted (unaudited)	(688,740)	688,740	9.41		
Options exercised (unaudited)	—	(15,000)	1.34		147
Options expired (unaudited)	72,833	(72,833)	1.80		
Options forfeited (unaudited)	436,951	(436,951)	7.09		
Balances at June 30, 2019 (unaudited)	399,886	2,192,230	$ 6.10	8.78	$ 15,319
Exercisable, December 31, 2018		603,141	$ 1.56	7.64	$ 4,733
Vested and expected to vest, December 31, 2018		2,028,274	$ 5.00	8.97	$ 8,939
Exercisable, June 30, 2019 (unaudited)		696,012	$ 3.78	7.45	$ 7,540
Vested and expected to vest, June 30, 2019 (unaudited)		2,192,230	$ 6.10	8.78	$ 15,319

The following table is a summary of stock compensation expense for employees and nonemployees by function (in thousands):

	Year Ended December 31, 2017	Year Ended December 31, 2018	Six Months Ended June 30, 2018 (Unaudited)	Six Months Ended June 30, 2019 (Unaudited)
Research and development	$ 188	$ 695	$ 184	$ 950
General and administrative	68	682	219	522
Total stock-based compensation	$ 256	$ 1,377	$ 403	$ 1,472

During the years ended December 31, 2017 and 2018, the Company granted 153,000 and 1,234,173 stock options to employees with a weighted-average grant date fair value of $1.12 and $5.50 per share, respectively, and 10,000 and 220,000 stock options to nonemployees with a weighted-average grant date fair value of $1.32 and $3.38, respectively. During the six month ended June 30, 2018 and 2019, the Company granted 298,436 (unaudited) and 653,740 (unaudited) stock options to employees with a weighted-average grant date fair value of $2.30 (unaudited) and $7.32 (unaudited) per share, respectively, and 190,000 and 35,000 stock options to nonemployees with a weighted-average grant date fair value of $2.67 and $8.43 and respectively. The total fair value of options vested during the years ended December 31, 2017 and 2018 was $0.3 million and $0.8 million, respectively, and $0.3 million (unaudited) and $0.6 million (unaudited) during the six months ended June 30, 2018 and 2019, respectively. As of December 31, 2018 and June 30, 2019, the unrecognized stock-based compensation of unvested options was $8.0 million and $9.4 million (unaudited), respectively, and is expected to be recognized over a weighted-average period of 3.4 years and 3.2 years (unaudited), respectively. Stock-based compensation expense recorded for employee options was $0.2 million and $0.6 million for the years end December 31, 2017 and 2018 and $0.2 million (unaudited) and $1.1 million (unaudited) for the six months ended June 30, 2018 and June 30, 2019, respectively. Stock-based compensation expense recorded for nonemployee consultants was $0.1 million and $0.8 million for years ended December 31, 2017 and 2018, respectively, and $0.2 million (unaudited) and $0.4 million (unaudited) for the six months ended June 30, 2018 and 2019, respectively.

The Company is a privately held company with no active public market for the Company's common stock. 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*.

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, 2017 and 2018 and six months ended June 30, 2018 and 2019 (unaudited), respectively:

	Year Ended December 31, 2017		Year Ended December 31, 2018		Six Months Ended June 30, 2018		Six Months Ended June 30, 2019	
	Employee	**Nonemployee**	**Employee**	**Nonemployee**	**Employee**	**Nonemployee**	**Employee**	**Nonemployee**
					(Unaudited)		**(Unaudited)**	
Expected term	5.6 –5.9 years	7.7 –10.0 years	5.5 –6.3 years	6.7 –9.9 years	5.5 –6.3 years	7.2 –9.9 years	5.3 –6.3 years	6.2 –9.7 years
Expected volatility	84.7% –84.9%	81.9% –85.6%	81.4% –84.1%	80.8% –83.9%	83.4% –84.1%	81.8% –83.9%	82.8% –83.0%	81.5% –83.7%
Risk-free interest rate	1.9% –1.9%	2.2% – 2.4%	2.7% –3.0%	2.6% –3.2%	2.8% –2.9%	2.7% –2.9%	2.3% –2.3%	1.8% –2.4%
Dividend yield	0%	0%	0%	0%	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 any 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. 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. In 2018, 15,000 of these warrant shares became exercisable upon the completion of the Series B financing and the $13,000 fair value of these warrant shares, as determined under the Black-Scholes Model, was recorded within operating expenses in the statements of operations and comprehensive loss and within additional paid-in-capital in the balance sheets. The Company has not recognized expense for the remaining 30,000 warrant shares that become exercisable upon completion of an IPO as the vesting condition was not considered probable as of December 31, 2018 and June 30, 2019 (unaudited). If an IPO had occurred on June 30, 2019 (unaudited), the Company would have recorded less than $0.1 million within operating expenses in the statements of operations and comprehensive loss and within additional paid-in-capital in the balance sheets for the 30,000 warrant shares becoming exercisable. The warrant expires in 2023.

The Company also agreed to issue a warrant for 23,669 common stock shares with an exercise price of $3.19 per share to a third-party. As the Company had not issued the warrant as of December 31, 2017, the obligation to issue this common stock warrant was remeasured to its fair value of $60,000 as of December 31, 2017 using the Black-Scholes option pricing model. The warrant was issued in May 2018 and the obligation to issue the common stock warrant was remeasured at the fair value of $59,000 and recorded within additional paid-in-capital in the balance sheets upon issuance of the warrants. The warrant expires in 2025.

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, 2017	Year Ended December 31, 2018	Six Months Ended June 30, 2018 (Unaudited)	Six Months Ended June 30, 2019 (Unaudited)
Numerator				
Net loss attributable to common stockholders	$ (11,223)	$ (9,551)	$ (5,186)	$ (16,516)
Denominator				
Weighted average shares outstanding	5,054,375	5,090,988	5,077,668	5,135,166
Less: weighted average shares subject to repurchase used in computing net loss per share attributable to common stockholders, basic and diluted	(100,956)	(41,785)	(56,665)	(2,452)
Weighted average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	4,953,419	5,049,203	5,021,003	5,132,714
Net loss per share attributable to common stockholders – basic and diluted	$ (2.27)	$ (1.89)	$ (1.03)	$ (3.22)

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 anti-dilutive:

	Year Ended December 31, 2017	Year Ended December 31, 2018	Six Months Ended June 30, 2018 (Unaudited)	Six Months Ended June 30, 2019 (Unaudited)
Redeemable convertible preferred stock	2,220,999	7,375,631	2,220,999	7,375,631
Options to purchase common stock	792,290	2,028,274	1,154,988	2,192,230
Unvested restricted stock awards	73,964	14,793	44,379	—
Common stock warrant	68,669	68,669	68,669	68,669
Total	3,155,922	9,487,367	3,489,035	9,636,530

Unaudited Pro Forma Net Loss Per Share

Unaudited pro forma basic and diluted net loss per share were computed to give effect to the automatic one-for-one conversion of all outstanding shares of redeemable convertible preferred stock into shares of common stock in connection with the closing of the planned IPO, using the as-converted method as though the conversion had occurred as of the beginning of the period presented or the date of issuance, if later.

Unaudited pro forma basic and diluted loss per share is computed as follows (in thousands, except share and per share data):

	Year Ended December 31, 2018	Six Months Ended June 30, 2019
Numerator		
Net loss attributable to common stockholders		
Denominator		
Weighted-average shares used in computing net loss per share, basic and diluted		
Adjust: Conversion of redeemable convertible preferred stock		
Weighted-average shares used in computing pro forma net loss per share, basic and diluted		
Pro forma net loss per share, basic and diluted		

15. Derivative Liability

The Company identified an embedded derivative resulting from the change of control provision in the CFFT collaboration 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 CFFT, the probability of a change of control event, the probability of the product achieving development or commercial status at time of change of control and the discount rate. The Company determined the estimated fair value of this liability as of the inception date of the CFFT 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, 2017, December 31, 2018 and June 30, 2019 (unaudited).

16. Related Party Transactions

In January 2014, in connection with the performance obligations under the uniQure Agreement, the founders of the Company 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 and one of the founders of the Company agreed to serve as a director of uniQure. The accounting for this arrangement is discussed in Note 6. See Note 17 for subsequent events related to the Company's agreements with uniQure.

In 2015, the Company signed a collaboration and license agreement with Pfizer and recorded deferred revenue of $5.0 million related to the upfront payment received from Pfizer under the arrangement. In 2018, Pfizer terminated this agreement for convenience. Upon the termination of the agreement, the Company recognized revenue on the $5.0 million upfront payment. As of December 31, 2018 and June 30, 2019 (unaudited), Pfizer owns 1,474,992 shares of the Company's redeemable convertible preferred stock and has a representative director on the Company's board of directors.

The Company's former Chief Operating Officer, who was employed at the Company through November 2017, was the Executive Chairman of Dark Horse Consulting. During the year ended December 31, 2017, the Company paid $0.2 million to Dark Horse Consulting under a consulting agreement to design and implement pharmaceutical quality manufacturing of and controls for drug products. The consulting agreement terminated in December 2017.

In each of the years ended December 31, 2017 and 2018, the Company paid $56,500 and $50,000, respectively, and $25,000 (unaudited) in each of the six months ended June 30, 2018 and 2019 to the co-founder and Chief Scientific Advisor of the Company for consulting services. In April 2019, the Company entered into two sponsored research agreements with the UC Regents. See Note 17 for further details of this transaction involving the co-founder and Chief Scientific Advisor of the Company.

In 2016, the Company entered into a consulting agreement with one its former directors, who resigned as a director in December 2018, to provide business development strategy services. In connection with this agreement, the former director was granted stock options. In the years ended December 31, 2017 and 2018, the Company recorded $14,700 and $219,500 of stock-based compensation expense related to such stock options. In the six months ended June 30, 2018, the Company recorded $61,400 (unaudited) of stock-based compensation expense related to such stock options.

In 2016, the Chief Executive Officer and several other employees of the Company founded Ignite Immunotherapy ("Ignite"). The Company's Chief Executive Officer also serves as the Chief Executive Officer and Executive Chairman of Ignite. Certain executives of the Company hold ownership interests in Ignite and are members of the board of directors of Ignite. Additionally, Pfizer, who is a related party of the Company holds a significant equity stake in Ignite. There have been no transactions between the Company and Ignite in the years ended December 31, 2017 and 2018.

17. Subsequent Events

The Company evaluated subsequent events through August 2, 2019, the date on which the financial statements were available for issuance.

In January 2019, the Company entered into a license agreement with the UC Regents relating to the use of certain patents and intellectual property surrounding its core technologies. The Company paid a non-refundable license fee of $50,000 to the UC Regents upon execution of the agreement.

In March 2019, the Benitec Agreement was terminated based on mutual agreement between the Company and Benitec.

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 Professor David Schaffer, the Company's co-founder and Chief Scientific Advisor. 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 $0.4 million was paid upon the execution of the SRAs. 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 May 2019, the Company amended the lease agreement executed in October 2018 to add 17,497 square feet to the space being leased in Emeryville, California. The amendment extended the term of the lease to December 31, 2029. The Company does 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 $1.6 million.

From January 1, 2019 through August 2, 2019, the Company has granted options for the purchase of 1.0 million shares of common stock at an exercise price ranging from $9.41 to $10.10 per share. These options vest over a period of one to four years.

18. Subsequent Events (unaudited)

In connection with the issuance of the unaudited interim financial statements, the Company has evaluated subsequent events through August 30, 2019, the date the financial statements were available to be issued.

In August 2019, the Company entered into an Amended and Restated Collaboration and License Agreement (“amended uniQure Agreement”) with uniQure which amended and restated the uniQure Agreement. Under the amended uniQure Agreement, the Company granted uniQure a license for select AAV capsid variants (Selected Variants) in the central nervous system and the liver (together the uniQure Field). uniQure is solely responsible, at its cost and expense, to develop and commercialize the compounds and products containing the Selected Variants.

Also in August 2019, the Company 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) in the uniQure Field and that affect certain targets (uniQure Targets). The Company is responsible for the research of the New Variants. The Company granted uniQure a license for a certain number of the New Variants (uniQure New Variants) that affect the uniQure Targets. uniQure is solely responsible, at its cost and expense, to develop and commercialize the compounds and products containing the uniQure New Variants that affect the uniQure Targets.

Under both the Amended and Restated 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 a portion of the amounts it receives for sublicensing to third parties the Company’s intellectual property rights licensed under the agreement at a rate between mid-single digit to mid-twenties percentages.

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Shares

4D Molecular Therapeutics, Inc.

Common Stock

Goldman Sachs & Co. LLC **Evercore ISI** **William Blair**

Chardan

Through and including , 2019 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

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PART II INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the costs and expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the sale of common stock being registered. All amounts are estimates except for the SEC registration fee, the Financial Industry Regulatory Authority, Inc. (FINRA) filing fee and The Nasdaq Global Market listing fee.

Item	Amount paid or to be paid
SEC registration fee	$ *
FINRA filing fee	*
The Nasdaq Global Market listing fee	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Blue Sky, qualification fees and expenses	*
Transfer Agent fees and expenses	*
Miscellaneous fees and expenses	*
Total	$ *

* To be completed by amendment.

Item 14. Indemnification of Directors and Officers.

As permitted by Section 102 of the Delaware General Corporation Law, we have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws, to be in effect immediately prior to the consummation of this offering, that will limit or eliminate the personal liability of our directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, directors exercise an informed business judgment based on all material information reasonably available to them. Consequently, a director will not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for 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;
- any act related to unlawful stock repurchases, redemptions or other distributions or payment of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not affect the availability of equitable remedies such as injunctive relief or rescission. Our amended and restated certificate of incorporation will also authorize us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws will provide that:

- we may indemnify our directors, officers, and employees to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions;

- we may advance expenses to our directors, officers and employees in connection with a legal proceeding to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions; and
- the rights provided in our amended and restated bylaws are not exclusive.

Our amended and restated certificate of incorporation, to be attached as Exhibit 3.2 hereto, and our amended and restated bylaws, to be attached as Exhibit 3.4 hereto, will provide for the indemnification provisions described above and elsewhere herein. We have entered into separate indemnification agreements with our directors and officers which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements generally require us, among other things, to indemnify our officers and directors against liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct. These indemnification agreements also generally require us to advance any expenses incurred by the directors or officers as a result of any proceeding against them as to which they could be indemnified. In addition, we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment in some circumstances. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of our officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act.

The form of Underwriting Agreement, to be attached as Exhibit 1.1 hereto, provides for indemnification by the underwriters of us and our officers who sign this Registration Statement and directors for specified liabilities, including matters arising under the Securities Act.

Item 15. Recent Sales of Unregistered Securities.

The following list sets forth information as to all securities we have sold since January 1, 2016, which were not registered under the Securities Act.

1. On August 27, 2018 and August 28, 2018, we issued an aggregate of 5,154,632 shares of our Series B redeemable convertible preferred stock at a price per share of $17.46 for aggregate proceeds to us of $89,999,874.72.
2. On June 30, 2016, we issued a warrant to purchase 45,000 shares of our common stock at a per share exercise price of $1.14.
3. On May 18, 2018, we issued a warrant to purchase 23,669 shares of our common stock at a per share exercise price of $3.19.
4. We granted stock options and stock awards to employees, directors and consultants under our 2015 Equity Incentive Plan, covering 3,239,613 shares of common stock, at a weighted-average exercise price of $6.32 per share. Of these, options covering an aggregate of 848,397 shares of common stock were cancelled without being exercised.

We claimed exemption from registration under the Securities Act for the sale and issuance of securities in the transactions described in paragraphs (1) through (3) by virtue of Section 4(a)(2) 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.

We claimed exemption from registration under the Securities Act for the sales and issuances of securities in the transactions described in paragraph (4) above under Section 4(a)(2) of the Securities Act in that such sales and issuances did not involve a public offering or under Rule 701 promulgated under the Securities Act, in that they were offered and sold either pursuant to written compensatory plans or pursuant to a written contract relating to compensation, as provided by Rule 701.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit Number	Exhibit Description
1.1*	Form of Underwriting Agreement.
3.1^	Amended and Restated Certificate of Incorporation, currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation, to be in effect immediately prior to the consummation of this offering.
3.3^	Bylaws, currently in effect.
3.4*	Form of Amended and Restated Bylaws, to be in effect immediately prior to the consummation of this offering.
4.1	Reference is made to exhibits 3.1 through 3.4.
4.2*	Form of Common Stock Certificate.
4.3^	Amended and Restated Investors' Rights Agreement, dated as of August 27, 2018, among the Registrant and the investors party thereto.
5.1*	Opinion of Latham & Watkins LLP.
10.1(a)#^	2015 Equity Incentive Plan.
10.1(b)#^	Form of Stock Option Agreement under 2015 Equity Incentive Plan.
10.2(a)#*	2019 Incentive Award Plan.
10.2(b)#*	Form of Stock Option Grant Notice and Stock Option Agreement under the 2019 Incentive Award Plan.
10.2(c)#*	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2019 Incentive Award Plan.
10.2(d)#*	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Incentive Award Plan.
10.3#*	2019 Employee Stock Purchase Plan.
10.4*	Form of Indemnification Agreement for directors and officers.
10.5*†	Collaboration and License Agreement, dated November 16, 2017, among the Registrant, F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.
10.6*†	Collaboration and Option Agreement, dated December 22, 2017, between the Registrant and MedImmune, LLC.
10.7*†	Amended and Restated Collaboration and License Agreement, dated August 6, 2019, between the Registrant and uniQure biopharma B.V.
10.8*†	Collaboration and License Agreement, dated August 6, 2019, by and between the Registrant and uniQure biopharma B.V.

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Exhibit Number	Exhibit Description
10.9*†	Exclusive License and Bailment Agreement, dated December 13, 2013, between the Registrant and The Regents of the University of California.
10.10*†	Exclusive License and Bailment Agreement, dated December 19, 2013, between the Registrant and The Regents of the University of California.
10.11#*	Offer Letter, dated March 20, 2015 between David Kirn, M.D. and the Registrant.
10.12#*	Employment Agreement, dated January 15, 2019 between Peter Francis, M.D., Ph.D. and the Registrant.
10.13#*	Offer Letter, dated July 31, 2018 between Fred Kamal, Ph.D. and the Registrant.
23.1*	Consent of independent registered public accounting firm.
23.2*	Consent of Latham & Watkins LLP (included in Exhibit 5.1).
24.1*	Power of Attorney. Reference is made to the signature page to the Registration Statement.

* To be filed by amendment.
† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.
\# Indicates management contract or compensatory plan.
^ Previously filed.

(b) Financial Statement Schedules. Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer, or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

1. For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.

2. For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in Emeryville, California on , 2019.

4D Molecular Therapeutics, Inc.

By: ____________________________
David Kirn, M.D.
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints David Kirn, M.D. and August J. Moretti, and each of them acting individually, as his or her true and lawful attorneys-in-fact and agents, each with full power of substitution, for him or her in any and all capacities, to sign any and all amendments to this Registration Statement, including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought, and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorneys-in-fact and agents, with full power of each to act alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he might or could do in person, hereby ratifying and confirming all that 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 Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
David Kirn, M.D.	Chairman and Chief Executive Officer *(Principal Executive Officer)*	, 2019
August J. Moretti	Chief Financial Officer *(Principal Financial and Accounting Officer)*	, 2019
David Schaffer, Ph.D.	Director	, 2019
Bill Burkoth	Director	, 2019
Jacob Chacko, M.D.	Director	, 2019
Charles P. Theuer, M.D., Ph.D.	Director	, 2019
Tony Yao, Ph.D.	Director	, 2019