Filed Pursuant to Rule 424(b)(4)
Registration No. 333-238608

Prospectus

10,526,316 shares

generation bio™

Common stock

This is Generation Bio Co.'s initial public offering. We are selling 10,526,316 shares of our common stock.

The public offering price is $19.00 per share. Currently, no public market exists for the shares. The shares will trade on the Nasdaq Global Select Market under the symbol "GBIO."

Investing in the common stock involves risks that are described in the "Risk factors" section beginning on page 12 of this prospectus.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings. See "Prospectus summary—Implications of being an emerging growth company."

	Per Share	Total
Public offering price	$ 19.00	$200,000,004
Underwriting discount(1)	$ 1.33	$ 14,000,000
Proceeds, before expenses, to us	$ 17.67	$186,000,004

(1) See "Underwriting" for a description of all compensation payable to the underwriters.

The underwriters may also exercise their option to purchase up to an additional 1,578,947 shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about June 16, 2020.

Joint bookrunning managers

J.P. Morgan **Jefferies** **Cowen**

Lead manager

Wedbush PacGrow

June 11, 2020

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Neither we nor the underwriters have authorized anyone to provide you with any information other than that contained in this prospectus, any amendment or supplement to this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside 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 in the United States. Persons outside 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 the United States.

Through and including July 6, 2020, (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 delivery requirement 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.

We own or have rights to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. The service marks and trademarks that we own include the mark Generation Bio™ and the Generation Bio logo. Other trademarks, service marks and trade names appearing in this prospectus are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this prospectus are listed without the ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names.

Prospectus summary

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, including our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the information set forth in the sections titled "Risk factors" and "Management's discussion and analysis of financial condition and results of operations." As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our" and "Generation Bio Co." refer to the consolidated operations of Generation Bio Co. and its wholly owned subsidiary.

Overview

We are an innovative genetic medicines company creating a new class of gene therapy utilizing our proprietary non-viral gene therapy platform to provide durable, redosable treatments for millions of patients living with rare and prevalent diseases. Our non-viral gene therapy platform incorporates our high-capacity DNA construct called closed-ended DNA, or ceDNA; our cell-targeted lipid nanoparticle delivery system, or ctLNP; and our established, scalable capsid-free manufacturing process. Using our approach, we are developing novel gene therapies to provide targeted delivery of genetic payloads that include large and multiple genes to a range of tissues across a broad array of diseases. We are also engineering our gene therapies to be redosable, which may enable individualized patient titration to reach the desired level of therapeutic expression and to maintain efficacy throughout a patient's life.

We are advancing a broad and expansive portfolio including eight programs for rare and prevalent diseases of the liver and retina. We are focused on diseases with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches. We are initially prioritizing rare monogenic diseases of the liver and retina, which result from mutations in a single gene, that have well-established biomarkers and clear clinical and regulatory pathways. We plan to expand our portfolio to include additional programs in rare and prevalent diseases of the liver and retina, as well as in diseases of the skeletal muscle, the central nervous system, or CNS, and oncology by developing discrete ctLNPs, each engineered to reach a different tissue. In parallel, we are developing the constructs and manufacturing capacity to rapidly advance new disease programs in a tissue or area once human proof of concept is established.

While we are currently a preclinical stage company and have not yet identified a product candidate, we believe that our new class of gene therapy has the potential to reach previously untreatable or under-treated patients and address new indications, including those with large patient populations, thereby unlocking the full potential of genetic medicine.

Our non-viral gene therapy platform

Our non-viral gene therapy platform is comprised of three essential components: our high-capacity ceDNA construct, which can accommodate large or multiple genes as well as native regulatory elements; our ctLNP delivery system, which enables highly specific delivery of ceDNA to a range of tissues; and our established, scalable capsid-free manufacturing process, that uses a cost-effective biologics infrastructure with the potential to reach patients with rare diseases and to expand access to patients with prevalent diseases requiring millions of doses on a sustainable basis.

ceDNA—Our high-capacity ceDNA is an engineered, double-stranded, linear, covalently closed-ended DNA construct that includes the gene of interest and associated regulatory sequences. We have produced ceDNA

constructs of 12 kilobases, or kb, which have almost three times the capacity of adeno-associated virus, or AAV, gene therapy approaches. We believe ceDNA can deliver a significant majority of the human coding sequences known to be relevant for the treatment of diseases that result from mutations in a single gene, in multiple genes, or in those requiring more than one type of genetic correction.

ctLNP—Our ctLNP delivery system builds upon clinically validated lipid nanoparticles, or LNPs, and is designed to allow for repeat dosing of a genetic payload without stimulating an immune response, such as antibody production. We have taken a significant step beyond current LNP technologies by adding a biological targeting molecule, called a ligand, on the surface of our LNPs to direct their biodistribution to specific tissues. Different targeting ligands may enable our ctLNPs to actively target specific cell receptors in the liver, retina, skeletal muscle, CNS and tumors. In addition, our ctLNP delivery system may confer the advantages of predictable behavior across species, minimal off-target effects and a foundational platform approach that unlocks the ability to target the widest possible spectrum of diseases with our therapies.

Manufacturing process—Our established, scalable manufacturing employs a proprietary, capsid-free process and utilizes standard biologics infrastructure, unlike traditional viral gene therapy manufacturing. Viral gene therapy relies on a protein capsid for therapeutic delivery of a viral vector, and as a result, the manufacturing process for viral gene therapies requires the production of protein capsids, which limit process scalability and consistency. Our capsid-free manufacturing process is an efficient and reproducible process that includes rigorous, industrial-scale purification that consistently yields greater than 99% pure ceDNA.

We have established a current Good Manufacturing Practices-ready process at the 200-liter scale. Our ability to conduct the manufacturing process at the 200-liter scale with high product quality suggests that further scaling to thousands of liters per batch is feasible using standard biological production equipment and engineering methods. We believe the combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases.

Advantages of our non-viral gene therapy platform

Our non-viral gene therapy platform is designed to overcome the limitations of current gene therapy approaches and we believe will disrupt the field of genetic medicine. While our platform is still in an early stage of development, we believe that our platform may provide the following advantages:

- *Durable expression.* Our ceDNA is highly stable and potentially enables years-long expression for patients with each dose, minimizing treatment burden.
- *Redosable administration*. Our ctLNP delivery system has been designed to avoid stimulating an antibody response in patients, thereby enabling redosing, which may allow for individualized patient titration to reach desired expression levels as well as extended therapeutic expression and the ability to treat pediatric patients.
- *Greater opportunity to demonstrate efficacy in first-in-human trials*. Because we may be able to redose, we believe that a greater proportion of patients participating in our early clinical trials may achieve the desired level of gene expression.
- *Addressing untreated or under-treated patients*. Our therapy may be used to treat patients with pre-existing immunity to AAV viral capsids or whose efficacy outcomes on current gene therapies were insufficient in level of duration or expression.

- *Delivery of large genetic payloads*. The payload capacity of ceDNA enables our constructs to carry larger genes and/or multiple genes, or to incorporate native regulatory elements.
- *Targeted, multi-tissue delivery*. Our ctLNP delivery system has been engineered to use biological ligands to reach receptors in a specific tissue.
- *Scale to reach millions of patients*. We believe the combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases.
- *A sustainable payer model*. Our cost-effective manufacturing process, combined with the potential to redose patients as needed to extend expression, may allow payers to better predict clinical outcomes and, as a result, to cover our therapies within the current reimbursement paradigm.

Our portfolio

We are advancing a broad and expansive portfolio, including eight programs for rare and prevalent diseases of the liver and retina. We are focused on diseases with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches. We are initially prioritizing rare monogenic diseases of the liver and retina that have well-established biomarkers and clear clinical and regulatory pathways. We plan to expand our portfolio by pursuing additional programs in rare and prevalent diseases of the liver and retina, as well as in skeletal muscle, the CNS and oncology by developing discrete ctLNPs, each engineered to reach a different tissue. As shown in the figure below, our most advanced liver disease programs are in phenylketonuria, or PKU, and hemophilia A, which are in the preclinical stage of development, and our most advanced retina disease programs are in Leber's Congenital Amaurosis, or LCA10, and Stargardt disease, which are in the lead optimization stage of development. In the lead optimization stage, we are seeking to identify ceDNA constructs that provide disease relevant expression in an animal model, and in the preclinical stage of development, we are conducting additional *in vivo* studies to identify development candidates and are assessing these candidates in investigational new drug, or IND, -enabling studies.

We believe our non-viral gene therapy platform may allow patients to produce antibody therapies from their own cells for years at a time from a single dose, and plan to advance antibody gene therapy programs across multiple therapeutic areas.

Over the course of 2020, we expect to obtain additional preclinical *in vivo* data and to identify development candidates for PKU and hemophilia A, positioning us to undertake IND-enabling studies for these programs in 2021 and to submit IND applications for these programs in 2022. We anticipate submitting IND applications for additional programs in 2023 and beyond.

Liver diseases

For the majority of our liver programs, we have designed and manufactured disease-modifying ceDNAs that have shown expression *in vitro* and/or disease correction *in vivo*. To drive ctLNP biodistribution to the liver, we have employed GalNAc, a ligand that binds to the asialoglycoprotein receptor on liver cells called hepatocytes, because the biology of this selective ligand-receptor pair for delivery to hepatocytes has been well-validated in human clinical trials. GalNAc targeting has been demonstrated to efficiently deliver nucleic acid payloads to up to 100% of hepatocytes, and we believe that broad biodistribution of ctLNP-GalNAc to hepatocytes will be a key strength of our pipeline programs since current gene therapy approaches deliver payload to 30% or fewer hepatocytes with a single dose. Additionally, our potential to redose patients until they are in the therapeutic range of expression may enable early and robust human proof of concept in early clinical trials and is a key differentiator from current gene therapy approaches.

Our most advanced liver disease programs include:

- *Phenylketonuria,* or PKU, is a rare autosomal recessive genetic disorder caused by deficiency of the hepatic enzyme phenylalanine hydroxylase, which results in metabolic abnormalities and neurocognitive deficits. PKU affects approximately 15,000 individuals in the United States and 41,000 individuals in the European Union. Our approach seeks to achieve sustained metabolic correction for patients of all ages upon initial dose or through individualized patient dose titration, normalizing their diet, eliminating the burden of ongoing treatment and stabilizing and/or preserving neurocognitive function.
- *Hemophilia A* is a rare X-linked hereditary bleeding disorder characterized by impaired blood coagulation as a result of deficiency in the production or function of coagulation Factor VIII that affects approximately 16,000 individuals in the United States and 320,000 individuals worldwide. Our approach aims to achieve therapeutic Factor VIII levels in patients of all ages resulting in normalization of bleeding risk to prevent irreversible tissue and organ dysfunction.

Retinal diseases

Approximately 200 million individuals suffer from inherited retinal diseases, in which a gene mutation leads to degeneration of the retina. Many of these diseases are caused by genes too large to be enclosed within AAV, including several types of LCA10 and Stargardt disease. We believe using ceDNA to deliver large gene payload efficiently and specifically to relevant cell types in the retina by minimally invasive routes represents an important therapeutic approach.

Our most advanced retinal disease programs include:

- *LCA10* is the most common genetic cause of childhood vision loss and affects approximately 2,200 individuals in the United States and 3,400 individuals in the European Union. Our approach may deliver the full gene to photoreceptors to correct the full spectrum of mutations with a single ceDNA construct in order to halt visual decline and restore vision.
- *Stargardt disease* is the most common inherited macular dystrophy and affects approximately 37,000 individuals in the United States and 66,000 individuals in the European Union. Our approach aims to deliver

the full gene to photoreceptors and retinal pigment epithelial cells in order to halt disease progression and preserve vision.

Our strategy

Our goal is to become an industry leader in the field of genetic medicine, advancing our non-viral gene therapy platform to discover, develop, manufacture and globally commercialize a new class of gene therapy that is durable, redosable and specifically delivered to a range of tissues for the treatment of diseases caused by single, large or multiple gene defects. We aim to provide sustainable, life-long treatment for millions of patients living with rare and prevalent diseases.

Key components of our strategy are to:

- Establish ceDNA as a new class of non-viral gene therapy, initially demonstrating its potential across rare monogenic diseases of the liver and retina;
- Leverage our non-viral gene therapy platform to advance additional programs for diseases of the liver and retina and to expand quickly into additional tissues;
- Utilize our eight-week research cycle to rapidly design, produce and screen ceDNA constructs to enable new disease programs within a tissue or therapeutic area;
- Expand manufacturing scale to access previously unattainable markets for gene therapy;
- Expand patient access to our non-viral gene therapy through a high-value network of alliances and collaborations; and
- Build a sustainable leadership position in non-viral gene therapy as a fully integrated innovative biotechnology company.

Our organization is composed of more than 85 talented individuals with significant experience across discovery, preclinical research, manufacturing and clinical development. Our research and development efforts have resulted in numerous innovations and breakthroughs across every aspect of our platform. We own or exclusively license patent applications in 37 patent application families covering our programs and technology, including our ceDNA platform, ctLNP delivery system and manufacturing processes, and have taken other steps to protect our proprietary position with respect to these innovations and breakthroughs. Our wholly owned intellectual property, combined with the background technology we have licensed from the National Institutes of Health and the University of Massachusetts Medical School and Voyager Therapeutics, Inc. based on our co-founder’s prior work, supports the leading position of our platform and provides a strong foundation for its continued advancement.

To fund our operations, we have raised approximately $227.3 million from investors, premier venture capitalists and institutional investors, including Atlas Venture, Fidelity, T. Rowe Price, Invus, Farallon, Wellington, Deerfield, Casdin Capital, Foresight Capital and Leerink Partners.

Risks associated with our business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the “Risk factors” section of this prospectus. These risks include, but are not limited to, the following:

- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts;

- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability;
- We are very early in our development efforts. We have not identified any product candidates for IND-enabling studies or clinical development. As a result it will be many years before we commercialize a product candidate, if ever. If we are unable to identify and advance product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed;
- We may encounter substantial delays in commencement, enrollment or completion of our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, any of which could prevent us from commercializing any product candidates we may develop on a timely basis, if at all;
- Our non-viral gene therapy platform is based on novel technologies that are unproven, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all;
- If any product candidates we may develop cause undesirable side effects or have other unexpected adverse properties, such side effects or properties could delay or prevent regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval;
- The outcome of preclinical studies may not be predictive of later preclinical studies or clinical trials;
- Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate we may develop, or the approval may be for a more narrow indication than we expect;
- The manufacture of genetic medicine products is complex and difficult and is subject to a number of scientific and technical risks, some of which are common to the manufacture of drugs and biologics and others of which are unique to the manufacture of gene therapies. We could experience manufacturing problems that result in delays in our development or commercialization programs;
- We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research, preclinical and clinical testing, and these third parties may not perform satisfactorily;
- If we fail to comply with our obligations under our existing license agreements, or under any future intellectual property licenses, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business;
- If we are unable to obtain and maintain patent protection for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop and technology may be adversely affected; and
- The ongoing COVID-19 pandemic and its effects on our business and operations are uncertain. We and our contract development and manufacturing organizations and contract research organizations have experienced a reduction in the capacity to undertake research scale production and to execute some preclinical studies, and we may face disruptions that affect our ability to initiate and complete preclinical studies and to procure items that are essential for our research and development activities.

Our corporate information

We were incorporated under the laws of the state of Delaware on October 21, 2016 under the name Torus Therapeutics, Inc. On November 17, 2017 we changed our name to Generation Bio Co. Our principal executive offices are located at 301 Binney Street, Cambridge, MA 02142 and our telephone number is (617) 655-7500. Our website address is http://www.generationbio.com. The information contained on, or accessible through, our website does not constitute part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Implications of being an emerging growth company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. As a result, we may take advantage of reduced reporting requirements that are otherwise applicable generally to public companies, including delaying auditor attestation of internal control over financial reporting, exemption from the requirements to hold non-binding advisory votes on executive compensation and golden parachute payments, providing only two years of audited financial statements and related Management’s discussion and analysis of financial condition and results of operations in this prospectus and reducing executive compensation disclosures.

We may remain an emerging growth company until the end of 2025. We will cease to be an emerging growth company prior to the end of 2025 if we become a “large accelerated filer,” our annual gross revenue exceeds $1.07 billion, or we issue more than $1.0 billion of non-convertible debt in any three-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected not to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we can adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (1) irrevocably elect to “opt out” of such extended transition period or (2) no longer qualify as an emerging growth company.

The offering

Common stock offered by us	10,526,316 shares
Common stock to be outstanding after this offering	44,634,420 shares
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase up to 1,578,947 additional shares of our common stock.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $183.0 million (or approximately $210.9 million if the underwriters exercise their option to purchase additional shares in full), based on the initial public offering price of $19.00 per share after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds to us from this offering, together with our existing cash and cash equivalents, for continued research and development of our programs, including preclinical research, completion of IND-enabling studies in our most advanced liver programs and initiation of a clinical trial in each of these programs; continued development and enhancement of our platform technologies; and for working capital and other general corporate purposes. See “Use of proceeds” for more information.
Risk factors	You should read the “Risk factors” section of this prospectus beginning on page 12 for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	“GBIO”

The number of shares of our common stock to be outstanding after this offering is based on 7,014,019 shares of our common stock outstanding as of April 30, 2020, which includes 1,233,488 shares of unvested restricted stock subject to repurchase by us, and after giving effect to the conversion of all outstanding shares of our preferred stock into an aggregate of 27,094,085 shares of common stock upon the closing of this offering, and excludes:

- 4,805,609 shares of common stock issuable upon exercise of stock options outstanding as of April 30, 2020, under our 2017 Stock Incentive Plan, as amended, or the 2017 Plan, at a weighted-average exercise price of $4.92 per share;

- 1,172,297 shares of common stock available for future issuance as of April 30, 2020 under our 2017 Plan, which shares will become available for issuance under our 2020 Stock Incentive Plan, or the 2020 Plan, at the time our 2020 Plan becomes effective; and
- 2,547,698 and 481,231 additional shares of common stock available for issuance under our 2020 Plan and our 2020 Employee Stock Purchase Plan, respectively, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans. Of the shares available under our 2020 Plan, we have granted options to purchase an aggregate of approximately 648,481 shares of our common stock, at an exercise price equal to the initial public offering price in this offering, to certain of our directors, employees and consultants.

Unless otherwise indicated, all information in this prospectus:

- assumes the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 27,094,085 shares of our common stock upon the closing of the offering;
- assumes no exercise of the outstanding options described above;
- assumes no exercise by the underwriters of their option to purchase additional shares of our common stock;
- gives effect to a one-for-1.7663 reverse stock split of our common stock, and a proportionate adjustment in the ratio at which our preferred stock is convertible into our common stock, that became effective on June 5, 2020; and
- assumes the filing and effectiveness of our restated certificate of incorporation and the adoption of our amended and restated bylaws upon the closing of this offering.

Summary consolidated financial data

You should read the following summary consolidated financial data, together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the "Selected consolidated financial data" and "Management's discussion and analysis of financial condition and results of operations" sections of this prospectus. We have derived the following consolidated statement of operations data for the years ended December 31, 2018 and 2019 from our audited consolidated financial statements appearing elsewhere in this prospectus. The consolidated statement of operations data for the three months ended March 31, 2019 and 2020 and the consolidated balance sheet data as of March 31, 2020 have been derived from our unaudited condensed consolidated financial statements appearing elsewhere in this prospectus and have been prepared on the same basis as our audited consolidated financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future.

	Year ended December 31,		Three months ended March 31,	
(in thousands, except per share data)	**2018**	**2019**	**2019**	**2020**
Consolidated statement of operations data:				
Revenue	$ 36	$ —	$ —	$ —
Operating expenses:				
Research and development	28,152	50,134	11,719	13,394
General and administrative	9,178	12,168	2,757	4,642
Total operating expenses	37,330	62,302	14,476	18,036
Loss from operations	(37,294)	(62,302)	(14,476)	(18,036)
Other income (expense):				
Interest income and other income (expense), net	1,491	985	382	319
Net loss and net loss attributable to common stockholders	$ (35,803)	$ (61,317)	$ (14,094)	$ (17,717)
Net loss per share attributable to common stockholders, basic and diluted	$ (10.69)	$ (12.96)	$ (3.29)	$ (3.22)
Weighted average common shares outstanding, basic and diluted	3,351	4,732	4,284	5,495
Pro forma net loss per share attributable to common stockholders, basic and diluted(1)		$ (3.11)		$ (0.56)
Pro forma weighted average common shares outstanding, basic and diluted(1)		19,693		31,389

(1) See Notes 2 and 12 to our consolidated financial statements appearing elsewhere in this prospectus for details on the calculation of unaudited pro forma net loss per share attributable to common stockholders.

(in thousands)	As of March 31, 2020		
	Actual	Pro forma(2)	Pro forma as adjusted(3)
Consolidated balance sheet data:			
Cash and cash equivalents	$ 104,473	$ 104,473	$ 287,473
Working capital(1)	100,199	100,199	283,857
Total assets	132,636	132,636	314,978
Convertible preferred stock	224,425	—	—
Total stockholders' equity (deficit)	(114,651)	109,774	292,774

(1) We define working capital as current assets less current liabilities.
(2) The pro forma consolidated balance sheet data give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 27,094,085 shares of common stock upon the closing of this offering.
(3) The pro forma as adjusted balance sheet data give further effect to our issuance and sale of 10,526,316 shares of our common stock in this offering at the initial public offering price of $19.00 per share after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Risk factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing elsewhere in prospectus, before deciding to invest in our common stock. The risks described below are not the only risks facing our company. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us or that we currently believe to be immaterial, could cause our business, prospects, operating results and financial condition to suffer materially. In such event, the trading price of our common stock could decline, and you might lose all or part of your investment.

Risks related to our financial position and need for additional capital

We have incurred significant losses since our inception, have no products approved for sale and we expect to incur losses over the next several years.

Since inception, we have incurred significant operating losses. Our net losses were $61.3 million for the year ended December 31, 2019 and $17.7 million for the three months ended March 31, 2020. As of March 31, 2020, we had an accumulated deficit of $126.2 million. To date, we have financed our operations with the proceeds from instruments convertible into convertible preferred stock (which converted into convertible preferred stock in 2017) and the sale of convertible preferred stock. We have devoted substantially all of our financial resources and efforts to research and development. We are still in the early stages of development of our product candidates, and we have not commenced or completed clinical development. We expect to continue to incur significant expenses and operating losses over the next several years. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue our current research programs and conduct additional research programs;
- advance any product candidates we identify through our research programs into preclinical and clinical development;
- expand the capabilities of our proprietary non-viral gene therapy platform;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- obtain, expand, maintain, defend and enforce our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- establish a commercial manufacturing source and secure supply chain capacity sufficient to provide commercial quantities of any product candidates we may develop for which we may obtain regulatory approval; and
- add operational, legal, compliance, financial and management information systems and personnel to support our research, product development, future commercialization efforts and operations as a public company.

Even if we obtain regulatory approval of and are successful in commercializing one or more of any product candidates we may develop, we will continue to incur substantial research and development and other

expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

We have never generated revenue from product sales and may never achieve or maintain profitability.

We have not initiated clinical development of any product candidate and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must succeed in developing, obtaining the necessary regulatory approvals for and eventually commercializing a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including:

- identifying product candidates and completing preclinical and clinical development of any product candidates we may identify;
- obtaining regulatory approval for any product candidates we may develop;
- manufacturing, marketing and selling any products for which we may obtain regulatory approval;
- achieving market acceptance of any product candidates we may develop for which we obtain regulatory approval as a viable treatment option; and
- satisfying any post-marketing requirements.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. We are currently only in the preclinical stage of our research programs. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

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 depress the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate preclinical testing and clinical trials of and potentially seek marketing approval for any product candidates we may develop. In addition, if we obtain marketing approval for any product candidates we may develop, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed, on attractive terms or at all, we may be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

As of March 31, 2020, we had cash and cash equivalents of $104.5 million. We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating

expenses and capital expenditure requirements into 2023. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect and could be forced to seek additional funding sooner than planned.

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

- the identification of additional research programs and additional product candidates;
- the scope, progress, costs and results of preclinical and clinical development for any product candidates we may develop;
- the costs, timing and outcome of regulatory review of any product candidates we may develop;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidates we may develop for which we receive marketing approval;
- the costs and scope of the continued development of our non-viral gene therapy platform;
- the costs of satisfying any post-marketing requirements;
- the revenue, if any, received from commercial sales of product candidates we may develop for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting applications for patents, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including claims of infringement, misappropriation or other violations of third-party intellectual property;
- the costs of operational, financial and management information systems and associated personnel;
- the associated costs in connection with any acquisition of in-licensed products, intellectual property and technologies; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully identify and develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all, and such revenues may not be sufficient to sustain our operations. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize any product candidates. We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and, 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 our product candidates or other research and development initiatives. We could be required to seek collaborators for product candidates we may develop at an earlier stage than otherwise would be desirable or on terms that are

less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates we may develop in markets where we otherwise would seek to pursue development or commercialization ourselves.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate we may develop, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Raising additional capital may cause dilution to our stockholders, including purchasers of our common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we would be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2016, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting research activities and filing and prosecuting patent applications. All of our research programs are still in the research or preclinical stage of development, and their risk of failure is high. We have not yet demonstrated our ability to initiate or complete any clinical trials, obtain marketing approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing genetic medicine products.

Our limited operating history, particularly in light of the rapidly evolving genetic medicine field, may make it difficult to evaluate our technology and industry and predict our future performance. Our limited history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

In addition, as our business grows, we may encounter unforeseen expenses, restrictions, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research focus to a company capable of conducting development activities and then to a company supporting commercial activities. We may not be successful in such transitions.

Our ability to utilize our net operating loss carryforwards may be subject to limitations.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating losses, or NOLs, or research and development tax credit carryforwards. As of December 31, 2019, we had federal NOLs of $91.9 million and state NOLs of $90.6 million.

In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an “ownership change,” generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of this offering or of subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described below in “Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition,” the Tax Cuts and Jobs Act, or the Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Risks related to discovery and development

We are very early in our development efforts. We have not identified any product candidates for IND-enabling studies or clinical development and as a result it will be years before we commercialize a product candidate, if ever. If we are unable to identify and advance product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts and have invested our research efforts to date in developing our platform. We have a portfolio of programs, including those listed in the “Business—Our pipeline” section of this prospectus, that are in early stages of preclinical development and have not identified any product candidates for IND-enabling studies or clinical development. We may never identify any product candidates or advance to clinical-stage development. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

Commencing clinical trials in the United States is subject to acceptance by the U.S. Food and Drug Administration, or FDA, of an investigational new drug application, or IND, and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our first clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union.

Commercialization of any product candidates we may develop will require preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the European Medicines Agency, or EMA; obtaining manufacturing supply, capacity and expertise; building of a commercial organization; and significant marketing efforts. The success of product candidates we may identify and develop will depend on many factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any product candidates we may develop;
- successful enrollment and completion of clinical trials, including under the FDA's current Good Clinical Practices, or GCPs, current Good Laboratory Practices, or cGLPs, and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical programs that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations of any product candidates we may develop;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any product candidates we may develop;
- commercial launch of any product candidates we may develop, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates we may develop, including method of administration, if and when approved, by patients, the medical community and third-party payers;
- effective competition with other therapies;
- maintenance of a continued acceptable safety, tolerability and efficacy profile of any product candidates we may develop following approval; and
- establishment and maintenance of healthcare coverage and adequate reimbursement by payers.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates we may develop, which would

materially harm our business. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We may encounter substantial delays in commencement, enrollment or completion of our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing any product candidates we determine to develop on a timely basis, if at all.

The risk of failure for any product candidates we determine to develop is high. It is impossible to predict when or if any product candidate would prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of product candidates in humans. We have not yet begun or completed a clinical trial of any product candidate. Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our INDs and other regulatory filings. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of any product candidates. As a result, we cannot be sure that we will be able to submit INDs for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs will result in the FDA allowing clinical trials to begin. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits.

Identifying and qualifying patients to participate in clinical trials of any product candidates we may develop is critical to our success. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment and trial completion is affected by factors including:

- perceived risks and benefits of novel genetic medicine-based approaches;
- size of the patient population, in particular for rare diseases, and process for identifying patients;
- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials;
- severity of the disease or disorder under investigation;
- proximity and availability of clinical trial sites for prospective patients;
- ability to obtain and maintain patient consent;

- risk that enrolled patients will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would harm our business, financial condition, results of operations and prospects.

Other events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CLROs, and clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board, or IRB, or independent ethics committee approval, or the equivalent review groups for sites outside the United States, at each clinical trial site;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;
- failure by us, any CLROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's GCPs;
- failure by physicians to adhere to delivery protocols leading to variable results;
- delays in the testing, validation, manufacturing and delivery of any product candidates we may develop to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events associated with a product candidate in development by another company, which are viewed to outweigh its potential benefits, and which may negatively impact the perception of our product due to a similarity in technology or approach;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the legal or regulatory regimes domestically or internationally related to patient rights and privacy; or
- lack of adequate funding to continue the clinical trial.

Any inability to successfully complete preclinical studies and clinical trials could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and

royalties. In addition, if we make manufacturing or formulation changes to any product candidates we may develop, we may need to conduct additional studies or trials to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we may develop or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize any product candidates we may develop and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of future clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with any product candidates we may develop, we may:

- be delayed in obtaining marketing approval for product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Genetic medicine is an emerging area of drug development that poses many scientific and other risks. We have only limited prior experience in genetic medicine research and manufacturing and no prior experience in genetic medicine clinical development. Our lack of experience for our genetic medicine programs may limit our ability to be successful or may delay our development efforts.

Genetic medicine is an emerging field of drug development with only a small number of genetic medicines having received FDA or EMA approval to date. Our genetic medicine research programs are still at an early stage, and there remain several areas of drug development risk, which pose particular uncertainty for our programs given the relatively limited development history of, and our limited prior experience with, genetic medicines. Translational science, manufacturing materials and processes, safety concerns, regulatory pathway and clinical trial design and execution all pose particular risk to our drug development activities. Furthermore, the medical community's understanding of the genetic causes of many diseases continues to evolve and further research may change the medical community's views on what therapies and approaches are most effective for addressing certain diseases.

As an organization, we have not previously conducted any IND-enabling studies or clinical trials, including any later stage or pivotal clinical trials. In pursuing our new technologies, we have begun to establish our own genetic medicine technical capabilities, but we will need to continue to expand those capabilities by either hiring internally or seeking assistance from outside service providers. Genetic medicine is an area of significant investment by biotechnology and pharmaceutical companies and there may be a scarcity of talent available to us in these areas. If we are not able to expand our genetic medicine capabilities, we may not be able to develop in the way we intend or desire any promising product candidates that emerge from our program or our other collaborative genetic medicine sponsored research programs, which would limit our prospects for future

growth. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we may develop. Failure to commence or complete, or delays in, our clinical trials, could prevent us from or delay us in commercializing our product candidates.

We will need to build our internal and external capabilities in designing and executing a genetic medicine clinical trial. There are many known and unknown risks involved in translating preclinical development of gene therapies to clinical development, including selecting appropriate endpoints and dosage levels for dosing humans based on preclinical data. Furthermore, our genetic medicine programs are initially targeting rare diseases with relatively small populations, which limits the pool of potential subjects for our genetic medicine clinical trials. If we are unable to initiate and conduct our genetic medicine clinical trials in a manner that satisfies our expectations or regulatory requirements, the value of our genetic medicine programs may be diminished.

Our non-viral gene therapy platform is based on novel technologies that are unproven, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all.

We have concentrated our research and development efforts on our non-viral gene therapy platform, and our future success depends on the successful development of our platform.

However, the technologies that comprise our platform are new and largely unproven. These technologies have not been clinically tested and the scientific evidence to support the feasibility of developing product candidates based on those technologies is both preliminary and limited. Successful development of product candidates by us will require solving a number of issues, including the expansion of our cell-targeted lipid nanoparticle delivery system, or ctLNP, delivery system to tissues beyond the liver and retina and obtaining expression levels sufficient to address or ameliorate each target disease or indication. There can be no assurance we will be successful in solving any or all of these issues. We have concentrated our research efforts to date on developing the components of our platform, and our future success is highly dependent on the successful development of our ceDNA constructs, our ctLNP delivery system and therapeutic applications of these technologies. We may decide to alter or abandon our initial programs as new data become available and we gain experience in developing our therapeutics. We cannot be sure that our technologies will yield satisfactory products that are safe and effective, scalable or profitable in any indication we pursue.

There can be no assurance that any development problems we experience in the future related to our non-viral gene therapy platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from initiating or conducting clinical trials or commercializing our products on a timely or profitable basis, if at all. In addition, the clinical trial requirements of the FDA, the EMA 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 can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. Only a small number of non-viral gene therapies have successfully reached the clinical trial phase of development, limiting insight into the regulatory review process for this field of genetic medicine. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals in either the United States or the European Union for any product candidates we may develop or how long it will take to commercialize any product candidate that receives marketing approval.

If any product candidates we may develop cause undesirable side effects or have other unexpected adverse properties, such side effects or properties could delay or prevent regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

We have not evaluated any product candidates in human clinical trials. Moreover, there have been only a limited number of clinical trials involving the use of non-viral gene therapies and none involving ceDNA constructs or other technology similar to our technology. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. In the genetic medicine field, there have been several significant adverse events from gene therapy treatments in the past, including reported cases of leukemia and death. There can be no assurance that our technologies will not cause undesirable side effects.

We use a ctLNP delivery system to deliver our ceDNA constructs. Lipid nanoparticles have been shown to induce necrosis in the liver at certain doses and induce infusion related reactions, as well as to initiate systemic inflammatory responses. While our ctLNPs are a new generation of LNP, there can be no assurance that our ctLNPs will not have undesired effects. Our ctLNPs could contribute, in whole or in part, to immune reactions, infusion reactions, complement reactions or antibody reactions. In addition, certain aspects of our non-viral gene therapies may induce immune reactions from the lipid as well as adverse reactions within liver pathways or degradation of the LNP into its component molecules or metabolites, any of which could lead to significant adverse events in one or more of our future clinical trials. Many of these types of side effects have been seen for LNPs. Once delivered to target cells, DNA-based payloads, such as those carried by our ceDNA constructs, may interact with host proteins or chromosomal DNA in the cell endosome, cytosol or nucleus.

Adeno-associated virus, or AAV, genomes have been shown in some cases to initiate intracellular immune activation, which can lead to transcriptional changes, and local tissue interferon responses, which may lead to immune infiltrates and tissue damage. AAV genetic material may also integrate into the host chromosome, which could contribute to modified cell function transformation. There may be uncertainty as to the underlying cause of any such adverse event, which would make it difficult to accurately predict side effects in future clinical trials and would result in significant delays in our programs.

If any product candidates we develop are associated with serious adverse events, undesirable side effects or unexpected characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects. Many product candidates that initially showed promise in early stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further clinical development of the product candidates.

If in the future we are unable to demonstrate that such side effects were caused by factors others than our product candidates, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates for any or all targeted indications. Even if we are able to demonstrate that any future serious adverse events are not product-related, and regulatory authorities do not order us to cease further development of our product candidates, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

Regulatory approval of and/or demand for our potential products will depend in part on public acceptance of the use of genetic medicine for the prevention or treatment of human diseases. Safety issues that might arise in

trials for gene therapies other than our own could adversely impact public attitudes towards our platform and product candidates notwithstanding that the gene therapies we are developing are non-viral.

There are a number of clinical trials of gene therapies ongoing. There is a potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry genetic material. Possible adverse side effects that may occur with treatment with gene therapy products include an immunologic reaction early after administration that could substantially limit the effectiveness of the treatment or represent safety risks for patients.

Any of these events could prevent us from achieving or maintaining market acceptance of any product candidates we may develop and could significantly harm our business, prospects, financial condition and results of operations.

The outcome of preclinical studies and earlier-stage clinical trials may not be predictive of future results or the success of later preclinical studies and clinical trials.

We are in the early stage of research in the development of our platform and have not identified any product candidates or conducted any IND-enabling studies or any clinical trials. As a result, our belief in the capabilities of our platform is based on early research and preclinical studies. However, the results of preclinical studies may not be predictive of the results of preclinical studies or clinical trials, and the results of any early-stage clinical trials may not be predictive of the results of later clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any product candidates we may develop. There is a high failure rate for product candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business and results of operations.

We may not be successful in our efforts to identify, discover or develop potential product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates based on our non-viral gene therapy platform. All of our product development programs are still in the research or preclinical stage of development. Our research programs may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates, our potential product candidates may be shown to have harmful side effects in preclinical *in vitro* experiments or animal model studies, they may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture, unmarketable or unlikely to receive marketing approval.

In addition, although we believe our platform will position us to rapidly expand our portfolio of programs beyond our current programs, we have not yet successfully developed any product candidate and our ability to expand our portfolio may never materialize. The process by which we identify and disclose product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;

- potential product candidates we develop may nevertheless be covered by third parties' patents or other intellectual property rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;
- potential product candidates may not be effective in treating their targeted diseases or disorders;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is too complex and difficult to navigate successfully or economically.

If we are unable to identify and discover suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations.

The genetic medicine field is relatively new and evolving rapidly. We are focusing our research and development efforts on our non-viral gene therapy platform, but other gene therapy technologies may be discovered that provide significant advantages over our platform, which could materially harm our business.

To date, we have focused our efforts on the advancement of our non-viral gene therapy platform, which is designed to overcome the limitations of current viral gene therapy approaches. However, while these modalities have demonstrated their limitations, there are many companies that are developing new genetic medicines, including viral gene therapies, gene editing and messenger RNA, or mRNA. There can be no certainty that these companies will not develop genetic medicines that address some of these limitations and will be considered to have advantages over our non-viral gene therapy platform. For example, in December 2019, Dyno Therapeutics announced a new technique for AAV delivery, labeled BRAVE, that allows the researchers to engineer the virus shell to deliver the gene package to the exact cell type in the body they intend to treat. This new method may reduce concerns about off-target AAV delivery and make it a more attractive delivery system.

We may expend our limited resources to pursue a particular program, product candidate or indication and fail to capitalize on programs, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and expect to focus on product candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential, or we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of any product candidates we may develop.

We will face an inherent risk of clinical trial and product liability exposure related to the testing of any product candidates we may develop in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no product candidates in clinical trials or that have been approved for commercial sale, the future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any product candidates we may develop.

We will need to increase our insurance coverage if we commence clinical trials or if we commence commercialization of any product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks relating to manufacturing

The manufacture of genetic medicine products is complex and difficult and is subject to a number of scientific and technical risks, some of which are common to the manufacture of drugs and biologics and others of which are unique to the manufacture of gene therapies. We could experience manufacturing problems that result in delays in our development or commercialization programs.

Genetic medicine drug products are complex and difficult to manufacture. We have an established current Good Manufacturing Practices, or cGMP, -ready process at the 200-liter scale which we have successfully transferred to external contract development and manufacturing organizations, or CDMOs, to supply our gene therapies for IND-enabling preclinical studies and early clinical trials. We believe that we will be able to enter into arrangements with existing and/or additional CDMOs to provide commercial supply. We may also seek to eventually establish our own manufacturing facility for long-term commercial supply.

A number of factors common to the manufacturing of biologics and drugs could also cause production issues or interruptions for our gene therapies, including raw material or starting material variability in terms of quality, cell line viability, productivity or stability issues, shortages of any kind, shipping, distribution, storage and supply chain failures, growth media contamination, equipment malfunctions, operator errors, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of god that are beyond our or our contract manufacturer’s control. It is often the case that early stage process development is conducted with materials that are not manufactured using cGMP starting materials, techniques or processes and which are not subject to the same level of analysis that would be required for clinical grade

material. We may encounter difficulties in translating the manufacturing processes used to produce research grade materials to cGMP compliant processes, and any changes in the manufacturing process may affect the safety and efficacy profile of our product candidates.

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 that we anticipate will be required in our manufacturing process, such as Sf9 cells, are derived from biologic sources. Such raw materials may be 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 any product candidates we may develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations and prospects.

Our non-viral gene therapy platform is novel, and the combination of novel constructs with untested scaling may cause us to experience delays in satisfying regulatory authorities or production problems that result in delays in our development or commercialization programs, limit the supply of any product candidates we may develop or otherwise harm our business.

Our non-viral gene therapy platform is novel and the manufacture of products on the basis of our platform is untested at a large scale. 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, insufficient inventory or potentially delay progression of our preclinical or clinical development of any product candidates we may develop. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. The ability to scale our manufacturing and maintain the manufacturing process at the same levels of quality and efficacy that we are currently manufacturing is yet to be tested. If we or our CDMOs are unable to scale our manufacturing at the same levels of quality and efficiency, we may not be able to supply the required number of doses for clinical trials or commercial supply, and our business could be harmed.

Manufacturing the ctLNP component of a potential product candidate may be complex and difficult, and we could experience delays in satisfying regulatory authorities or production problems that result in delays in our development or commercialization, limit the supply of any product candidates we may develop or otherwise harm our business.

Many product candidates we may develop will require the manufacture of the ctLNP component, which may require processing steps that are more complex than those required for current products that utilize LNPs. In order to manufacture ctLNPs that are specialized for a given platform program, we may need to add biologic ligands to existing LNPs. This process is challenging and may pose a risk to our ability to manufacture on a scale sufficient to meet clinical and commercial needs.

Testing of and changes to methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are tested and then altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives.

An important part of the manufacturing of our potential product candidates is analytical testing. Analytical testing of gene therapies involves tests that are more numerous, more complex in scope and take a longer time

to develop and to conduct as compared to traditional dugs. We and our CDMOs may need to expend considerable time and resources to develop assays and other analytical tests for our product candidates, including assays to assess the potency of our product candidates. Some assays may need to be outsourced to specialized testing laboratories. Even when assays are developed, they may need to be further tested, qualified and validated, which may take substantial time and resources. Because of the lagging nature of analytical testing, we may proceed with additional manufacturing and other development activities without having first fully characterized our manufactured materials. If the results of the testing fail to meet our expectations, we may need to delay or repeat certain manufacturing and development activities.

We may make changes to our manufacturing methods as part of our product development activities. Any such changes could cause any product candidates we may develop to perform differently and affect the results of clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

In addition, the FDA, the EMA, and other regulatory authorities may require us to submit samples of any lot of and approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA, or other 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 product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We currently depend on a small number of third-party suppliers for our drug substance and drug product, and we expect to continue to depend on third-party suppliers for materials used in the manufacture of any product candidates we may develop, and the loss of these third-party suppliers or their inability to supply us with adequate materials, particularly those raw materials that are in short supply, could harm our business.

We currently rely on a small number of third-party suppliers for our drug substance and drug product and expect to continue to rely on third-party suppliers for certain materials and components required for the production of any product candidates we may develop. Our dependence on these third-party suppliers and the challenges we may face in obtaining and maintaining adequate supplies of materials involve several risks, including limited control over pricing, availability and quality and delivery schedules. There is substantial demand and limited supply for certain of the raw materials used to manufacture genetic medicine products and these raw materials are usually sole-sourced, as there are a limited number of qualified suppliers. This limited supply, combined with any problems that may arise during the manufacturing process development, may create long lead times to manufacture or procure starting materials. The progress of our non-viral gene therapy platform is highly dependent on these suppliers providing us or our contract manufacturer with the necessary starting materials that meet our requirements in a timely manner. As a small company, our negotiation leverage is limited, and we are likely to get lower priority than our competitors that 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 supply interruption in limited or sole-sourced raw materials could materially harm our ability to manufacture any product candidates we may develop until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel 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 any product candidates we may develop, including limiting

supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks related to our dependence on third parties

We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our product manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to many of these items, including CDMOs for the manufacturing of any product candidates we test in preclinical or clinical development, as well as contract research organizations, or CROs for the conduct of our animal testing and research. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols.

Although we intend to design the clinical trials for any product candidates we may develop, CLROs will conduct some or all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CLROs and other third parties do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of any product candidates we may develop may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CLROs and other third parties, we could be required to repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures.

If third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND submissions and approval of any product candidates we may develop.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including any contract manufacturers of any product candidates we may develop, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturer must supply all necessary documentation in support of a biologics license application, or BLA, on a timely basis and must adhere to the FDA's cGLP and cGMP regulations enforced through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of any product candidates we may develop or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms or at all if they are affiliated with our competitors;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities, particularly if they are under contract with our competitors;
- termination or nonrenewal of manufacturing 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 or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies or trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

We may from time to time be dependent on single-source suppliers for some of the components and materials used in, and the processes required to develop, our development candidates and investigational medicines.

We may from time to time depend on single-source suppliers for some of the components and materials used in, and manufacturing processes required to develop, our development candidates and investigational medicines. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes and finished goods exposes us to several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

If we have to switch to a replacement supplier, the manufacture and delivery of our development candidates or investigational medicines could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers for any of the components or processes used in our investigational medicines, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single source components and materials used in our products, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our investigational medicines.

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 have a material adverse effect on the success of 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 third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific 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 have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations and permitting requirements. These current or future laws, regulations and permitting requirements may impair our research, development or production efforts. Failure to comply with these laws, regulations and permitting requirements also may result in substantial fines, penalties or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We expect to rely on third parties to conduct, supervise and monitor IND-enabling studies and clinical studies, and if these third parties perform in an unsatisfactory manner, it may harm our business.

We expect to rely on CROs and CLROs and research and clinical trial sites to ensure our IND-enabling studies and clinical trials are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs and CLROs' activities. Nevertheless, we will be responsible for ensuring that each of these studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs and CLROs does not relieve us of our regulatory responsibilities.

We and our CROs and CLROs will be required to comply with the FDA's GCPs for conducting, recording and reporting the results of IND-enabling studies and clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these GCPs through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our CROs or CLROs fail to comply with applicable GCPs, the preclinical and clinical data generated in our studies may be deemed unreliable and the FDA may require us to perform additional

studies before approving any marketing applications. Upon inspection, the FDA may determine that our studies did not comply with GCPs.

Our CLROs and CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CLROs and CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our CROs or CLROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements, or for any other reasons, our studies may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidates we may develop. As a result, our financial results and commercial prospects would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We may enter into 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 capitalize on the market potential of those product candidates.

We may seek third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or any product candidates we may develop pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of any product candidates we may 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 programs, preclinical studies or clinical trials, provide insufficient funding for programs, preclinical studies or clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with any product candidates we may develop if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may be acquired by a third party having competitive products or different priorities;
- collaborators with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines;

- collaborators may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our medicines or any product candidates we may develop or that result in costly litigation or arbitration that diverts management attention and resources;
- we may lose certain valuable rights under certain circumstances, including if we undergo a change of control;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates we may develop; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

If our collaborations do not result in the successful development and commercialization of product candidates, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus apply to the activities of our collaborators.

These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the product candidates we may develop that are the subject of these collaborations with us. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates we may develop.

Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into

collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, fail to devote sufficient resources to the development and commercialization of products, or merge with or be acquired by a third party who may do any of these things. Any of these developments could harm our product development efforts.

If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our product development and research programs and the potential commercialization of any product candidates we may develop will require substantial additional cash to fund expenses. For some of the product candidates we may develop, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, reduce the scope of any sales or marketing activities, or increase our own expenditures on the development of the product candidate.

Risks related to commercialization

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to any product candidates that we may develop from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disorders for which we are conducting research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

There are numerous companies that are selling or developing genetic medicines, including in indications for which we may develop our non-viral gene therapies. These companies include viral gene therapy companies such as BioMarin Pharmaceuticals, Inc., Homology Medicines, Inc., Adverum Biotechnologies, Inc. and Hoffmann La Roche Ltd; gene editing companies such as Crispr Therapeutics AG, Intellia Therapeutics, Inc. and Editas Medicine, Inc.; and mRNA companies such as Moderna, Inc. See ‘‘Business—Competition’’ for additional information regarding competition.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product candidates or that would render any product candidates that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if any product candidate that we may develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payers and others in the medical community necessary for commercial success.

If any product candidate we may develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payers and others in the medical community. Sales of medical products depend in part on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost-effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians’ organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost-effective as compared with competing treatments. Efforts to educate the medical community and third-party payers on the benefits of any product candidates we may develop may require significant resources and may not be successful. If any product candidates we may develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of 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 clinical trials;
- the potential advantages and limitations compared to alternative treatments;
- the effectiveness of sales and marketing efforts;

- the cost of treatment in relation to alternative treatments;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products, if approved, together with other medications.

The pricing, insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our future product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

The initial target platforms in our pipeline are indications with small patient populations. For product candidates that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such product candidates must be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third-party payers, the adoption of those product candidates and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved.

We expect that coverage and reimbursement by third-party payers will be essential for most patients to be able to afford these treatments. Accordingly, sales of our future product candidates will depend substantially, both domestically and internationally, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payers. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement by government authorities for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, since CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payers tend to follow CMS to a substantial degree. However, one payer’s determination to provide coverage for a product does not assure that other payers will also provide coverage for the drug product. Further, a payer’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement agencies in the European Union may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of

therapeutics such as any product candidates we may develop. In many countries, particularly the countries of the European Union, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product, possibly for lengthy periods of time. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for product candidates. Accordingly, in markets outside the United States, the reimbursement for any product candidates we may develop may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payers, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for any product candidates we may develop. We expect to experience pricing pressures in connection with the sale of any product candidates we may develop due to the trend toward managed healthcare, the increasing influence of certain third-party payers, such as health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market. Recently there have been instances in which third-party payers have refused to reimburse treatments for patients for whom the treatment is indicated in the FDA-approved product label. Even if we are successful in obtaining FDA approvals to commercialize our product candidates, we cannot guarantee that we will be able to secure reimbursement for all patients for whom treatment with our product candidates is indicated.

In addition to CMS and private payers, professional organizations such as the American Medical Association, or the AMA, can influence decisions about reimbursement for new products by determining standards for care. In addition, many private payers contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our product candidates. Even if favorable coverage and reimbursement status is attained for one or more product candidates for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any product candidates we may develop 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 product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we may build a sales and marketing infrastructure to market some of the product candidates we may develop if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and

time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

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

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

Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Amendment, or the PPACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. 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 the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes

intended to implement BPCIA may be fully adopted by the FDA, any such processes could have an adverse effect on the future commercial prospects for our biological products.

There is a risk that any product candidates we may develop that are approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider any product candidates we may develop to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for nonbiological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If the market opportunities for any product candidates we may develop are smaller than we believe they are, our potential revenues may be adversely affected, and our business may suffer. Because the target patient populations for many of the initial product candidates we may develop are small, we must be able to successfully identify patients and achieve a significant market share to maintain profitability and growth.

We are focusing our initial research and product development on treatments for rare genetically defined diseases; as a result, the relevant patient population may be small. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with our product candidates we may develop, or may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations and prospects. Additionally, because of the potential that any product candidates we may develop could cure a target disease, we may not receive recurring revenues from patients and may deplete the patient population prevalence through curative therapy.

Risks related to our intellectual property

Although we own and license a number of pending patent applications which have not yet issued as patents, we do not currently own or exclusively in-license any issued patents relating to any product candidates we may develop or technology, including with respect to our ceDNA constructs, ctLNP delivery system and manufacturing process. If we or our licensors are unable to obtain, maintain and defend patent and other intellectual property protection for our product candidates and technology, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully develop and commercialize any product candidates we may develop or our technology may be adversely affected due to such competition.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and other jurisdictions with respect to any product candidates we may develop and our technology, including our ceDNA constructs, ctLNP delivery system, manufacturing processes and their respective components, formulations, combination therapies, methods of treatment, processes and development that are important to our business, as well as successfully defending these patents and other intellectual property against third-party challenges. We and our licensors have sought, and will seek, to protect our proprietary position by filing patent applications in the United States and abroad

related to certain technologies and our platform that are important to our business. However, our patent portfolio is at an early stage and we currently do not own or exclusively license any issued patents in any jurisdiction. Moreover, there can be no assurance as to whether or when our patent applications will issue as granted patents. Our ability to stop third parties from making, using, selling, marketing, offering to sell, importing and commercializing any product candidates we may develop and our technology is dependent upon the extent to which we have rights under valid and enforceable patents and other intellectual property that cover our platform and technology. If we are unable to secure, maintain, defend and enforce patents and other intellectual property with respect to any product candidates we may develop and technology, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

We own certain patent applications, and exclusively in-license from University of Massachusetts as represented by and solely on behalf of its Medical School, or UMass, and Voyager Therapeutics, Inc. certain other patent applications, which cover our ceDNA platform structure, use and/or function, our ctLNP platform and its use, and ceDNA manufacturing processes, as applicable. Our pending Patent Cooperation Treaty, or PCT, patent applications are not eligible to become issued patents until, among other things, we file a national stage patent application within 30 to 32 months, depending on the jurisdiction, from such application's priority date in the jurisdictions in which we are seeking patent protection. Similarly, our pending provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of such provisional patent application's filing date. If we do not timely file such national stage patent applications or non-provisional patent applications, we may lose our priority date with respect to such PCT or provisional patent applications, respectively, and any patent protection on the inventions disclosed in such PCT or provisional patent applications, respectively. While we and our licensors intend to timely file national stage and non-provisional patent applications relating to our PCT and provisional patent applications, respectively, we cannot predict whether any such patent applications will result in the issuance of patents. If we or our licensors do not successfully obtain issued patents, or, if the scope of any patent protection we or our licensors obtain is not sufficiently broad, we will be unable to prevent others from using any product candidates we may develop or our technology or from developing or commercializing technology and products similar or identical to ours or other competing products and technologies. Any failure to obtain or maintain patent protection with respect to our ceDNA constructs, ctLNP delivery system, manufacturing processes or our other product candidates and technology would have a material adverse effect on our business, financial condition, results of operations and prospects.

The patent prosecution process is expensive, time-consuming and complex, and we and our licensors may not be able to file, prosecute, maintain, defend, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. We and our licensors may not be able to obtain, maintain or defend patents and patent applications due to the subject matter claimed in such patents and patent applications being in the public domain. For example, in some cases, the work of certain academic researchers in the genetic medicine field has entered or will enter the public domain, which may compromise our and our licensors' ability to obtain patent protection for certain inventions related to or building upon such prior work. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we would not able to prevent any third party from using any of our technology that is in the public domain to compete with our product candidates.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of patent rights are highly uncertain. Our pending and future owned and licensed patent applications may not result in patents being issued which protect our technology or product candidates, effectively prevent others from commercializing competitive technologies and product or otherwise provide any competitive advantage. In fact, patent applications may not issue as patents at all, and even if such patent applications do issue as patents, they may not issue in a form, or with a scope of claims, that will provide us with any meaningful protection, prevent others from competing with us or otherwise provide us with any competitive advantage. In addition, the scope of claims of an issued patent can be reinterpreted after issuance, and changes in either the patent laws or interpretation of the patent laws in the United States and other jurisdictions may diminish the value of our patent rights or narrow the scope of our patent protection. Furthermore, our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

Third parties have developed technologies that may be related or competitive to our own technologies and product candidates and may have filed or may file patent applications, or may have obtained issued patents, claiming inventions that may overlap or conflict with those claimed in our owned or licensed patent applications or issued patents. We may not be aware of all third-party intellectual property rights potentially relating to our current and future product candidates and technology. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know for certain whether the inventors of our owned or licensed patents and patent applications were the first to make the inventions claimed in any owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or ruled unenforceable.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and other jurisdictions. For example, we may be subject to a third-party submission of prior art to the United States Patent and Trademark Office, or USPTO, challenging the validity of one or more claims of our owned or licensed patents. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our owned or licensed pending patent applications. We may become involved in opposition, derivation, re-examination, *inter partes* review, post-grant review or interference proceedings and similar proceedings in foreign jurisdictions (for example, opposition proceedings) challenging our owned or licensed patent rights. In addition, a third party may claim that our owned or licensed patent rights are invalid or unenforceable in a litigation. An adverse result in any litigation or patent office proceeding could put one or more of our owned or licensed patents at risk of being invalidated, ruled unenforceable or interpreted narrowly and could allow third parties to commercialize products identical or similar to any product candidates we may develop and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges and proceedings may result in loss of patent rights, exclusivity, freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and any product candidates we may develop. Such challenges and proceedings may also result in substantial cost and require significant time from

our scientists and management, even if the eventual outcome is favorable to us. Moreover, there could be public announcements of the results of hearings, motions or other interim proceedings or developments related to such challenges and proceedings 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.

Furthermore, patents have a limited lifespan. In the United States, the expiration of a patent is generally 20 years from the earliest date of filing of the first non-provisional patent application to which the patent claims priority. Patent term adjustments and extensions may be available; however, the overall term of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent and other intellectual property rights may not provide us with sufficient rights to exclude others from commercializing products similar or identical to our technology and any product candidates we may develop. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Our rights to develop and commercialize any product candidates are subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

We are reliant upon licenses from third parties for certain patent and other intellectual property rights that are important or necessary to the development of our technology and product candidates. For example, we rely on a license from the National Institutes of Health, or NIH, and the Association Institut de Myologie, Universite Pierre et Marie Curie, Centre National de la Recherche Scientifique and Inserm Transfert SA, which we refer to as the French Institutions, pursuant to which we have been granted a non-exclusive, worldwide, royalty-bearing license to certain patent rights related to our ceDNA construct, to make and have made, research and have researched, use and have used, sell and have sold, offer to sell and to import products for the treatment, prevention or palliation of any human disease, disorder or condition. In addition, we rely on a license from UMass pursuant to which we have been granted an exclusive, worldwide, royalty-bearing license to certain patent rights related to our ceDNA construct to research, develop, manufacture, have manufactured, use, offer for sale, sell and import products in the treatment, prevention or palliation of any human disease, disorder or condition. Our existing license agreements, including our license agreements with NIH and UMass, impose, and we expect that future license agreements will impose, specified diligence, milestone payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. For more information on the terms of the license agreements with NIH and UMass, see “Business—Intellectual property—License agreements.” We may enter into additional license agreements in the future.

Furthermore, the licensors of our license agreements have the right to terminate the agreement if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. If our license agreements are terminated, we may lose our rights to develop and commercialize any product candidates we may develop and technology, lose patent protection any product candidates we may develop and our technology, experience significant delays in the development and commercialization of our product candidates and technology and incur liability for damages. If these in-licenses are terminated, or if the

underlying intellectual property fails to provide the intended exclusivity, our competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our product candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with any product candidates we may develop and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology, product candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other intellectual property rights under our license agreements;
- our diligence, development, regulatory, commercialization, financial or other obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, our license agreements are, and future license agreements are likely to be, complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If disputes over intellectual property that we have licensed or any other dispute described above related to our license agreements prevent or impair our ability to maintain our current license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our license agreement with NIH is, and other license agreements we may enter into in the future may be, non-exclusive. Accordingly, third parties may also obtain non-exclusive licenses from such licensors, including NIH, with respect to the intellectual property licensed to us under such license agreements, including our NIH license agreement. Accordingly, our NIH license agreement does not, and other license agreements may not, provide us with exclusive rights to use such licensed patent and other intellectual property rights, or may not provide us with exclusive rights to use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and any product candidates we may develop in the future.

Moreover, some of our in-licensed patent and other intellectual property rights are, and may in the future be, subject to third party interests such as co-ownership. If we are unable to obtain an exclusive license to such third-party co-owners' interest, in such patent and other intellectual property rights, such third-party co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. We or our licensors may need the cooperation of any such co-owners of our licensed patent and other intellectual property rights in order to enforce them against third parties, and such cooperation may not be provided to us or our licensors.

Additionally, we do not have complete control over the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. For example, pursuant to each of our intellectual property licenses with NIH and UMass, our licensors retain control of preparation, filing, prosecution and maintenance, and, in certain circumstances, enforcement and defense of their patents and patent applications. It is possible that our licensors' filing, prosecution and maintenance of the licensed patents and patent applications, enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, and accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to file, prosecute, maintain, enforce and defend such patents and patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our technology and any product candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors or other third parties from making, using and selling competing products. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Furthermore, our owned and in-licensed patent rights may be subject to a reservation of rights by one or more third parties. For example, inventions contained within some of our in-licensed patent rights may be made using U.S. government funding. When new technologies are developed with government funding, in order to secure ownership of patent rights related to the technologies, the recipient of such funding is required to comply with certain government regulations, including timely disclosing the inventions claimed in such patent rights to the U.S. government and timely electing title to such inventions. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, including such timely disclosure and election of title. The failure of our licensors to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents or patent applications. In addition, the U.S. government has certain rights in such in-licensed patent rights, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. If the U.S. government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The U.S. government's rights may also permit it to disclose the funded inventions and technology, which may include our confidential information, to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we or our licensors failed to achieve practical application of the U.S. 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 in-licensed U.S. government-funded inventions may be subject to certain requirements to manufacture any product candidates we may develop embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations and prospects significantly.

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

Filing, prosecuting, maintaining, enforcing and defending patents and other intellectual property rights on our technology and any product candidates we may develop in all jurisdictions throughout the world would be prohibitively expensive, and accordingly, our intellectual property rights in some jurisdictions outside the United States could be less extensive than those in the United States. In some cases, we or our licensors may not be able to obtain patent or other intellectual property protection for certain technology and product candidates outside the United States. In addition, the laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we and our licensors may not be able to obtain issued patents or other intellectual property rights covering any product candidates we may develop and our technology in all jurisdictions outside the United States and, as a result, may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Third parties may use our technologies in jurisdictions where we and our licensors have not pursued and obtained patent or other intellectual property protection to develop their own products and, further, may export otherwise infringing, misappropriating or violating products to territories where we have patent or other intellectual property protection, but enforcement is not as strong as that in the United States. These products may compete with any product candidates we may develop and our technology and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Additionally, many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain jurisdictions, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violation of our patent and other intellectual property rights or marketing of competing products in violation of our intellectual property rights generally. For example, an April 2019 report from the Office of the United States Trade Representative identified a number of countries, including China, Russia, Argentina, Chile and India, where challenges to the procurement and enforcement of patent rights have been reported. Proceedings to enforce our or our licensors' patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patent and other intellectual property rights at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We or our licensors may not prevail in any lawsuits that we or our licensors initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many jurisdictions have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many jurisdictions limit the enforceability of patents against government agencies or government contractors. In these jurisdictions, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or patent applications will be due to be paid to the USPTO and various government patent agencies outside of the

United States over the lifetime of our owned or licensed patent rights. We rely on our outside counsel and other professionals or our licensing partners to pay these fees due to the USPTO and non-U.S. government patent agencies. The USPTO and various non-U.S. government patent agencies also require compliance with several procedural, documentary and other similar provisions during the patent application process. We rely on our outside counsel and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment, loss of priority or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

We may not be successful in obtaining necessary rights to product candidates we may develop through acquisitions and in-licenses.

We currently have rights to certain intellectual property through licenses from third parties. Because our programs may require the use of additional intellectual property rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these intellectual property rights. In addition, with respect to any patent or other intellectual property rights that we co-own with third parties, we may require exclusive licenses to such co-owners' interest in such patent or other intellectual property rights. However, we may be unable to secure such licenses or otherwise acquire or in-license any intellectual property rights related to compositions, methods of use, processes or other components from third parties that we identify as necessary for any product candidates we may develop and our technology on commercially reasonable terms, or at all. Even if we are able to in-license any such necessary intellectual property, it could be on non-exclusive terms, thereby giving our competitors and other third parties access to the same intellectual property licensed to us, and the applicable licensors could require us to make substantial licensing and royalty payments. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to third parties, potentially blocking our ability to pursue our research program and develop and commercialize our product candidates.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have licensed, we may be required to expend significant time and resources to redesign any product candidates we may develop or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Issued patents covering any product candidates we may develop could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

Our owned and licensed patent rights may be subject to priority, validity, inventorship and enforceability disputes. If we or our licensors are unsuccessful in any of these proceedings, such patent rights may be narrowed, invalidated or held unenforceable, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or we may be required to cease the development, manufacture and commercialization of one or more of our product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If one of our licensing partners, one of our co-owners, we or our licensor's other licensees initiate legal proceedings against a third party to enforce a patent covering any of any product candidates we may develop or our technology, the defendant could counterclaim that the patent covering the product candidate or technology is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, interference proceedings, derivation proceedings, post grant review, *inter partes* review and equivalent proceedings such as opposition, invalidation and revocation proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover any product candidates we may develop or our technology or prevent third parties from competing with any product candidates we may develop or our technology. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates or technology. Such a loss of patent protection could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, contractors and other parties who have access to such technology and processes. However, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breach or violate the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets and third parties could use our trade secrets to compete

with any product candidates we may develop and our technology. Additionally, we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems; however, such systems and security measures may be breached, and we may not have adequate remedies for any breach.

In addition, our trade secrets may otherwise become known or be independently discovered by competitors or other third parties. Competitors or third parties could purchase any product candidates we may develop or our technology and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our intellectual property rights or develop their own competitive technologies that fall outside the scope of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate such trade secrets, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, our business, financial condition, results of operations and prospects could be materially and adversely affected.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may become party to, or be threatened with, adversarial proceedings or litigation in which third parties may assert infringement, misappropriation or other violation claims against us, alleging that any product candidates we may develop, manufacturing methods, formulations or administration methods are covered by their patents. Given the vast number of patents and other intellectual property in our field of technology, we cannot be certain or guarantee that we do not infringe, misappropriate or otherwise violate patents or other intellectual property. Other companies and institutions have filed, and continue to file, patent applications that may be related to our technology and, more broadly, to gene therapy and related manufacturing methods. Some of these patent applications have already been allowed or issued and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. If a patent holder believes the manufacture, use, sale or importation of any product candidates we may develop or our technology infringes its patent, the patent holder may sue us even if we have licensed other patent rights for our technology.

It is also possible that we have failed to identify relevant third-party patents or applications. Because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of any product candidates we may develop or our technology and we may not be aware of such patents. Furthermore, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States may remain confidential until a patent issues. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to any product candidates we may develop and our technologies

because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, any product candidates we may develop or the use of any product candidates we may develop.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could adversely affect our ability to commercialize any product candidates we may develop or any other of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing any product candidates we may develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing any product candidates we may develop or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other proceedings could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Competitors may challenge the validity and enforceability of our patent rights or those of our licensing partners, infringe, misappropriate or otherwise violate our or our licensors' patent and other intellectual property rights, or we may be required to defend against claims of infringement, misappropriation or other violation. Litigation and other proceedings in connection with any of the foregoing claims can be unpredictable, expensive and time consuming. Even if resolved in our favor, litigation or other proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our scientific, technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors or other third parties may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could adversely affect our ability to compete in the marketplace and could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or be required to obtain licenses to such intellectual property rights, which may not be available on commercially reasonable terms or at all. An inability to incorporate such intellectual property rights would harm our business and may prevent us from successfully commercializing any product candidates we may develop or at all. In addition, we may lose personnel as a result of such claims and any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize any product candidates we may develop and our technology, which would have a material adverse effect on our business, results of operations, financial condition and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our scientific and management personnel.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. Moreover, even when we obtain agreements assigning intellectual property to us, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have pre-existing or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. Disputes about the ownership of intellectual property that we own may have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, we or our licensors may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our owned or licensed patent rights. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and any product candidates we may develop. Such challenges may also result in our inability to develop, manufacture or commercialize our technology and product candidates without infringing third-party patent rights. In addition, if the breadth or

strength of protection provided by our owned or licensed patent rights are threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technology and product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in patent law in the United States or worldwide could diminish the value of patents in general, thereby impairing our ability to protect any product candidates we may develop and our technology.

Changes in either the patent laws or interpretation of patent laws in the United States and worldwide, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of any owned or in-licensed patent applications and the maintenance, enforcement or defense of any current in-licensed issued patents and issued patents we may own or in-license in the future. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our in-licensed issued patents and issued patents we may own or in-license in the future, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. As one example, in the case Assoc. for Molecular Pathology v. Myriad Genetics, Inc., the U.S. Supreme Court held that certain claims to DNA molecules are not patentable simply because they have been isolated from surrounding material. Moreover, in 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to patent-ineligible subject matter. Accordingly, in view of the guidance memo, there can be no assurance that claims in our patent rights covering any product candidates we may develop or our technology will be held by the USPTO or equivalent foreign patent offices or by courts in the United States or in foreign jurisdictions to cover patentable subject matter. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop and our technology, one or more of our U.S. patents that we license or may own in the future may be eligible for limited patent term extension under Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patent rights, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates or technology. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patent rights, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of or right to use intellectual property that is important to any product candidates we may develop or our technology. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have filed trademark applications with the USPTO for the mark "Generation Bio" and the Generation Bio logo. Our current and future trademark applications in the United States and other foreign jurisdictions may not be allowed or may be subsequently opposed. Once filed and registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time-consuming, particularly for a company of our size. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of

interest. At times, third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to any product candidates we may develop but that are not covered by the intellectual property, including the claims of the patents, that we own or license currently or in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or license currently or in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating our owned or licensed intellectual property rights;
- it is possible that our or our licensors' current or future pending patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by third parties;
- third parties might conduct research and development activities in jurisdictions where we do not have patent or other intellectual property rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents or other intellectual property rights of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

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

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

Because we currently rely on certain third parties to manufacture all or part of our drug product and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our product engine and pipeline, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements and other similar agreements with our collaborators, advisors, employees, consultants and contractors prior to beginning research or disclosing any 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 or other third parties, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets by third parties. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's or other third party's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may harm our business, financial condition, results of operations and prospects.

Risks related to regulatory approval and other legal compliance matters

Regulatory requirements governing genetic medicine products, and in particular any novel gene therapy products we may develop, have changed frequently and may continue to change in the future.

Regulatory requirements governing gene and cell therapy products, and in particular any novel gene therapy products we may develop, have changed frequently and may continue to change in the future. We are aware of a limited number of gene therapy products that have received marketing authorization from the FDA and EMA. Even with respect to more established products in the gene therapy field, the regulatory landscape is still developing. For example, the FDA has established the Office of Tissues and Advanced Therapies (formerly the Office of Cellular, Tissue and Gene Therapies) within its Center for Biologics Evaluation and Research, or 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. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or the NIH, also are potentially subject to review by the Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC; however, the NIH announced that the RAC will soon only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks.

The same applies in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the Committee for Medicinal Products for Human Use, or CHMP, before CHMP adopts its final opinion. In the European Union, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy

products and cell therapy products may be applied to any product candidates we may develop, but that remains uncertain at this point.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post-approval limitations or restrictions. As we advance any product candidates we may develop, 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 these product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

Although the FDA decides whether individual genetic medicine protocols may proceed, the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's institutional biosafety committee, or IBC, as well as its IRB would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of genetic medicine products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any product candidates we may develop. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for genetic medicine products and require that we comply with these new guidelines.

As we are initially seeking to identify and develop product candidates to treat diseases using novel technologies, there is heightened risk that the FDA, the EMA or other regulatory authority may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. Even if the endpoints are deemed clinically meaningful, we may not achieve these endpoints to a degree of statistical significance, particularly because many of the diseases we are targeting with our platform have small patient populations, making development of large and rigorous clinical trials more difficult.

Adverse developments in post-marketing experience or in clinical trials conducted by others of gene therapy products or cell therapy products may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for development or approval of any product candidates we may develop or limit the use of products utilizing non-viral gene therapy technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities 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 the product candidates we may develop can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing non-viral gene therapy technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the commercialization of resulting products.

In addition, ethical, social and legal concerns about genetic medicine, genetic testing and genetic research could result in additional regulations or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed their intentions to further regulate biotechnology. More restrictive regulations or claims that any product candidates we may develop are unsafe or

pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of any product candidates we may develop under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

As we advance any product candidates we may develop through clinical development, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. These regulatory review committees and advisory groups and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post-approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates we may develop. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, product candidates we may develop, and our ability to generate revenue will be materially impaired.

Any product candidates we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate we may develop will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CLROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate’s safety, purity and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we may develop may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be

limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact public perception of our future product candidates.

Our potential therapeutic products involve introducing genetic material into patients' cells. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene regulation are unsafe, unethical or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products once approved. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although our delivery system is non-viral, any product candidates we may develop may be associated with such viral delivery systems as a gene therapy platform. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical trials. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. If any such adverse events occur, commercialization of our product candidates or further advancement of our clinical trials could be halted or delayed, which would have a negative impact on our business and operations.

Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates we may develop from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell any product candidates we may develop in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in

other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Political and socioeconomic factors can adversely affect our business. For example, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for any product candidates we may develop, which could significantly and materially harm our business.

Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process and does not assure FDA approval of any product candidates we may develop.

If any product candidate we may develop is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical need for this condition, the sponsor may apply for FDA fast track designation. However, a fast track designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. As a result, while we may seek and receive fast track designation for any product candidates we may develop, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

Breakthrough or RMAT therapy designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of any product candidates we may develop.

If any product candidate we may develop is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development, the sponsor may apply for FDA breakthrough designation or a regenerative medicine advanced therapy, or RMAT, designation. However, neither a breakthrough designation nor an RMAT designation ensures that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. As a result, while we may seek and receive breakthrough or RMAT designation for any product candidates we may develop, we may not experience a faster development process, review or approval compared to conventional

FDA procedures. In addition, the FDA may withdraw breakthrough or RMAT designation if it believes that the designation is no longer supported by data from our clinical development program. Neither breakthrough nor RMAT designation alone guarantees qualification for the FDA's priority review procedures.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of any product candidates we may develop.

If the FDA determines that a product candidate we may develop offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for any product candidates we may develop. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate we may develop is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

We may not be able to obtain orphan drug exclusivity for any product candidates we may develop, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and the FDA has issued recent draft guidance suggesting that it would not consider two genetic medicine products to be different drugs solely based on minor differences in the transgenes or vectors. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

In 2017, the Congress passed the FDA Reauthorization Act of 2017, or the FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same

rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate we may develop or the approval may be for a more narrow indication than we expect.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if any product candidates we may develop demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop. For example, our development of any product candidates for pediatric use is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

Even if we, or any collaborators we may have, obtain marketing approvals for any product candidates we may develop, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The FDA typically advises that patients treated with genetic medicine undergo follow-up observations for potential adverse events for a 15-year period. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we may develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we and such collaborators are not able to comply with

post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition and prospects.

If we fail to comply with applicable regulatory requirements following approval of any product candidates we may develop, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or supplements to a BLA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any product candidates we may develop and generate revenues.

Any product candidate we may develop for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with our medicines, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;

- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any product candidates we develop and adversely affect our business, financial condition, results of operations and prospects.

Additionally, if any product candidates we may develop receive marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients and a communication plan to healthcare practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

We are affected by the political environment and changes that may be made to regulatory regimes. The efforts of the current presidential administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The current presidential administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. On January 30, 2017, the president issued an executive order, applicable to all executive agencies, including the FDA, that required that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that required the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management on February 2, 2017, the administration indicated that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our relationships with healthcare providers, physicians and third-party payers will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payers play a primary role in the recommendation and prescription of any product candidates that we develop for which we obtain marketing approval. Our future arrangements with third-party payers and customers may expose us to broadly applicable fraud and abuse and

other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid or other government payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $11,181 to $22,363 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers;
- the federal false statements statute, which prohibits 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;
- the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services, or HHS, information related to payments and other transfers of value to physicians and teaching hospitals and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payers, including private insurers, and certain 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 in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the

European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Violation of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations 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 these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, 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 be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Recently enacted and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of any product candidates we may develop, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payers.

The PPACA, which became law in 2010, contains provisions of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any product candidates we may develop and that are approved for sale, the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of federal healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the PPACA during the next Congressional session.

Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the PPACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the PPACA. The Congress will likely consider other legislation to replace elements of the PPACA, during the next Congressional session. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace PPACA provisions is highly uncertain in many respects, it is also possible that some of the PPACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with PPACA coverage expansion provision.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our potential products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers.

The current presidential administration has also taken executive actions to undermine or delay implementation of the PPACA. Since January 2017, the president has signed two executive orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. One executive order directs federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices. The second executive order terminates the cost-sharing subsidies that reimburse insurers under the PPACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in PPACA risk corridor payments to third-party payers who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payers, the viability of the PPACA marketplace, providers, and potentially our business, are not yet known.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States, and members of Congress and the executive branch have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the current presidential administration has pressed for drug price control measures that could be enacted during the 2019 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. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current presidential administration have

each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for any product candidates we may develop or additional pricing pressures.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants and partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA and other anti-corruption laws potentially applicable to our business is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, compliance with the FCPA and other anti-corruption laws presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the European Union General Data Protection Regulation (EU) 2016/679, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that such rules should apply to transfers of personal data from clinical trial sites located in the EEA to the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements are rigorous and time intensive and require significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act of 2018, or the CCPA, which became effective on January 1, 2020, requires companies that process information on California residents to make new disclosures to consumers about their data collection, use and sharing practices, allow consumers to opt out of certain data sharing with third parties and provide a new cause of action for data breaches. Many other states are considering similar legislation, and a broad range of legislative measures also have been introduced at the federal level.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information, including certain laws that regulate the use and disclosure of personal health information. In particular, regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996, or HIPAA, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. These provisions may be applicable to our business in the future. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have violated these privacy and security laws and/or breached certain contracts with our business partners. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

It is possible that new and existing laws may be interpreted and applied in a manner that is inconsistent with our practices and our efforts to comply with the evolving data protection rules may be unsuccessful. If so, this could result in government-imposed fines or penalties or orders requiring that we change our practices, which could adversely affect our business. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with federal, state and international laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. We also face a threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business, financial condition, results of operations or prospects.

Risks related to employee matters and managing growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment offer letters with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate we may develop receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

As a growing biotechnology company, we are actively pursuing new platforms and product candidates in many therapeutic areas and across a wide range of diseases. Successfully developing product candidates for and fully understanding the regulatory and manufacturing pathways to all of these therapeutic areas and disease states requires a significant depth of talent, resources and corporate processes in order to allow simultaneous execution across multiple areas. Due to our limited resources, we may not be able to effectively manage this simultaneous execution and the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, legal or regulatory compliance failures, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively and commercialize our product candidates, if approved, will depend in part on our ability to effectively manage the future development and expansion of our company.

Future acquisitions or strategic alliances could disrupt our business and harm our financial condition and results of operations.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions, include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations.

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

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information.

Despite the implementation of security measures, given the size and complexity of our internal information technology systems and those of our current and any future third-party vendors, collaborators and other contractors and consultants, and the increasing amounts of confidential information that they maintain, such information technology systems are vulnerable to damage or interruption from computer viruses, computer hackers, malicious code, employee theft or misuse, denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies.

While we seek to protect our information technology systems from system failure, accident and security breach, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary or confidential information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we were to experience a significant cybersecurity breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the breach to counterparties and data subjects could be material. In addition, our remediation efforts may not be successful. Moreover, if the information technology systems of our third-party vendors, collaborators and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our third-party vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation based primarily on the laws and regulations discussed above in the privacy discussion, our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed. Furthermore, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our customers or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a natural disaster, pandemic or other catastrophic event.

We depend on our employees, consultants, CDMOs, CLROs, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions we take for natural disasters or other catastrophic events, these events, including terrorist attack, pandemics, hurricanes, fire, floods and ice and snowstorms, could result in significant disruptions to our research and development, preclinical studies, clinical trials, and, ultimately, commercialization of our products. Long-term disruptions in the infrastructure caused by events, such as natural disasters, the outbreak of war, the escalation of hostilities and acts of terrorism or other ‘‘acts of God,’’ particularly involving cities in which we have offices, manufacturing or clinical trial sites, could adversely affect our businesses. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not respond or be adequate to compensate us for all losses that may occur. Any natural disaster or catastrophic event affecting us, our CDMOs, our CLROs, regulatory agencies or other parties with which we are engaged could have a significant negative impact on our operations and financial performance.

Risks related to this offering, ownership of our common stock and our status as a public company

We do not know whether a 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.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock was determined through negotiations with the underwriters. Although our common stock has been approved for listing on the Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares or at all.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock is substantially higher than the pro forma as adjusted net tangible book value per share of our common stock after this offering. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after this offering. Based on our capitalization as of March 31, 2020 and the initial public offering price of $19.00 per share, you will experience immediate dilution of $12.44 per share. To the extent outstanding options are exercised, you will incur further dilution.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume 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 would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provide more favorable relative recommendations about our competitors, 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 and trading volume to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of any product candidates we may develop or those of our competitors or potential collaborators;
- timing of the results of our preclinical studies and clinical trials or those of our competitors;
- our success in commercializing any product candidates we may develop, if and when approved;
- the success of competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any product candidates we may develop;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of common stock by us, our executive officers, directors or principal stockholders or others;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, political and market conditions; and
- the other factors described in this “Risk factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and divert management’s attention and resources.

The COVID-19 pandemic, which began in late 2019 and has spread worldwide, may affect our ability to initiate and complete preclinical studies, delay the initiation of our planned clinical trial or future clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, each of which could result in adverse effects on our business, on raising capital and on our operations.

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, is causing many governments to implement measures to slow the spread of the outbreak through quarantines, travel restrictions, heightened border scrutiny and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the outbreak and its effects on our business and operations are uncertain. We and our CDMOs, and CROs, have experienced a reduction in the capacity to undertake research-scale production and to execute some preclinical studies, and we may face disruptions that affect our ability to initiate and complete preclinical studies, and disruptions in procuring items that are essential for our research and development activities, such as raw materials used in the manufacture of any product candidates we may develop, laboratory supplies used in our preclinical studies, or animals that are used for preclinical testing for which there are shortages because of ongoing efforts to address the outbreak. We and our CROs and CDMOs may face disruptions related to our future IND-enabling studies and clinical trials arising from delays in preclinical studies, manufacturing disruptions, and the ability to obtain necessary IRB, IBC or other necessary site approvals, as well as other delays at clinical trial sites. The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions. The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations and prospects.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the 2008 global financial crisis, could result in a variety of risks to our business, including, weakened demand for any product candidates we may develop and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. 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. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

After this offering, our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to control all matters submitted to stockholders for approval.

Upon the closing of this offering, based on the number of shares outstanding as of April 30, 2020, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately 58.38% of our common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

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

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

A significant portion of our total outstanding shares is 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 drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have 44,634,420 shares of common stock outstanding based on the number of shares outstanding as of April 30, 2020 after giving effect to the automatic conversion of our preferred stock. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. The remaining 34,108,104 shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times after the offering as described in the section of this prospectus titled “Shares eligible for future sale.” The representatives of the underwriters may release some or all of the shares of common stock subject to lock-up agreements at any time and without notice, which would allow for earlier sales of shares in the public market.

Moreover, beginning 180 days after the completion of this offering, holders of an aggregate of 31,887,648 shares of our common stock will have rights, along with holders of an additional shares of our common stock issuable upon exercise of outstanding options, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of 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, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriters" section of this prospectus.

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

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until the end of the fiscal year in which the fifth anniversary of this offering occurs, although if the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have annual gross revenues of $1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1.0 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- being permitted to provide only two years of audited financial statements in this prospectus, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Even after we no longer qualify as an emerging growth company, we may continue to qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of SOX Section 404 and reduced disclosure obligations regarding executive compensation. In reliance on these exemptions, we have taken advantage of reduced reporting obligations in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an EGC or a smaller reporting company.

We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we

will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either irrevocably elect to "opt out" of such extended transition period or no longer qualify as an EGC. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an EGC or a smaller reporting company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, in our second annual report due to be filed with the SEC after becoming a public company, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC or a smaller reporting company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to

implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an EGC under the JOBS Act or a smaller reporting company, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation, which could have a negative effect on the trading price of our stock.

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

Upon completion of this offering, we will become subject to certain reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Act, which significantly reformed the Code. The Tax Act, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for NOLs arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of NOL carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such NOLs may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the CARES Act was enacted on March 27, 2020. Both contain

numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of NOLs, which was enacted as part of the Tax Act. It also provides that NOLs arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the Tax Act, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the FFCR Act or the CARES Act.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws that will become effective upon the closing of this offering.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation that will become effective upon the closing of this offering designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation that will become effective upon the closing of this offering provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of proceedings:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders;
- any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or
- any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction. Furthermore, our certificate of incorporation that will become effective upon the closing of this offering provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find the choice of forum provisions contained in our 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 materially adversely affect our business, financial condition and operating results.

Cautionary note regarding forward-looking statements and industry data

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- the initiation, timing, progress and results of our research and development programs and preclinical studies and clinical trials;
- our estimates regarding expenses, future revenue, capital requirements, need for additional financing and the period over which we believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operating expenses and capital expenditure requirements;
- our plans to develop and, if approved, subsequently commercialize any product candidates we may develop;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for any product candidates we may develop;
- the potential advantages of our non-viral gene therapy platform;
- our estimates regarding the potential addressable patient populations for our programs;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection;
- our intellectual property position;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our expectations related to the use of proceeds from this offering;
- the impact of government laws and regulations;
- our competitive position and expectations regarding developments and projections relating to our competitors and any competing therapies that are or become available;
- developments and expectations regarding developments and projections relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could

differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments we may make or enter into.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus are made as of the date of this prospectus, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This prospectus includes statistical and other industry and market data that we obtained from independent industry publications and research, surveys and studies conducted by independent third parties as well as our own estimates of the prevalence of certain diseases and conditions. The market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the patient population with the potential to benefit from treatment with any product candidates we may develop include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect the addressable patient population. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Use of proceeds

We estimate that the net proceeds to us from our issuance and sale of 10,526,316 shares of our common stock in this offering will be approximately $183.0 million, based on the initial public offering price of $19.00 per share after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $210.9 million.

As of March 31, 2020, we had cash and cash equivalents of $104.5 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $75.0 million for continued research and development of our programs, including preclinical research, completion of IND-enabling studies in our most advanced liver programs and initiation of a clinical trial in each of these programs;
- approximately $130.0 million for continued development and enhancement of our platform technologies; and
- the remainder for working capital and other general corporate purposes.

Our expected use of net proceeds from this offering and our existing cash and cash equivalents represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the scope, progress, costs and results of our research and development efforts and manufacturing activities, as well as any collaborations that we may enter into with third parties for any product candidates we may develop, and any unforeseen cash needs. We believe opportunities may exist from time to time to expand our current business through acquisitions of complementary companies, products or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions at this time, we may also use a portion of the net proceeds for these purposes.

We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to complete our anticipated IND-enabling studies in PKU and hemophilia A and to initiate a clinical trial in each of these programs. However, all of our programs are currently in the early stage of development, including our programs in PKU and hemophilia A, and we have not yet identified a product candidate for any of our programs. As a result, we are unable to specify the portion of the net proceeds from this offering and our existing cash and cash equivalents that will be allocated to any specific program. The specific allocation of the net proceeds from this offering and our existing cash and cash equivalents to any program will depend on, among other things, the results of our research and development efforts for each program, the timing and success of our preclinical studies in the program and the timing and outcome of regulatory submissions.

Based on our current plans, we believe that anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2023. We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong. We could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing, which may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Our management will retain broad discretion over the allocation of the net proceeds from this offering. Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

Dividend policy

We have never declared or paid cash dividends on our common stock since our inception. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Capitalization

The following table sets forth our cash and cash equivalents and our capitalization as of March 31, 2020:

- on an actual basis;
- on a pro forma basis to give effect to the conversion of all outstanding shares of our preferred stock into an aggregate of 27,094,085 shares of common stock upon the closing of this offering, and the filing and effectiveness of our amended and restated certificate of incorporation; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 10,526,316 shares of our common stock in this offering at the initial public offering price of $19.00 per share after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the information in this table, together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the "Selected consolidated financial data" and "Management's discussion and analysis of financial condition and results of operations" sections of this prospectus.

	As of March 31, 2020		
(in thousands, except share and per share data)	**Actual**	**Pro forma**	**Pro forma as adjusted**
Cash and cash equivalents	$ 104,473	$ 104,473	$ 287,473
Convertible preferred stock (Series A, B and C), $0.0001 par value; 46,361,960 shares authorized, 46,361,960 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	224,425	—	—
Stockholders' equity (deficit)			
Preferred stock, $0.0001 par value; no shares authorized, issued or outstanding, actual; 5,000,000 shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, $0.0001 par value; 75,000,000 shares authorized, 7,010,906 shares issued and 5,570,652 shares outstanding at March 31, 2020, actual; 150,000,000 shares authorized, 34,104,991 shares issued and 32,664,737 shares outstanding, pro forma; 150,000,000 shares authorized, 44,631,307 shares issued and 43,191,053 shares outstanding, pro forma as adjusted	1	3	4
Additional paid-in capital	11,517	235,940	418,939
Accumulated deficit	(126,169)	(126,169)	(126,169)
Total stockholders' equity (deficit)	(114,651)	109,774	292,774
Total capitalization	$ 109,774	$ 109,774	$ 292,774

The table above is based on 7,010,906 shares of common stock outstanding as of March 31, 2020, which includes 1,440,254 shares of unvested restricted stock subject to repurchase by us, and excludes:

- 5,034,210 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2020 under our 2017 Stock Incentive Plan, or the 2017 Plan, at a weighted average exercise price of $4.89 per share;
- 946,809 shares of common stock available for future issuance as of March 31, 2020 under our 2017 Plan; and

- 2,547,698 and 481,231 additional shares of common stock available for issuance under our 2020 Stock Incentive Plan and our 2020 Employee Stock Purchase Plan, respectively, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans. Of the shares available under our 2020 Stock Incentive Plan, we have granted options to purchase an aggregate of approximately 648,481 shares of our common stock, at an exercise price equal to the initial public offering price in this offering, to certain of our directors, employees and consultants.

Dilution

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

Our historical net tangible book value (deficit) as of March 31, 2020 was $(115.3) million, or $(16.45) per share of common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and the carrying value of our preferred stock, which is not included within stockholders' equity (deficit). Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by the 7,010,906 shares of common stock outstanding as of March 31, 2020, including 1,440,254 shares of unvested restricted stock subject to repurchase by us.

Our pro forma net tangible book value as of March 31, 2020 was $109.1 million, or $3.20 per share of common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 27,094,085 shares of common stock upon the closing of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of March 31, 2020, after giving effect to the pro forma adjustment described above.

After giving further effect to our issuance and sale of 10,526,316 shares of our common stock in this offering at the initial public offering price of $19.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2020 would have been $292.8 million, or $6.56 per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of $3.36 to existing stockholders and immediate dilution of $12.44 in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$19.00
Historical net tangible book value (deficit) per share as of March 31, 2020	$(16.45)	
Increase per share attributable to the pro forma adjustment described above	19.65	
Pro forma net tangible book value per share as of March 31, 2020	3.20	
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing common stock in this offering	3.36	
Pro forma as adjusted net tangible book value per share after this offering		6.56
Dilution per share to new investors purchasing common stock in this offering		$12.44

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be $6.94 representing an immediate increase in pro forma as adjusted net tangible book value per share of $3.74 to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of $12.06 to new investors purchasing common stock in this offering, at the initial public offering price of $19.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes, as of March 31, 2020, on the pro forma as adjusted basis described above, the total number of shares of common stock purchased from us on an as converted to common stock basis, the total consideration paid or to be paid and the average price per share paid or to be paid by existing stockholders and by new investors in this offering at the initial public offering price of $19.00 per share before deducting underwriting discounts and commissions and estimated offering expenses payable by us. As the table shows, new investors purchasing common stock in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percentage	
Existing stockholders	34,104,991	76.4%	$227,647,532	53.2%	$ 6.67
Investors participating in this offering	10,526,316	23.6	200,000,004	46.8	$ 19.00
Total	44,631,307	100%	$427,647,536	100%	

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to 73.8% of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors purchasing common stock in this offering would be increased to 26.2% of the total number of shares of our common stock outstanding after this offering.

The tables and discussion above are based on 7,010,906 shares of common stock outstanding as of March 31, 2020, which includes 1,440,254 shares of unvested restricted stock subject to repurchase by us, and excludes:

- 5,034,210 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2020 under our 2017 Stock Incentive Plan, or 2017 Plan, at a weighted average exercise price of $4.89 per share;
- 946,809 shares of common stock available for future issuance as of March 31, 2020 under our 2017 Plan; and
- 2,547,698 and 481,231 additional shares of common stock available for issuance under our 2020 Stock Incentive Plan and our 2020 Employee Stock Purchase Plan, respectively, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans. Of the shares available under our 2020 Stock Incentive Plan, we have granted options to purchase an aggregate of approximately 648,481 shares of our common stock, at an exercise price equal to the initial public offering price in this offering, to certain of our directors, employees and consultants.

To the extent that outstanding stock options are exercised, new stock options or warrants are issued, or we issue additional shares of common stock in the future, there will be further dilution to new investors. 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 consolidated financial data

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the "Management's discussion and analysis of financial condition and results of operations" section of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2018 and 2019 and the consolidated balance sheet data as of December 31, 2018 and 2019 from our audited consolidated financial statements appearing elsewhere in this prospectus. The consolidated statement of operations data for the three months ended March 31, 2019 and 2020 and the consolidated balance sheet data as of March 31, 2020 have been derived from our unaudited condensed consolidated financial statements appearing elsewhere in this prospectus and have been prepared on the same basis as the audited consolidated financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future.

	Year ended December 31,		Three months ended March 31,	
(in thousands, except per share data)	**2018**	**2019**	**2019**	**2020**
Consolidated statement of operations data:				
Revenue	$ 36	$ —	$ —	$ —
Operating expenses:				
Research and development	28,152	50,134	11,719	13,394
General and administrative	9,178	12,168	2,757	4,642
Total operating expenses	37,330	62,302	14,476	18,036
Loss from operations	(37,294)	(62,302)	(14,476)	(18,036)
Other income (expense):				
Interest income and other income (expense), net	1,491	985	382	319
Net loss and net loss attributable to common stockholders	$ (35,803)	$ (61,317)	$ (14,094)	$ (17,717)
Net loss per share attributable to common stockholders, basic and diluted	$ (10.69)	$ (12.96)	$ (3.29)	$ (3.22)
Weighted average common shares outstanding, basic and diluted	3,351	4,732	4,284	5,495
Pro forma net loss per share attributable to common stockholders, basic and diluted(1)		$ (3.11)		$ (0.56)
Pro forma weighted average common shares outstanding, basic and diluted(1)		19,693		31,389

(1) See Notes 2 and 12 to our consolidated financial statements appearing elsewhere in this prospectus for details on the calculation of unaudited pro forma net loss per share attributable to common stockholders.

(in thousands)	As of December 31, 2018	As of December 31, 2019	As of March 31, 2020
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 7,305	$ 15,076	$ 104,473
Marketable securities	67,565	—	—
Working capital(1)	70,371	8,998	100,199
Total assets	83,519	42,140	132,636
Convertible preferred stock	115,593	115,593	224,425
Total stockholders' deficit	(41,591)	(98,592)	(114,651)

(1) We define working capital as current assets less 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 the "Selected consolidated financial data" section of this prospectus and our consolidated financial statements and the related notes and other financial information 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, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk factors" section of this prospectus, 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.

Overview

We are an innovative genetic medicines company creating a new class of gene therapy utilizing our proprietary non-viral gene therapy platform to provide durable, redosable treatments for millions of patients living with rare and prevalent diseases. Our non-viral gene therapy platform incorporates our high-capacity DNA construct called closed-ended DNA, or ceDNA; our cell-targeted lipid nanoparticle delivery system, or ctLNP; and our established, scalable capsid-free manufacturing process. Using our approach, we are developing novel gene therapies to provide targeted delivery of genetic payloads that include large and multiple genes to a range of tissues across a broad array of diseases. We are also engineering our gene therapies to be redosable, which may enable individualized patient titration to reach the desired level of therapeutic expression and to maintain efficacy throughout a patient's life.

Since our inception in October 2016, we have focused substantially all of our resources on building our non-viral gene therapy platform, establishing and protecting our intellectual property portfolio, conducting research and development activities, developing our manufacturing process, organizing and staffing our company, business planning, raising capital and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations with proceeds from instruments convertible into convertible preferred stock (which converted into convertible preferred stock in 2017) and the sales of convertible preferred stock. Through March 31, 2020, we had received gross proceeds of $227.3 million from sales of preferred stock and instruments convertible into preferred stock. Since our inception, we have incurred significant operating losses. Our ability to generate any product revenue or product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more product candidates we may develop. For the years ended December 31, 2018 and 2019, we reported net losses of $35.8 million and $61.3 million, respectively, and for the three months ended March 31, 2020, we reported net losses of $17.7 million. As of March 31, 2020, we had an accumulated deficit of $126.2 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly if and as we:

- continue our current research programs and conduct additional research programs;
- advance any product candidates we identify into preclinical and clinical development;
- expand the capabilities of our non-viral gene therapy platform;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- obtain, expand, maintain, enforce and defend our intellectual property portfolio;

- hire additional clinical, regulatory and scientific personnel;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- establish a commercial manufacturing source and secure supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain regulatory approval; and
- add operational, legal, compliance, financial and management information systems and personnel to support our research, product development, future commercialization efforts and operations as a public company.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for any product candidates we may develop. If we obtain regulatory approval for any product candidates we may develop, we expect to incur significant expenses related to developing our commercial capability to support product sales, marketing and distribution. Further, following the completion of this offering, we expect to incur additional costs associated with operating as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements when needed or on terms acceptable to us, we would be required to delay, limit, reduce or terminate our product development or future commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditures into 2023. We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong. We could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing, which may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. See “—Liquidity and capital resources.”

Components of our results of operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for our product candidates are successful and result in regulatory approval or license or collaboration agreements with third parties, we may generate revenue in the future from product sales, payments from collaboration or license agreements that we may enter into with third parties, or any combination thereof.

We have previously generated a small amount of revenue by providing services to pharmaceutical and life sciences companies. We did not generate any such revenue in 2019 or in in the first quarter of 2020.

Operating expenses

Research and development expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our programs, which include:

- personnel-related costs, including salaries, benefits and stock-based compensation expense, for employees engaged in research and development functions;
- expenses incurred in connection with our research programs, including under agreements with third parties, such as consultants and contractors and contract research organizations, or CROs;
- the cost of developing and scaling our manufacturing process and manufacturing drug substance and drug product for use in our research and preclinical studies, including under agreements with third parties, such as consultants and contractors and contract development and manufacturing organizations, or CDMOs;
- laboratory supplies and research materials;
- facilities, depreciation and amortization and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Our external research and development expenses consist of costs that include fees and other costs paid to consultants, contractors, CDMOs and CROs in connection with our preclinical and manufacturing activities. We do not allocate our research and development costs to specific programs because costs are deployed across multiple programs and our platform and, as such, are not separately classified. We expect that our research and development expenses will increase substantially as we advance our programs into clinical development and expand our discovery, research and preclinical activities in the near term and in the future. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any product candidates we may develop. The successful development of any of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development, including the following:

- the timing and progress of preclinical studies, including investigational new drug, or IND, -enabling studies;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising additional funds necessary to complete preclinical and clinical development of our product candidates;
- the timing of filing and acceptance of INDs or comparable foreign applications that allow commencement of future clinical trials for our product candidates;
- the successful initiation, enrollment and completion of clinical trials, including under current good clinical practices;
- our ability to achieve positive results from our future clinical programs that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended patient populations of any product candidates we may develop;

- the availability of specialty raw materials for use in production of our product candidates;
- our ability to establish arrangements with third-party manufacturers for clinical supply;
- our ability to establish new licensing or collaboration arrangements;
- the receipt and related terms of regulatory approvals from the U.S. Food and Drug Administration, or FDA, and other applicable regulatory authorities;
- our ability to establish, obtain, maintain, enforce and defend patent, trademark, trade secret protection and other intellectual property rights or regulatory exclusivity for any product candidates we may develop and our technology; and
- our ability to maintain a continued acceptable safety, tolerability and efficacy profile of our product candidates following approval.

A change in the outcome of any of these variables with respect to any product candidates we may develop could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any product candidates we may develop.

General and administrative expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation, for employees engaged in executive, legal, finance and accounting and other administrative functions. General and administrative expenses also include professional fees for legal, patent, consulting, investor and public relations and accounting and audit services as well as direct and allocated facility-related costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our programs and platform. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, director and officer insurance costs and investor and public relations expenses associated with operating as a public company.

Other income (expense)

Interest income and other income (expense), net

Interest income consists of interest earned on our invested cash balances. We expect our interest income to increase as we invest the cash received from the sale of Series C preferred stock in January 2020 and the net proceeds from this offering.

Other income (expense) consists of miscellaneous income and expense unrelated to our core operations.

Income taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred or for the research and development tax credits earned in each year, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credit carryforwards will not be realized.

As of December 31, 2019, we had federal net operating loss carryforwards of $91.9 million, which may be available to offset future taxable income, of which $8.2 million of the total net operating loss carryforwards begin to expire in 2036, while the remaining $83.7 million do not expire but may be limited in their usage to an annual deduction equal to 80% of annual taxable income. In addition, as of December 31, 2019, we had state

net operating loss carryforwards of $90.6 million, which may be available to offset future taxable income and expire at various dates beginning in 2036. As of December 31, 2019, we also had federal and state research and development tax credit carryforwards of $4.0 million and $2.5 million, respectively, which may be available to reduce future tax liabilities and expire at various dates beginning in 2036 and 2032, respectively. Due to our history of cumulative net losses since inception and uncertainties surrounding our ability to generate future taxable income, we have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

Results of operations

Comparison of the three months ended March 31, 2019 and 2020

The following table summarizes our results of operations for the three months ended March 31, 2019 and 2020:

	Three months ended March 31,		
(in thousands)	**2019**	**2020**	**Change**
Operating expenses:			
Research and development	$ 11,719	$ 13,394	$ 1,675
General and administrative	2,757	4,642	1,885
Total operating expenses	14,476	18,036	3,560
Loss from operations	(14,476)	(18,036)	(3,560)
Other income (expense):			
Interest income and other income (expense), net	382	319	(63)
Net loss	$ (14,094)	$ (17,717)	$ (3,623)

Research and development expenses

The following table summarizes our research and development expenses for the three months ended March 31, 2019 and 2020:

	Three months ended March 31,		
(in thousands)	**2019**	**2020**	**Change**
Personnel related	$ 3,081	$ 3,819	$ 738
Stock-based compensation	676	827	151
Preclinical and manufacturing	3,675	3,472	(203)
Facilities	2,137	2,436	299
Lab supplies	1,171	1,278	107
Consulting and professional services	432	991	559
Other	547	571	24
Total research and development expenses	$ 11,719	$ 13,394	$ 1,675

Research and development expenses were $11.7 million for the three months ended March 31, 2019, compared to $13.4 million for the three months ended March 31, 2020. The increase in personnel-related costs of $0.7 million was primarily due to increased headcount in our research and development function. The increases in facility-related expenses and lab supplies of $0.3 million and $0.1 million, respectively, were primarily due to the increased costs of supporting a larger group of research and development personnel and their research efforts. The increase in consulting and professional services of $0.6 million was primarily due to consulting services to develop and scale our manufacturing process.

General and administrative expenses

The following table summarizes our general and administrative expenses for the three months ended March 31, 2019 and 2020:

(in thousands)	Three months ended March 31, 2019	2020	Change
Personnel related	$ 882	$ 1,566	$ 684
Stock-based compensation	317	677	360
Professional and consultant fees	1,030	1,860	830
Facilities	251	369	118
Other	277	170	(107)
Total general and administrative expenses	$ 2,757	$ 4,642	$ 1,885

General and administrative expenses for the three months ended March 31, 2019 were $2.8 million, compared to $4.6 million for the three months ended March 31, 2020. The increases in personnel-related costs and stock-based compensation costs of $0.7 million and $0.4 million, respectively, were primarily a result of an increase in headcount in our general and administrative function. Professional and consultant fees increased by $0.8 million primarily due to professional fees relating to accounting, audit and legal services as well as costs associated with ongoing business activities and our preparations to operate as a public company.

Other income and expense, net

Other income and expense, net for the three months ended March 31, 2019 was $0.4 million, compared to $0.3 million for the three months ended March 31, 2020 and consisted primarily of interest earned on invested cash balances.

Comparison of the years ended December 31, 2018 and 2019

The following table summarizes our results of operations for the years ended December 31, 2018 and 2019:

(in thousands)	Year ended December 31, 2018	2019	Change
Revenue	$ 36	$ —	$ (36)
Operating expenses:			
Research and development	28,152	50,134	21,982
General and administrative	9,178	12,168	2,990
Total operating expenses	37,330	62,302	24,972
Loss from operations	(37,294)	(62,302)	(25,008)
Other income (expense):			
Interest income and other income (expense), net	1,491	985	(506)
Net loss	$ (35,803)	$ (61,317)	$ (25,514)

Revenue

We recorded less than $0.1 million of revenue for the year ended December 31, 2018 for services rendered. We did not generate revenue in 2019.

Research and development expenses

The following table summarizes our research and development expenses for the years ended December 31, 2018 and 2019:

(in thousands)	Year Ended December 31, 2018	2019	Change
Personnel related	$ 8,705	$12,847	$ 4,142
Stock-based compensation	2,093	2,753	660
Preclinical and manufacturing	7,359	15,027	7,668
Facilities	2,835	9,553	6,718
Lab supplies	3,200	4,124	924
Consulting and professional services	2,377	2,629	252
Other	1,583	3,201	1,618
Total research and development expenses	$28,152	$50,134	$21,982

Research and development expenses were $28.2 million for the year ended December 31, 2018, compared to $50.1 million for the year ended December 31, 2019. The increase in personnel-related costs of $4.1 million was primarily due to increased headcount in our research and development function. The increase in preclinical and manufacturing expense of $7.7 million was primarily due to developing and scaling our manufacturing process, advancing our lead programs towards development candidates and advancing our discovery efforts. The increases in facility-related expenses and lab supplies of $6.7 million and $0.9 million, respectively, were primarily due to rent expense for our new facility in Cambridge, Massachusetts, for which we recorded a full year of rent expense in 2019 compared to a partial year in 2018, and the increased costs of supporting a larger group of research and development personnel and their research efforts. The increase in other expense of $1.6 million was primarily due to an increase in technology licensing fees.

General and administrative expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2018 and 2019:

(in thousands)	Year ended December 31, 2018	2019	Change
Personnel related	$2,997	$ 4,279	$ 1,282
Stock-based compensation	1,395	1,454	59
Professional and consultant fees	3,319	4,465	1,146
Facilities	623	1,217	594
Other	844	753	(91)
Total general and administrative expenses	$9,178	$12,168	$ 2,990

General and administrative expenses for the year ended December 31, 2018 were $9.2 million, compared to $12.2 million for the year ended December 31, 2019. The increase in personnel-related costs of $1.3 million was a result of an increase in headcount in our general and administrative function. Professional and consultant fees increased by $1.1 million primarily due to professional fees relating to accounting, audit and legal services as well as costs associated with ongoing business activities and our preparations to operate as a public company. The increase in facility-related expenses of $0.6 million was primarily due to rent expense for our new facility in Cambridge, Massachusetts.

Other income and expense, net

Other income and expense, net for the year ended December 31, 2018 was $1.5 million, compared to $1.0 million for the year ended December 31, 2019. The decrease was primarily due to a reduction in interest income as we had a lower average invested balance during 2019.

Other expense was not significant for either of the years ended December 31, 2018 or 2019.

Liquidity and capital resources

Since our inception in October 2016, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we support our continued research activities and development of our programs and platform. To date, we have funded our operations with proceeds from instruments convertible into convertible preferred stock (which converted into convertible preferred stock in 2017) and the sale of convertible preferred stock. Through March 31, 2020, we had received gross proceeds of $227.3 million from sales of convertible preferred stock and instruments convertible into convertible preferred stock.

As of December 31, 2019 and March 31, 2020, we had cash and cash equivalents of $15.1 million and $104.5 million, respectively.

Cash flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year ended December 31,		Three months ended March 31,	
(in thousands)	**2018**	**2019**	**2019**	**2020**
Cash used in operating activities	$ (28,119)	$ (40,346)	$ (12,094)	$ (17,780)
Cash provided by (used in) investing activities	(69,761)	47,985	15,447	(2,011)
Cash provided by financing activities	100,189	78	9	109,133
Net increase in cash, cash equivalents and restricted cash	$ 2,309	$ 7,717	$ 3,362	$ 89,342

Operating activities

During the three months ended March 31, 2020, operating activities used $17.8 million of cash, primarily resulting from our net loss of $17.7 million and net cash used by changes in our operating assets and liabilities of $2.2 million, partially offset by net non-cash charges of $2.2 million. Net cash used by changes in our operating assets and liabilities for the three months ended March 31, 2020 consisted primarily of a $2.2 million decrease in accounts payable and accrued expenses and other current liabilities, a decrease of $0.2 million in deferred rent and an increase of $0.2 million in prepaid expenses and other current assets, partially offset by a decrease of $0.4 million in tenant receivable.

During the three months ended March 31, 2019, operating activities used $12.1 million of cash, primarily resulting from our net loss of $14.1 million, partially offset by net non-cash charges of $1.0 million and net cash provided by changes in our operating assets and liabilities of $1.0 million. Net cash provided by changes in our operating assets and liabilities for the three months ended March 31, 2019 consisted primarily of a $6.1 million increase in deferred rent, partially offset by a $3.8 million increase in tenant receivable and a $1.0 million increase in prepaid expenses and other current assets.

During the year ended December 31, 2019, operating activities used $40.3 million of cash, primarily resulting from our net loss of $61.3 million, partially offset by net non-cash charges of $5.7 million and net cash provided

by changes in our operating assets and liabilities of $15.2 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2019 consisted primarily of a $13.0 million increase in deferred rent and a $3.2 million increase in accounts payable and accrued expenses and other current liabilities, partially offset by a $1.9 million increase in prepaid expenses and other current assets.

During the year ended December 31, 2018, operating activities used $28.1 million of cash, primarily resulting from our net loss of $35.8 million, partially offset by net non-cash charges of $3.0 million and net cash provided by changes in our operating assets and liabilities of $4.7 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2018 consisted primarily of a $3.0 million increase in deferred rent and a $3.5 million increase in accounts payable and accrued expenses and other current liabilities, partially offset by a $1.3 million increase in tenant receivable and a $0.5 million increase in prepaid expenses and other current assets.

Changes in accounts payable, accrued expenses and other current liabilities and prepaid expenses and other current assets in all periods were generally due to growth in our business, the advancement of our research programs and the timing of vendor invoicing and payments. The increase in deferred rent primarily related to a tenant improvement allowance from our landlord.

Investing activities

During the three months ended March 31, 2020, net cash used in investing activities was $2.0 million, due to the acquisition of property and equipment during the period. Property and equipment purchases during the three months ended March 31, 2020 were primarily related to leasehold improvements and lab equipment for our facility in Cambridge, Massachusetts.

During the three months ended March 31, 2019, net cash provided by investing activities was $15.4 million, due primarily to net sales and maturities of marketable securities of $21.3 million, partially offset by the acquisition of property and equipment during the period of $5.8 million. Property and equipment purchases during the three months ended March 31, 2019 were primarily related to leasehold improvements and lab equipment for our facility in Cambridge, Massachusetts.

During the year ended December 31, 2019, net cash provided by investing activities was $48.0 million, due primarily to net sales and maturities of marketable securities, partially offset by the acquisition of property and equipment during the year. Property and equipment purchases during the year ended December 31, 2019 primarily related to leasehold improvements and lab equipment for our new facility in Cambridge, Massachusetts.

During the year ended December 31, 2018, net cash used in investing activities was $69.8 million, due primarily to net purchases of marketable securities and property and equipment. Property and equipment purchases during the year ended December 31, 2018 primarily related to leasehold improvements and lab equipment for our new facility in Cambridge, Massachusetts.

Financing activities

During the three months ended March 31, 2020, net cash provided by financing activities was $109.1 million, consisting primarily of proceeds from the sale of our Series C preferred stock of $109.0 million and proceeds from the exercise of common stock options.

During the three months ended March 31, 2019, net cash provided by financing activities was less than $0.1 million, consisting of proceeds from the exercise of common stock options.

During the year ended December 31, 2019, net cash provided by financing activities was $0.1 million, consisting primarily of proceeds from the exercise of common stock options.

During the year ended December 31, 2018, net cash provided by financing activities was $100.2 million, consisting of net proceeds from the sale of our Series B preferred stock.

Funding requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and initiate clinical trials for our product candidates in development. The timing and amount of our operating expenditures will depend largely on:

- the identification of additional research programs and additional product candidates;
- the scope, progress, costs and results of preclinical and clinical development for any product candidates we may develop;
- the costs, timing and outcome of regulatory review of any product candidates we may develop;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidates we may develop for which we receive marketing approval;
- the costs and scope of the continued development of our non-viral gene therapy platform;
- the costs of satisfying any post-marketing requirements;
- the revenue, if any, received from commercial sales of product candidates we may develop for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting applications for patents, obtaining, maintaining, defending and enforcing our intellectual property rights and defending against any intellectual property-related claims, including claims of infringement, misappropriation or other violation of third-party intellectual property;
- the costs of operational, financial and management information systems and associated personnel;
- the associated costs in connection with any acquisition of in-licensed products, intellectual property and technologies; and
- the costs of operating as a public company.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into 2023. We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong. We could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing, which may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We do not have any committed external source of funds. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter would result in fixed payment obligations and may involve agreements that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, granting liens over our assets, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. Any debt financing or additional equity that we raise may contain terms that could adversely affect the holdings or the rights of our common stockholders.

If we are unable to raise sufficient capital as and when needed, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate we may develop, or be unable to expand our operations or otherwise capitalize on our business opportunities. If we raise additional funds through collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

See “Risk factors” for additional risks associated with our substantial capital requirements.

Contractual obligations and commitments

The following table summarizes our contractual obligations as of December 31, 2019 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

		Payments due by period			
(in thousands)	Total	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
Operating lease commitments(1)	$71,742	$ 6,867	$ 14,304	$ 15,120	$ 35,451
Total	$71,742	$ 6,867	$ 14,304	$ 15,120	$ 35,451

(1) Amounts in table reflect payments due for our lease of office and laboratory space in Cambridge, Massachusetts under an operating lease agreement that expires in April 2029.

We enter into contracts in the normal course of business with CROs, CDMOs and other third parties for preclinical research studies and manufacturing services. These contracts do not contain minimum purchase commitments and are cancelable by us upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation. These payments are not included in the table of contractual obligations above as the amount and timing of such payments are not known.

We have also entered into license agreements under which we are obligated to make specified milestone and royalty payments. We have not included future payments under these agreements in the table of contractual obligations above since the payment obligations under these agreements are contingent upon future events, such as our achievement of specified development, regulatory and commercial milestones, or generating product sales. As of December 31, 2019, we were unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. For additional information about our licenses agreements and amounts that could become payable in the future under such agreements, see “Business—Intellectual Property—License Agreements” and Note 10 to our consolidated financial statements appearing elsewhere in this prospectus.

Critical accounting policies and significant judgments and estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Accrued research and development expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate certain accrued research and development expenses. This process involves estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include those related to fees paid to:

- vendors in connection with discovery and preclinical development activities;
- CROs in connection with preclinical studies and testing; and
- CDMOs in connection with the process development and scale up activities and the production of materials.

We base the expense recorded related to contract research and manufacturing on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs and CDMOs that conduct services and supply materials. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses. While the majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; some require advance payments. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. We record these as prepaid expenses on our consolidated balance sheet.

Stock-based compensation

We measure all stock-based awards granted to employees, non-employees and directors based on their fair value on the date of the grant using the Black-Scholes option-pricing model for options or the difference between the purchase price, if any, and the fair value of our common stock for restricted stock awards. Compensation expense for awards with service-based vesting is generally recognized over the vesting period of the award using the straight-line method to record the expense. We use the graded-vesting method to record the expense of awards with both service-based and performance-based vesting conditions, commencing once achievement of the performance condition becomes probable. We account for forfeitures of share-based awards as they occur.

The Black-Scholes option-pricing model uses as inputs the fair value of our common stock and assumptions we make for the expected volatility of our common stock, the expected term of stock options, the risk-free interest rate for a period that approximates the expected term of our common stock options and our expected dividend yield.

Determination of fair value of common stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of common stock, and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common stock valuations were prepared using either an option pricing method, or OPM, or a hybrid method, both of which used market approaches to estimate our enterprise value. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. These third-party valuations were performed at various dates, which resulted in valuations of our common stock of $4.60 per share as of February 21, 2018, $6.36 per share as of May 31, 2019, $7.26 per share as of August 31, 2019, $5.16 per share as of January 31, 2020, and $5.25 per share as of March 25, 2020. In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies in our programs;
- our stage of development and our business strategy;
- external market conditions affecting the biotechnology industry and trends within the biotechnology industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biotechnology industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Once a public trading market for our common stock has been established in connection with the completion of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

Awards granted

The following table summarizes by grant date the number of stock-based awards granted between January 1, 2019 and June 11, 2020, the per share exercise price of options, the per share fair value of common stock on each grant date, and the per share estimated fair value of the awards:

Grant date	Number of shares subject to options granted	Per share exercise price of options	Per share fair value of common stock on grant date	Per share estimated fair value of options
February 21, 2019	506,142	$ 4.60	$ 6.36(1)	$ 4.26
August 12, 2019	296,523	$ 6.36	$ 6.36	$ 4.14
November 25, 2019	279,963	$ 7.26	$ 7.26	$ 4.77
December 6, 2019	118,326	$ 7.26	$ 7.26	$ 5.37
March 5, 2020	1,664,609	$ 5.16	$ 5.16	$ 3.46
March 31, 2020	63,834	$ 5.25	$ 5.25	$ 3.40

(1) At the time of the option grant on February 21, 2019, our board of directors determined that the fair value of our common stock of $4.60 per share calculated in the valuation as of February 21, 2018 reasonably reflected the fair value of our common stock as of the grant date. However, the fair value of common stock as of February 21, 2019 was adjusted for financial reporting purposes based, in part, upon our third-party valuation of our common stock prepared as of May 31, 2019.

Off-balance sheet arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Recently issued accounting pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this prospectus.

Emerging growth company status

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we can adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an emerging growth company.

Quantitative and qualitative disclosures about market risks

As of December 31, 2019, we had cash and cash equivalents of $15.1 million, which consisted of cash and money market funds. Interest income is sensitive to changes in the general level of interest rates; however, due to the nature of these investments, an immediate 10% change in market interest rates would not have a material effect on the fair market value of our investment portfolio. We are not currently exposed to significant market risk related to changes in foreign currency exchange rates. Our operations may be subject to fluctuations in foreign currency exchange rates in the future. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the year ended December 31, 2019.

Business

Overview

We are an innovative genetic medicines company creating a new class of gene therapy utilizing our proprietary non-viral gene therapy platform to provide durable, redosable treatments for millions of patients living with rare and prevalent diseases. Our non-viral gene therapy platform incorporates our high-capacity DNA construct called closed-ended DNA, or ceDNA; our cell-targeted lipid nanoparticle delivery system, or ctLNP; and our established, scalable capsid-free manufacturing process. Using our approach, we are developing novel gene therapies to provide targeted delivery of genetic payloads that include large and multiple genes to a range of tissues across a broad array of diseases. We are also engineering our gene therapies to be redosable, which may enable individualized patient titration to reach the desired level of therapeutic expression and to maintain efficacy throughout a patient's life.

We are advancing a broad and expansive portfolio of eight programs for rare and prevalent diseases of the liver and retina. We are focused on diseases with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches. We are initially prioritizing rare monogenic diseases of the liver and retina, which are diseases that result from mutations in a single gene, that have well-established biomarkers and clear clinical and regulatory pathways.

We plan to expand our portfolio to include rare and prevalent diseases of the skeletal muscle, the central nervous system, or CNS, and oncology by developing discrete ctLNPs, each engineered to reach a different tissue. In parallel, we are developing the constructs and manufacturing capacity to rapidly advance new disease programs in a tissue or area once human proof of concept is established.

We believe our non-viral gene therapy platform may allow patients to produce antibody therapies from their own cells for years at a time from a single dose, and plan to advance antibody gene therapy programs across multiple therapeutic areas. The combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases.

While we are currently a preclinical stage company and are early in our development efforts, we believe that our new class of gene therapy has the potential to reach previously untreatable or under-treated patients and address new indications, including those with large patient populations, thereby unlocking the full potential of genetic medicine. Specifically, we believe that our platform has the potential to provide durable and redosable therapies that will enable:

- expanded patient access, including the ability to treat children;
- delivery of large genetic payload, including large and multiple genes;
- native gene regulation;
- targeted delivery to a range of tissues;
- large-scale cost-effective production;
- treatment for millions of patients across the globe; and
- a sustainable payer model.

Our non-viral gene therapy platform

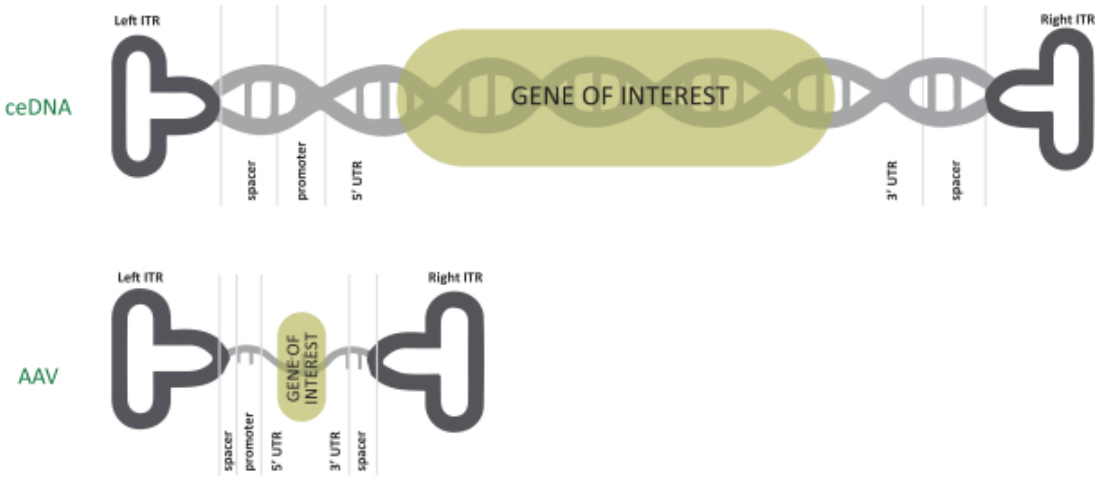
Our non-viral gene therapy platform is comprised of three essential components: our high-capacity ceDNA construct, which can accommodate large or multiple genes as well as native regulatory elements; our ctLNP delivery system, which enables highly specific delivery of ceDNA to a range of tissues; and our established,

scalable capsid-free manufacturing process, which uses a cost-effective biologics infrastructure that has the potential to reach patients with rare diseases and to expand access to patients with prevalent diseases, requiring millions of doses, on a sustainable basis.

ceDNA

Our high-capacity ceDNA is an engineered, double-stranded, linear, covalently closed-ended DNA construct that includes the gene of interest and associated regulatory sequences. We have produced ceDNA constructs of 12 kilobases, or kb, which have almost three times the 4.7 kb capacity of adeno-associated virus, or AAV, gene therapy approaches. The structure and relative size of ceDNA as compared to AAV is shown in the figure below. We believe ceDNA can deliver a significant majority of the human coding sequences known to be relevant for the treatment of diseases that result from mutations in a single gene or in multiple genes. ceDNA may address many diseases, including prevalent diseases and diseases requiring more than one type of genetic correction that are beyond the scope of current gene therapy. This capacity can also accommodate native or engineered regulatory elements, potentially enabling a powerful new dimension of gene therapy that responds to the body's own signals.

ceDNA structure and capacity



ctLNP

Our ctLNP delivery system builds upon clinically validated lipid nanoparticles, or LNPs, and is designed to allow for repeat dosing of a genetic payload without stimulating an immune response, such as antibody production. We have taken a significant step beyond current LNP technology by adding a biological targeting molecule, called a ligand, on the surface of our LNPs to direct their biodistribution to specific tissues. Different targeting ligands may enable our ctLNPs to actively target specific cell receptors in the liver, retina, skeletal muscle, CNS and tumors. In addition, our ctLNP delivery system may confer the advantages of predictable behavior across species, minimal off-target effects and a foundational platform approach that unlocks the ability to target the widest possible spectrum of diseases with our therapies.

Manufacturing process

Our established, scalable manufacturing employs a proprietary, capsid-free process and utilizes standard biologics infrastructure, unlike traditional viral gene therapy manufacturing. Viral gene therapy relies on a

protein capsid for therapeutic delivery of a viral vector, and as a result, the manufacturing process for viral gene therapies requires the production of protein capsids, which limit process scalability and consistency. Our capsid-free manufacturing process is an efficient and reproducible process that includes rigorous, industrial-scale purification that consistently yields greater than 99% pure ceDNA.

We have established a current Good Manufacturing Practices, or cGMP, -ready process at the 200-liter scale, which we have successfully transferred to external contract development and manufacturing organizations, or CDMOs, for production of clinical supply.

Our ability to conduct this manufacturing process at the 200-liter scale with high product quality suggests that further scaling to thousands of liters per batch is feasible using standard biological production equipment and engineering methods.

We believe the combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases. We also believe these features will allow the cost of production for our non-viral gene therapy platform to compare favorably to the cost of production of current biologic products.

Our portfolio

We are advancing a broad and expansive portfolio including eight programs for rare and prevalent diseases of the liver and retina. We are focused on diseases with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches. We are initially prioritizing rare monogenic diseases of the liver and retina that have well-established biomarkers and clear clinical and regulatory pathways.

We plan to expand our portfolio to include rare and prevalent diseases of the skeletal muscle, the CNS and oncology by developing discrete ctLNPs, each engineered to reach a different tissue. In parallel, we are developing the constructs and manufacturing capacity to rapidly advance new disease programs in a tissue or area once human proof of concept is established. As shown in the figure below, our most advanced liver disease programs are in phenylketonuria, or PKU, and hemophilia A, which are in the preclinical stage of development, and our most advanced retina disease programs are in Leber's Congenital Amaurosis, or LCA10, and Stargardt disease, which are in the lead optimization stage of development. In the lead optimization stage, we are seeking to identify ceDNA constructs that provide disease relevant expression in an animal model, and in the preclinical stage of development, we are conducting additional *in vivo* studies to identify development candidates and are assessing these candidates in investigational new drug, or IND, -enabling studies.

In December 2019, we held an Initial Targeted Engagement for Regulatory Advice on CBER Products, or INTERACT, meeting with the FDA's Office of Tissues and Advanced Therapies, or OTAT, to introduce our platform and align on the manufacturing and analytical control strategy to support clinical development in PKU. Over the course of 2020, we expect to obtain additional preclinical *in vivo* data and to identify development candidates for PKU and hemophilia A, positioning us to undertake studies enabling IND applications for these programs in 2021 and to submit IND applications for these programs in 2022. We anticipate submitting IND applications for additional programs in 2023 and beyond.

Our eight programs in the liver and retina as well as in our expansion opportunities are wholly owned by us. For the majority of our programs, we have designed and produced ceDNAs that have shown expression *in vitro* and/or disease correction *in vivo*.

Our strategy

Our goal is to become an industry leader in the field of genetic medicines, advancing our non-viral gene therapy platform to discover, develop, manufacture and globally commercialize a new class of gene therapy that is durable, redosable and specifically delivered to a range of tissues for the treatment of diseases caused by single, large or multiple gene defects. We aim to provide sustainable, life-long treatment for millions of patients living with rare and prevalent diseases.

Our research and development efforts have resulted in numerous innovations and breakthroughs across every aspect of our platform. We own or exclusively license patent applications in 36 patent application families covering our programs and technology, including our ceDNA platform, ctLNP delivery system and our manufacturing processes, and have taken other steps to protect our proprietary position with respect to these innovations and breakthroughs. Our wholly owned intellectual property, combined with the background technology we have licensed from the National Institutes of Health, or NIH, and the University of Massachusetts Medical School, or UMass, and Voyager Therapeutics, Inc., or Voyager, based on our co-founder's prior work, supports the leading position of our non-viral gene therapy platform and provides a strong foundation for its continued advancement.

To fund our operations, we have raised approximately $227.3 million from investors, premier venture capitalists and institutional investors, including Atlas Venture, Fidelity, T. Rowe Price, Invus, Farallon, Wellington, Deerfield, Casdin Capital, Foresight Capital and Leerink Partners.

Our culture and team

We have established a highly collaborative, patient-first culture that fuels our innovation. Our team learns, develops and thrives as a community guided by four core values: together we are thoughtful, inclusive, courageous and all-in for our mission to create solutions for patients and their families.

Our management team has extensive collective expertise in human genetics, rare disease drug development and commercialization and the manufacture and delivery of nucleic acid therapeutics. Geoff McDonough, M.D., our President and Chief Executive Officer, brings over 20 years of leadership experience with innovative life science companies across strategy, corporate and business development, program management and global drug development and launches. Douglas Kerr, M.D., Ph.D., M.B.A., our Chief Development Officer, is a pioneer in the development of rare neuroscience programs with more than 15 years of industry experience. Matthew Stanton, Ph.D., our Chief Scientific Officer, is an expert in nucleic acid therapeutic development and delivery platforms with over 20 years of experience across pharmaceutical and biotechnology companies. Mark Angelino, Ph.D., our Chief Operating Officer, has more than 25 years of experience in drug development and deep expertise in building and scaling gene therapy manufacturing processes and infrastructure.

In the aggregate, our management team has been involved in the filing of over 40 INDs and contributed to the development of 20 approved products, including Biogen's SPINRAZA (nusinersen); Sanofi Genzyme's FABRAZYME (agalsidase beta), ALDURAZYME (laronidase) and MYOZYME (alglucosidase alfa); Sobi and Biogen's ELOCTATE and ALPROLIX; Vertex Pharmaceuticals Inc.'s KALYDECO (ivacaftor), ORKAMBI (lumacaftor/ivacaftor) and SYMDEKO (tezacaftor/ivacaftor); bluebird bio, Inc.'s ZYNTEGLO (autologous CD34+ cells encoding bA-T87Q-globin gene); and Moderna, Inc.'s mRNA-1944, an investigational therapy for the chikungunya virus.

Our organization is comprised of more than 85 talented individuals with significant experience across discovery, preclinical research, manufacturing and clinical development. We have also established scientific and clinical advisory boards comprised of leading experts in the fields of human genetics, rare disease drug discovery and development and global regulatory engagement, who share our mission of providing sustainable, life-long treatment for millions of patients living with rare and prevalent diseases.

The genetic medicines industry

Background

The human genome is made up of approximately 25,000 genes, which act as a set of instructions to influence and determine every aspect of how the body functions. A genetic disease is caused by a change, or a mutation, in an individual's DNA sequence. Genetic diseases can be caused by a mutation in a single gene, known as a monogenic disorder, or by mutations in multiple genes, known as a multifactorial inheritance disorder. Current estimates suggest that there are more than 10,000 monogenic diseases. Many of these are rare, affecting hundreds or thousands of patients worldwide, such as PKU or hemophilia A. There are an even greater number of prevalent diseases whose genetics are multifactorial, affecting millions of people on a global scale, such as many types of metabolic disease and cancer.

Genetic medicines are designed to correct disease-causing dysfunction at the genetic level and utilize recombinant nucleic acids to regulate, repair, replace, add or delete a genetic sequence to achieve the desired therapeutic effect. Viral gene therapy, gene editing and messenger RNA, or mRNA, are genetic medicine modalities that specifically aim to replace the function of disease-causing genes by either inserting a gene, modifying the DNA, or inserting mRNA into a patient's cell.

Early gene therapy clinical trials in the 1990's used adenovirus to deliver genetic material. However, developers have moved away from using adenoviruses because they can trigger a strong immune reaction and their effect is short lived. Another form of viral gene therapy uses retroviral vectors, including lentiviral vectors, to incorporate DNA directly into a cell's chromosome upon infection, typically through *ex vivo* delivery. In *ex vivo* delivery, genetic modification of isolated patient or donor cells are conducted outside of the patient and then re-introduced to the patient. As an integrating virus, these vectors pose additional safety risks, and create the potential for disrupting genes or activating cancer-causing genes. In addition, *ex vivo* delivery poses a significant operational challenge and higher cost relative to *in vivo* therapies. As a result, AAV has become a preferred viral vector for gene therapy.

Significant progress has been made in the field of genetic medicine over the last decade with products approved in viral gene therapy, and several gene editing and mRNA programs in clinical development. While we expect that there will be further advancements in these modalities, each possesses distinct clinical and commercial limitations due to known safety, efficacy, therapeutic delivery and manufacturing scale challenges.

Current and emerging genetic medicines and their limitations

Viral gene therapy

Viral gene therapy, in which viral vectors are employed to deliver therapeutic genes to defective cells or tissues, has made significant progress in the past decade. The most advanced system for systemic administration is AAV gene therapy, which has demonstrated durable transduction of cells in several organ systems, with long-lasting expression in non-dividing cells. Several AAV gene therapy products have been approved, including LUXTURNA (voretigene neparvovec-rzyl) for the treatment of the rare inherited blindness disorder biallelic RPE65 mutation-associated retinal dystrophy and ZOLGENSMA (onasemnogene abeparvovec-xioi) for spinal muscular atrophy, or SMA.

However, current AAV gene therapy has demonstrated limitations, including:

- *Single dose administration only*: Following a single dose of AAV, antibodies are induced against the AAV capsid, the protein shell of the virus used for delivery. Because of these antibodies, AAV can only be dosed once, and it is typically dosed at the upper end of its therapeutic index to maximize potential efficacy across all treated patients.
    - *Variable expression*: Administration of a single fixed dose to all patients prevents repeat dosing to adjust the expression level in each patient, called titration, and leads to variable levels of expression, with many patients expressing the therapeutic protein above or below target levels.
    - *Inefficient clinical development*: Because patients cannot be redosed, those who do not achieve a therapeutic effect in early clinical trials cannot benefit from AAV therapy or contribute to further clinical development.
    - *Inability to extend expression*: The antibodies formed following a single dose of AAV prevent re-treatment to increase or extend efficacy for patients with inadequate initial response or declining levels of expression.
    - *Exclusion of pediatric patients*: The inability to redose precludes treatment of pediatric patients, whose organ growth and dividing cells would dilute expression over time.
- *Pre-existing immunity*: Up to half of patients have antibodies against AAV due to naturally acquired infections. These antibodies prevent them from receiving AAV gene therapy due to pre-existing AAV immunity to the capsid.
- *Payload capacity*: AAV constructs are limited to 4.7 kb in length, restricting both the size of genes and complexity of regulatory sequences that can be delivered. This restricts the diseases that can be addressed to those requiring single genes that can fit within this limited capacity and prevents the use of native regulatory sequences that may respond to the body’s own signals.
- *Off-target, multi-tissue delivery*: Due to the inherent features of AAV, off-target delivery to unintended tissues and cell-types can lead to adverse events.
- *Quality control*: A lack of process and analytic control over the composition of AAV vectors leads to batch-to-batch variation in potency and potentially contributes to inconsistency in patients’ responses.
- *Manufacturing scale*: The production systems for AAV gene therapies are limited in scale to 2,000 liters per batch or less. In general, the high doses required by AAV gene therapies and the low productivity of these systems combine to limit treatment to rare disease populations at a higher cost relative to other treatment modalities.

- *Payer coverage*: The relatively high cost of AAV gene therapies, combined with uncertain clinical durability and the inability to redose to extend expression, make it challenging for payers to predict clinical outcomes and, as a result, payers may be less inclined to pay for AAV gene therapies within the current reimbursement paradigm.

Gene editing

Gene editing is the process of deleting, modifying or replacing defective DNA directly in the native genomic location. Zinc finger nuclease, TALEN and CRISPR-based gene editing are the most advanced approaches to gene editing and are currently in early clinical trials. CRISPR uses a combination of a nuclease to make a double-stranded break in the DNA and a guide RNA to direct the nuclease to the correct location for editing. Given insertion of full-length genes into the chromosome has remained relatively inefficient for gene editing, particularly *in vivo*, these approaches have primarily focused on *ex vivo* therapeutic applications.

Moreover, viral vectors are used widely to deliver gene editing nucleases *in vivo*, thereby conveying many of the same clinical and commercial challenges as viral gene therapy. Additional limitations for gene editing include the potential for unwanted DNA modifications related to double-stranded DNA breaks, the inability to control the level and duration of protein expression and low efficiency of precise gene correction.

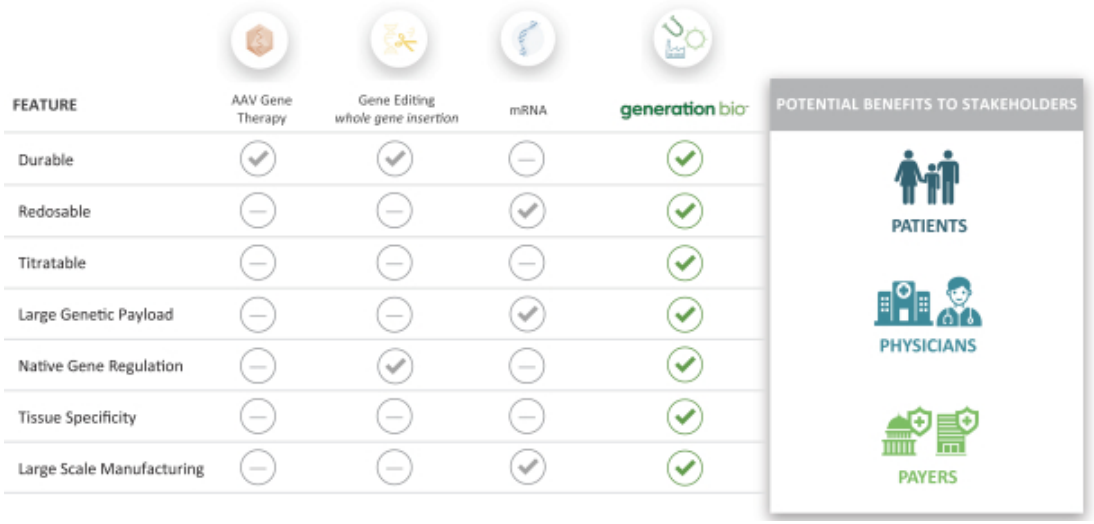
Messenger RNA therapies

Messenger RNA therapies are designed to increase mRNA levels by exogenous delivery of modified mRNA. However, the use of modified mRNA is limited by a lack of durable expression due to the half-life, or stability profile, of an mRNA transcript in the cell, which is approximately 10 hours. Due to the lack of durable expression for mRNA and the resulting requirement of frequent dosing, clinical development of mRNA therapies has focused primarily on novel vaccines. The safety of this frequent repeat dosing has yet to be proven clinically. In addition, the standard LNP approaches used for mRNA do not enable precise targeting of tissues.

Summary of limitations of current approaches

The advancements in gene therapy have demonstrated the potential of these modalities to replace full genes and the aggregate market capitalization of publicly traded gene therapy companies in the United States exceeds $50 billion. However, as illustrated in the figure below, the current approaches also have important limitations. While the development of our non-viral gene therapy platform is still in the early stage and we have not yet identified a product candidate, and thus contrasts with other approaches may not be a direct comparison, we have designed our platform to overcome the limitations of these gene therapy approaches.

Comparison of genetic medicine approaches



Advantages of our non-viral gene therapy platform

Our non-viral gene therapy platform, comprised of our ceDNA construct, our ctLNP delivery system and our established, scalable capsid-free manufacturing process, is designed to overcome the limitations of current gene therapy approaches and we believe will disrupt the field of genetic medicine. We believe that our platform may provide the following advantages:

- *Durable expression*: Our ceDNA is highly stable and establishes extra-chromosomal episomes in the nucleus of cells to drive durable expression of the gene of interest. This durability has the potential to enable years-long expression for patients with each dose, minimizing the treatment burden for patients.
- *Redosable administration*: Our ctLNP system has been designed to avoid stimulating an antibody response in patients, thereby enabling redosing. The ability to redose provides several advantages:
    - *Individualized patient titration to reach desired expression level*: We expect our gene therapies will enable individualized patient titration, allowing each patient to be redosed until they reach the expression level required to address their specific needs. Patients and physicians may achieve individual therapeutic goals in a predictable manner.
    - *Greater opportunity to demonstrate efficacy in first-in-human trials*: Because we may be able to redose, we expect that a greater proportion of patients participating in our early clinical trials may achieve the desired level of gene expression.

  - *Extending expression*: If expression of the gene of interest begins to wane for an individual patient, we expect that redosing could restore effective expression levels, prolonging the benefits of our therapies throughout the patient's life.
  - *Reach pediatric patients*: Rapidly waning expression due to organ growth and dividing cells in children limits the utility of a single administration of gene therapy. We expect that the properties of our therapies may allow us to initiate treatment in childhood and allow the patient to prolong the benefits thereafter. Early intervention near the onset of disease may enable a greater therapeutic benefit throughout the patient's life.
- *Address untreated or under-treated patients*: Our therapies may be used to treat patients with pre-existing immunity to the AAV viral capsid, and therefore, not able to receive AAV gene therapy treatments, as well as patients whose efficacy outcomes on current gene therapy were insufficient in level or duration of expression.
- *Delivery of large genetic payloads*: The large payload capacity of ceDNA enables our constructs to carry large genes, multiple genes or combinations of genes with regulatory elements. This capacity arises from the lack of capsid packaging constraints that limit DNA incorporation in AAV gene therapy to less than 4.7 kb. Our established, scalable manufacturing process routinely prepares constructs of up to 12 kb without loss in yield or quality. We have not identified an upper limit of construct length.
  - *More potent constructs*: Our ceDNA constructs have the potential to improve upon existing gene therapy modalities by utilizing novel expression elements that exceed the capacity of AAV gene therapy.
  - *Larger genes*: Our ceDNA constructs may enable treatment of monogenic diseases requiring larger genes that are not possible to deliver with current gene therapy.
  - *Multiple genes*: Our ceDNA constructs have the potential to include novel multi-gene constructs to produce complex biologics such as monoclonal antibodies, or to address conditions that need more than one type of genetic correction.
  - *Native gene regulation*: The large capacity of our constructs provides us the ability to incorporate native regulatory elements that are naturally associated with the gene we are replacing. We believe this will allow for activity of the replaced gene to increase or decrease in response to the body's own signals.
- *Targeted, multi-tissue delivery*: Our ctLNP delivery system has been engineered to use biological ligands to reach receptors in a specific tissue. We believe that highly specific targeting to the key cell type for therapeutic benefit with limited delivery to off-target cells will improve the safety profile of our products.
- *Expected scale to reach millions of patients*: The combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases.
- *Sustainable payer model*: Our cost-effective manufacturing process combined with the potential to redose patients to extend expression may allow payers to better predict clinical outcomes and, as a result, to cover our therapies within the current reimbursement paradigm.

We believe that our new class of gene therapy has the potential to reach previously untreatable or under-treated patients and address new indications, including those with large patient populations, thereby unlocking the full potential of genetic medicine.

Our strategy

Our goal is to become an industry leader in the field of genetic medicine, advancing our non-viral gene therapy platform to discover, develop, manufacture and globally commercialize a new class of gene therapy that is durable, redosable and specifically delivered to a range of tissues for the treatment of diseases caused by single, large or multiple gene defects. We aim to provide sustainable, life-long treatment for millions of patients living with rare and prevalent diseases.

Key components of our strategy include:

- ***Establish ceDNA as a new class of gene therapy, initially demonstrating its potential across rare monogenic diseases of the liver and retina.*** We are prioritizing rare monogenic diseases of the liver and retina with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches, beginning with PKU, hemophilia A, LCA10 and Stargardt disease. We believe our initial focus on these rare indications, which have well-established biomarkers and clear clinical and regulatory pathways, may enable us to achieve rapid human proof of concept, regulatory approval and eventually, commercialization. We expect to submit our first IND applications beginning in 2022.
- ***Leverage our non-viral gene therapy platform to advance additional programs for diseases of the liver and retina and to expand quickly into additional tissues.*** We are advancing additional programs for the liver and retina by making minimal changes to our ceDNA construct and by using the same ctLNP delivery system for each tissue. We believe this process can reduce the risk and accelerate the speed of development for subsequent indications in these tissues. We also plan to apply this approach as we develop biological ligands for our ctLNP delivery system to reach skeletal muscle, the CNS and tumors.
- ***Utilize our eight-week research cycle to rapidly design, produce and screen ceDNA constructs to enable new disease programs within a tissue or therapeutic area.*** We have established a highly efficient eight-week research cycle to rapidly design, produce and screen ceDNA constructs to enable new disease programs within a therapeutic area once human proof of concept is established in that area. We intend to invest in technologies to further accelerate our research cycle and create additional efficiency and scope for this process.
- ***Expand manufacturing scale to access previously unattainable markets for gene therapy.*** We have established a capsid-free manufacturing process for ceDNA that is scalable, cost-effective and yields a high-quality product using standard biological production equipment and engineering methods. We intend to further develop our internal manufacturing capabilities and to continue to expand our high-quality network of suppliers to increase capacity. We believe that our ability to conduct our manufacturing process at the 200-liter scale with high product quality suggests that further scaling to thousands of liters per batch is feasible using standard biological production equipment and engineering methods. We believe the combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases.
- ***Expand patient access to our non-viral gene therapies through a high-value network of alliances and collaborations.*** We are developing a broad and expandable portfolio of gene therapies that have the distinct opportunity to address rare monogenic diseases, as well as prevalent diseases. To help us realize the full breadth of opportunities and to expedite patient access to our gene therapies, we have established and plan to continue to explore a limited set of innovative collaborations and strategic alliances with biopharmaceutical companies whose capabilities and resources are additive or complementary to our own.
- ***Build a sustainable leadership position in non-viral gene therapy as a fully integrated innovative biotechnology company.*** We have established a leading position in non-viral gene therapy for gene transfer

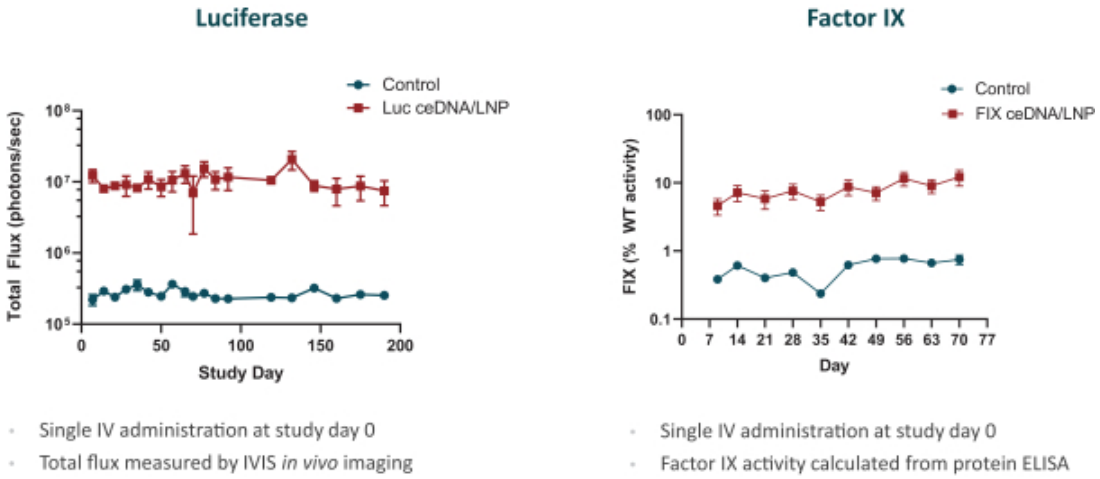
by investing in our ceDNA, ctLNP and manufacturing technologies and capabilities, and by rigorously protecting our innovations through an expanding intellectual property portfolio. We intend to evaluate and invest in new technologies that may further de-risk and accelerate the development of our new class of gene therapy, and to build out our capabilities to commercialize our gene therapies on our own.

Our non-viral gene therapy platform

Our non-viral gene therapy platform is comprised of three essential components: our high-capacity ceDNA construct, which can accommodate large or multiple genes as well as native regulatory elements; our ctLNP delivery system, which enables highly specific delivery of ceDNA to a range of tissues; and our established, scalable capsid-free manufacturing process, which uses a cost-effective biologics infrastructure that has the potential to reach patients with rare diseases and to expand access to patients with prevalent diseases, requiring millions of doses on a sustainable basis.

The three components of our platform are designed to enable critical features that address key limitations of existing genetic medicines. The ceDNA construct is designed to enable durable expression with a single dose. As shown in the figures below, in immunocompetent mice, a single intravenous dose of ceDNA formulated in an LNP provided months-long expression in the liver using both the reporter protein luciferase (denoted in the left figure below as Luc ceDNA/LNP) and human Factor IX, or FIX, the protein that is missing or defective in hemophilia B (denoted in the right figure below as FIX ceDNA/LNP).

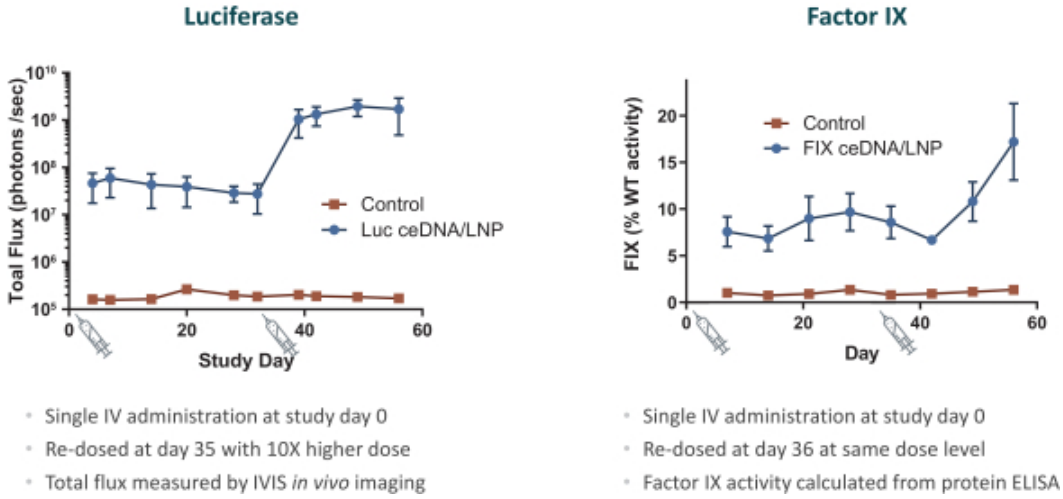
ceDNA-LNP: durable expression in immunocompetent mice after single IV administration



As shown in the figure below, ceDNA delivered in an LNP could be redosed in mice with normal immune systems because the first dose did not induce neutralizing antibodies. As the figure demonstrates, in immunocompetent mice, redosing ceDNA formulated in an LNP achieved increased expression using both reporter protein luciferase (denoted in the left figure below as Luc ceDNA/LNP) and human FIX (denoted in the right figure below as FIX ceDNA/LNP). In both studies, we intravenously administered ceDNA formulated in an LNP and then repeated the administration five weeks later. After the first administration of Luc ceDNA/LNP, mice demonstrated stable expression of luciferase protein and then higher, stable expression after repeat administration. After the first administration of FIX ceDNA/LNP, mice demonstrated 5-10% activity levels of FIX

protein in the blood and then 10-20% activity after repeat administration. These results support our belief that our platform may enable us to titrate every patient to the desired level of protein expression.

ceDNA-LNP: redosing achieves increased expression in immunocompetent mice



As shown in the figure below, our upstream manufacturing process is comparable to biologics manufacturing and includes accumulation of ceDNA in Sf9 cells, which are then lysed to harvest ceDNA. The downstream process includes high-capacity purification of ceDNA drug substance, followed by ctLNP formulation. We have successfully completed ceDNA drug substance and purification runs of one liter, 50 liters and 200 liters, with a consistent processing time in the manufacturing plant of three weeks per run. With the process and controls we have developed, we achieve greater than 99% purity ceDNA following the downstream purification process, and have consistently demonstrated this up to the 200-liter scale.

Overview of our capsid-free manufacturing process

Closed-ended DNA (ceDNA) construct

ceDNA was discovered by our scientific co-founder Robert Kotin, who during his two decades as a senior investigator at the National Institutes of Health also invented the Sf9 AAV production system and discovered

the insertion site for AAV on chromosome 19. We have continued to build upon Dr. Kotin's work by assembling an expert team of leaders in molecular biology in order to deepen our understanding of ceDNA biology. In addition, we are expanding on Dr. Kotin's early work to create a broad palette of structural and sequence motifs for ceDNA constructs to explore novel mechanisms and to address multiple diseases. We are also deepening our expertise in computational biology, virology and cell biology to exploit the potential of large genomic datasets to elucidate the mechanisms underlying large subsets of prevalent and complex diseases.

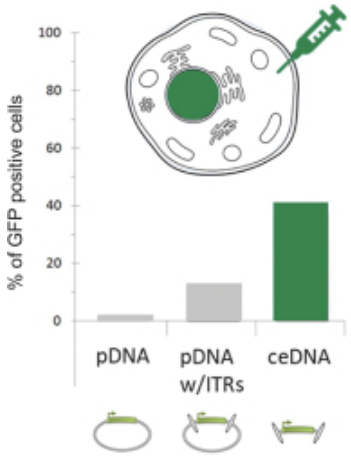
ceDNA is an engineered, double-stranded, linear, covalently closed-ended DNA construct, with no free ends or viral capsid. As shown in the figure below, ceDNA includes the target gene or genes of interest, along with key components of the expression cassette, which is the full genetic sequence necessary to derive transcription including spacers, promoters and untranslated regions flanked by two inverted terminal repeat, or ITR, sequences. By gene of interest, we specifically mean the transcribed region of the target gene. ITRs, which are also present in AAV technology, are thought to be critical for durable expression in the nucleus of cells. To date, we have designed, produced and purified ceDNA constructs of up to 12 kb and have not identified an upper limit of construct length.

ceDNA structure

Nuclear entry

In an AAV system, it is thought that the capsid mediates nuclear entry. For our capsid-free non-viral gene therapy, we believe our ceDNA accesses the nucleus due to a previously unrecognized function of the ITR structure. In an *in vitro* study, we injected plasmid lacking ITR sequences, plasmid containing ITR sequences and ceDNA into the cytoplasm of individual cells. As shown in the figure below, the plasmid lacking ITR sequences was not able to access the nucleus, and the plasmid containing ITR sequences resulted in low but measurable expression. By contrast, ceDNA displayed positive green fluorescent protein, or GFP, expression, indicating that the ceDNA had effectively translocated to the nucleus.

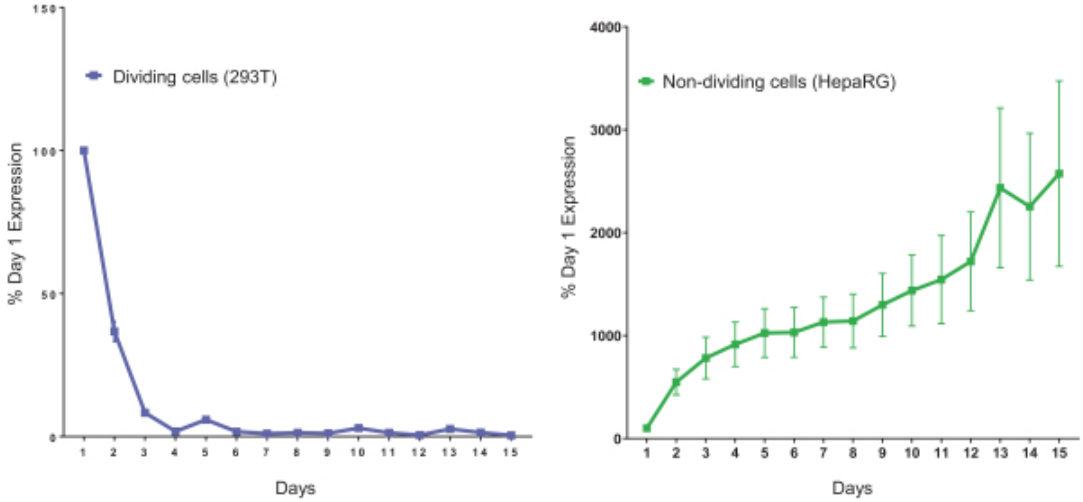
ceDNA's ITR structure drives translocation to the nucleus



Episomal expression

ceDNA-derived expression has been observed in *in vivo* and *in vitro* studies to be episomal, meaning that it can deliver genetic material outside of the chromosome without being directly incorporated into or altering the cell's genome. This characteristic of ceDNA is a potentially important safety feature of our redosable gene therapy platform. In cell culture studies, as depicted in the figure below, the expression in dividing cells transfected with ceDNA encoding GFP decayed rapidly as the cells divided, consistent with lack of genomic integration as each successive cell division effectively diluted the amount of ceDNA in new generations of cells. In contrast, in cells transfected with ceDNA encoding GFP which are post-mitotic and therefore not dividing, we observed sustained and durable GFP expression over the course of two weeks.

ceDNA-derived GFP expression observed to be episomal



ceDNA capacity

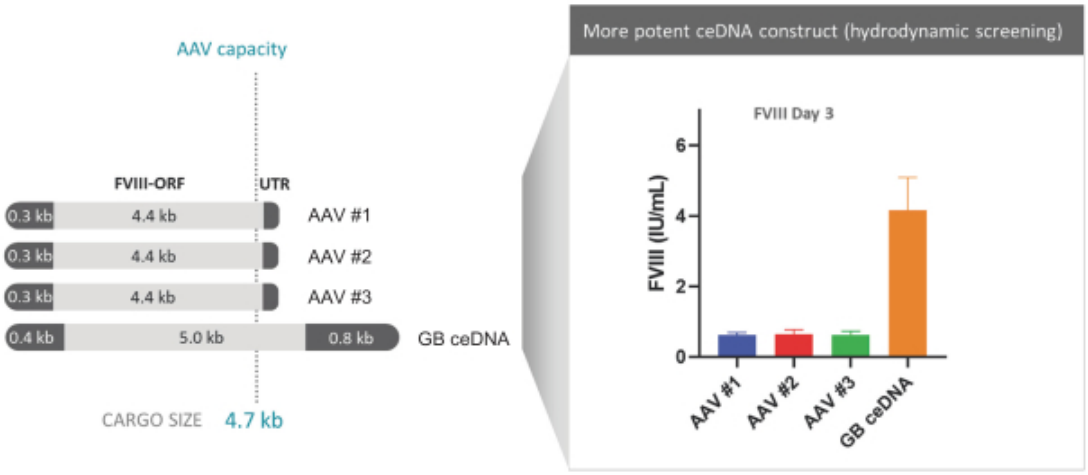
The large payload capacity of ceDNA enables our constructs to carry large genes, multiple genes, or combinations of genes with regulatory elements. This capacity arises from the lack of capsid packaging constraints that limit DNA incorporation in AAV gene therapy to less than 4.7 kb. Our established, scalable manufacturing process routinely prepares constructs of up to 12 kb in length without loss in yield or quality. We have not identified an upper limit of construct length. We believe ceDNA can deliver a significant majority of the human coding sequences known to be relevant for the treatment of diseases that result from mutations in a single gene or in multiple genes. The practical applications of increased capacity include the ability:

- to improve expression of existing targets of viral gene therapy and mRNA;
- to incorporate genes too large to be packaged in viral vectors;
- to include multiple genes, or to produce more than one transcript, which opens the possibility of creating several therapeutic molecules per ceDNA to address conditions that need more than one type of genetic correction; and
- to add native regulatory elements that are naturally associated with the gene we are replacing, which may allow for activity of the replaced gene to increase or decrease in response to the body's own signals.

We have observed the impact of the increased payload capacity of our constructs on improved expression efficiency in *in vitro* and *in vivo* studies. We undertook studies of Factor VIII, a protein involved in the coagulation cascade. Defects in Factor VIII are known to give rise to hemophilia A. Factor VIII is a large protein having a minimal gene of interest domain accounting for 4.4 kb (in the B-domain deleted format) which is almost the entire AAV capsid capacity. For this reason, AAV Factor VIII constructs currently in clinical development contain the minimal, B-domain deleted coding region along with a small core promoter of 0.3 kb and limited transcriptional enhancer regions.

We have designed ceDNA constructs that have larger promoter elements and more substantial transcriptional enhancer regions than can be accommodated within the payload capacity of AAV. We have observed in a mouse model that a ceDNA construct, labeled as GB ceDNA in the figure below, showed six-fold improved expression of Factor VIII relative to ceDNA constructs with the expression cassette of each of three AAV Factor VIII product candidates currently in clinical development. The identification of constructs with improved potency may enable us to lower the dose required to achieve therapeutic efficacy.

Increased ceDNA payload capacity enables the design of more potent constructs



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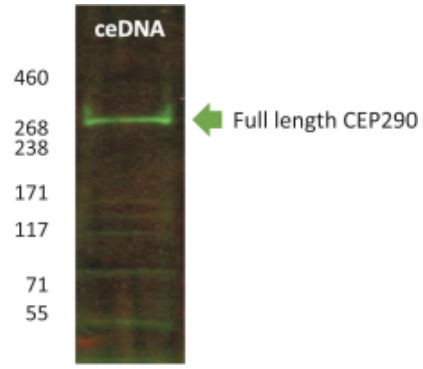
In addition to improving the activity of typical AAV target genes like Factor VIII, the capacity of ceDNA allows us to address monogenic diseases caused by large genes whose coding region is outside of the packaging capacity of AAV. One such example is LCA10, the most common genetic cause of childhood vision loss. LCA10 is caused by mutations in the CEP290 gene, which has a gene of interest region of 7.4 kb. Since this exceeds the payload capacity of AAV, there are no current transfer-based gene therapy programs in clinical trials for LCA10. By replacing the entire gene, gene therapy can potentially restore vision to patients with all forms of LCA10, irrespective of which mutation is present. We have created a ceDNA construct encoding the CEP290 gene that has demonstrated expression of full-length protein after transfection in cells, as shown in the immunoblot below.

Expression of full length CEP290 *in vitro*



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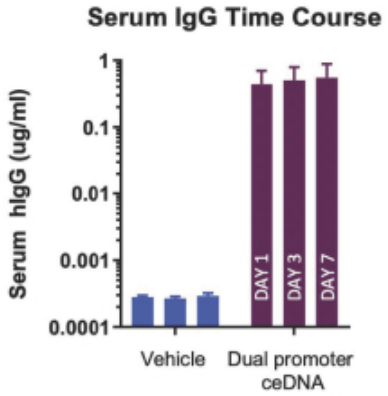
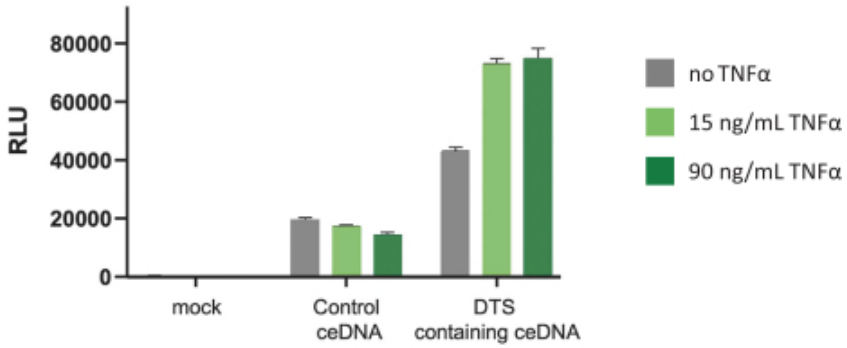
In *in vivo* studies, we have encoded and expressed two different proteins independently within the same ceDNA construct. To do this, we created a ceDNA that independently expressed heavy and light chain fragments of the antibody immunoglobulin, or IgG, with unique promoters for each, a requirement for producing distinct and separate proteins off one construct. Each promoter, a unique sequence that defines where DNA transcription starts, governs the independent production of its own transcript. This construct was able to produce fully formed and secreted IgG *in vivo,* as shown in the figure below. This ability to include novel multi-gene constructs to produce complex biologics, such as monoclonal antibodies, also opens the potential to address conditions that need more than one type of genetic correction, such as one that could knock down a gene and another that replaces a missing or defective gene.

ceDNA dual promoter construct produced fully formed and secreted IgG *in vivo*



We have also shown in *in vitro* studies that our constructs can establish context-dependent expression by inclusion of regulatory sequences. The inclusion of regulatory sequences may enable expression of the therapeutic protein to adjust in response to changes in the patient's body, an example of which might be an anti-inflammatory antibody that is only expressed when the patient is in an inflammatory state. For these studies, we created a construct that contained multiple simian virus 40, or SV40, -derived nuclear factor kappa-light-chain-enhancer of activated B cells, or NFkb, and DNA-targeting sequences, or DTS, that are known to be responsive to tumor necrosis factor alpha, or TNFa. As shown in the figure below, expression in HepG2 cells, as measured in reflected light units, or RLUs, was significantly increased in the presence of TNFa relative to control.

Regulatory elements increased expression with TNFa stimulus



We believe this finding supports the potential to develop context-dependent expression cassettes and to take advantage of the sequence capacity necessary to accomplish this. Another example of such an application would be the inclusion of the native promoter in a construct expressing ABCB4 for progressive familial intrahepatic cholestasis type III where the native promoter is approximately 3.0 kb in size, which restricts its application in viral gene therapy. We have prepared this ceDNA and demonstrated that it expresses protein in cell culture.

Our research and development of ceDNA has dramatically increased our understanding of the construct's properties, capabilities and *in vivo* functioning. We have filed numerous patent applications on our innovations in ceDNA structure, applications of the technology and specific classes of therapeutic ceDNA. We intend to continue investing in both ceDNA development and its intellectual property protection.

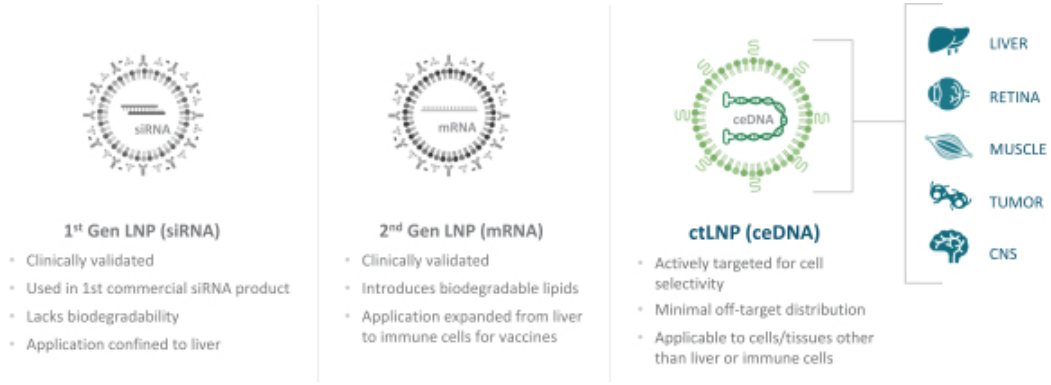
Cell-targeted LNP (ctLNP) delivery system

Lipid nanoparticle technology has been developed over the past two decades for the effective delivery of nucleic acids to the liver, culminating in the first approved small interfering RNA, or siRNA, therapy for the treatment of transthyretin amyloidosis. Second-generation LNP technologies incorporate novel lipid components that improve potency, increase tolerability and are biodegradable. A second-generation LNP was recently clinically validated in a Phase 1 study of a passive immunization approach to Chikungunya virus.

Our Chief Scientific Officer Matthew Stanton has been a leader in LNP technology for the past 12 years. Prior to joining us, he led nucleic acid delivery research at Merck and Co., Inc. and Moderna, Inc., resulting in the discovery and development of four distinct classes of second-generation LNPs currently in clinical development. We have hired a team of chemists and formulation scientists along with cellular biologists and pharmacologists to continue to advance our LNP technology and expertise.

Building on the attributes of both the first- and second-generation LNP technology, we have designed our ctLNP delivery platform so that its biodistribution can be selectively controlled through the addition of a targeting molecule, or ligand. In addition, our ctLNP may confer the advantages of predictable behavior across species, minimal off-target effects, and a foundational platform approach that unlocks the ability to delivery to other tissues, including retina, skeletal muscle, the CNS and tumors. The graphic below illustrates the evolution from first generation LNPs to ctLNP.

Novel ctLNP enables biologically-driven cell and tissue targeting



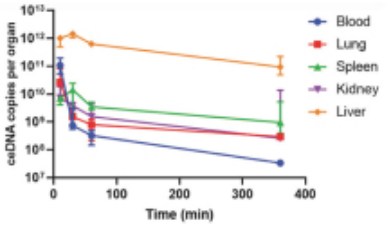
A key feature of our ctLNP technology is the use of biological targeting ligands. This is a strategy that is shared with antibody-drug conjugates and with oligonucleotide conjugates, both of which have demonstrated clinical success. The application of targeting ligand technology has historically been unavailable to nanoparticles. This is primarily due to the non-specific and efficient uptake of nanoparticles by cells of the reticuloendothelial system, or RES, a system of cells that removes immune complexes and foreign particulates from circulation in healthy persons, and historically overwhelms the effectiveness of the targeting ligand. We have applied our chemistry and formulation capabilities to identify LNPs that avoid RES-mediated clearance, which has enabled the use of biological targeting ligands. We have achieved proof of concept for tissue-specific delivery with ctLNP *in vivo* for liver and retina and *in vitro* for skeletal muscle.

Liver

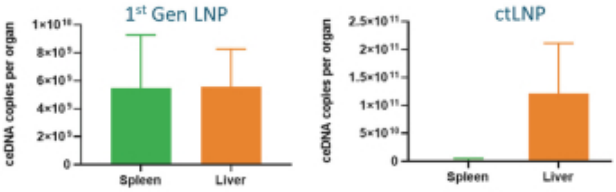
We have employed N-acetyl galactosamine, or GalNAc, as the ligand of choice for targeting the majority of liver cells, called hepatocytes, specifically in the liver through the asialoglycoprotein receptor, or ASGPr, a well validated, selective ligand-receptor pair for delivery to hepatocytes that is conserved across species including mouse, rat, non-human primates and humans. Prior third-party research has shown that the pharmacology of the ASGPr receptor in non-human primates is strongly correlated with the pharmacology of the ASGPr receptor in humans. GalNAc targeted oligonucleotides have also demonstrated broad distribution to all hepatocytes. When we dosed GalNAc targeted ctLNPs in mice, we observed a profound selectivity for ceDNA delivery to the liver. As shown in the left figure below, ceDNA was distributed selectively to the liver, with more than 97% of the total ceDNA copies in that tissue. By contrast, less than 3% of the copies per tissue was present in blood, lung, spleen and kidney combined. This stands in contrast to first generation LNPs, as shown in the middle and right figures below. At six hours post administration, first generation LNPs distribute equal ceDNA copies in spleen relative to liver. In contrast, distribution of ceDNA with ctLNP is highly selective for liver at this time point. This selectivity enhancement of ctLNP relative to first-generation LNP minimized off-target effects and enabled well-tolerated dosing up to 5.0 mg/kg in mice. When we examined the liver tissue by *in situ* hybridization, we observed up to

100% of hepatocytes transduced with ceDNA at early time points, highlighting the breadth of distribution of ctLNP. Additionally, we have demonstrated the successful dosing of a ctLNP in preliminary non-human primate experiments at doses up to 0.5 mg/kg. The 0.5 mg/kg ctLNP dose level was tolerated and not associated with signs of hepatotoxicity.

ctLNP Longitudinal PK in mice

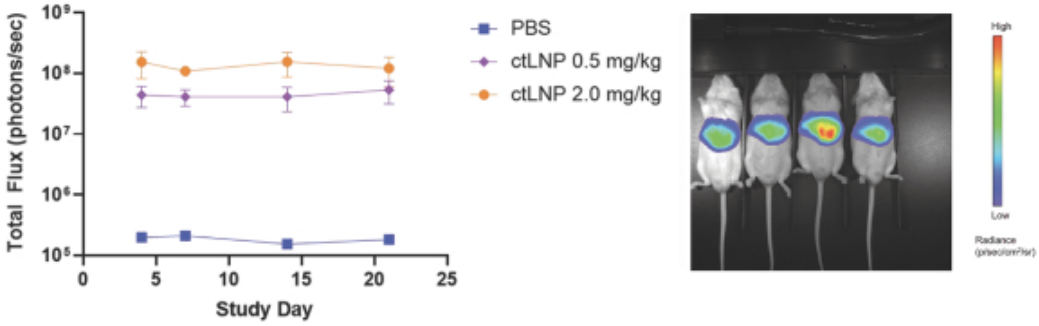


Biodistribution by tissue at 6hr for 1st Gen LNP



We have demonstrated in mice both high-level and dose-dependent expression from ceDNA incorporating our ctLNP system using a reporter ceDNA that expresses firefly luciferase after a single intravenous administration on day one. The expression was also determined to be dose proportional as we increased the ctLNP from 0.5 mg/kg to 2.0 mg/kg, as shown in the left figure below. The protein expression was specific to the liver region as determined by in-life imaging, as shown in the right figure below. We continue to apply chemistry and formulation optimization efforts to improve the activity of ctLNP, with our latest ctLNPs providing three to five times improvements in expression over our first iteration. We plan to continue to make further improvements in this technology.

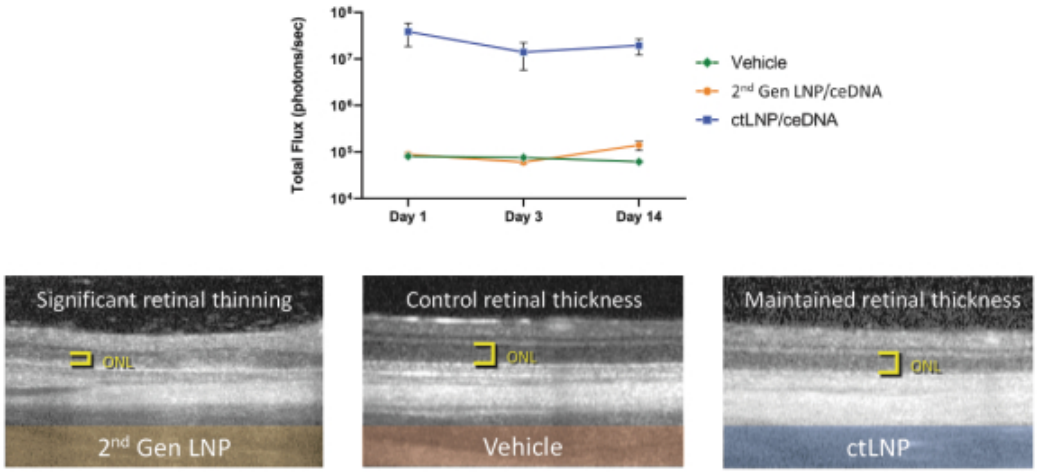
High-level and dose-dependent luciferase expression from ceDNA-ctLNP



Retina

In addition to assessing the specificity and activity of ctLNP established for systemic administration to the liver, we have also assessed ctLNP in local administration to the retina in the eye. Second-generation LNPs containing ceDNA, when dosed subretinally *in vivo* in rats, led to significant inflammation and retinal degeneration and failed to express protein. This degeneration is evident by measuring the thickness of the outer nuclear layer, or ONL, by optical coherence tomography imaging, shown in the yellow labels in the figures below. By contrast, administration of ctLNP subretinally *in vivo* in rats led to high levels of expression and lack of retinal degeneration at day 21. We believe this improved retinal tolerability profile is due to ctLNP avoiding off-target delivery to local immune cells. We have additionally demonstrated efficient transduction of retinal photoreceptor and retinal pigment epithelial, or RPE, cells with ctLNP, which we believe enables disease relevant expression for our lead retinal programs, LCA10 and Stargardt disease.

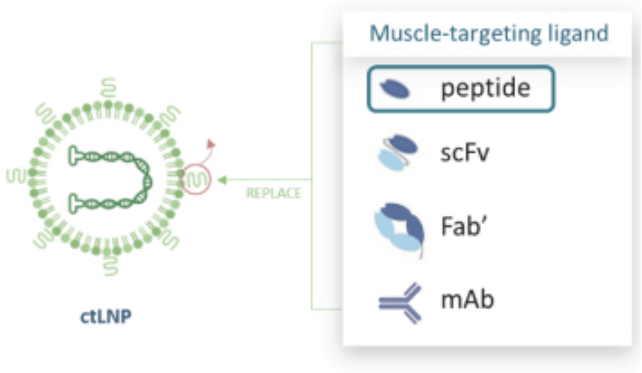
Subretinal injection of ceDNA-ctLNP led to high levels of expression and lack of retinal degeneration



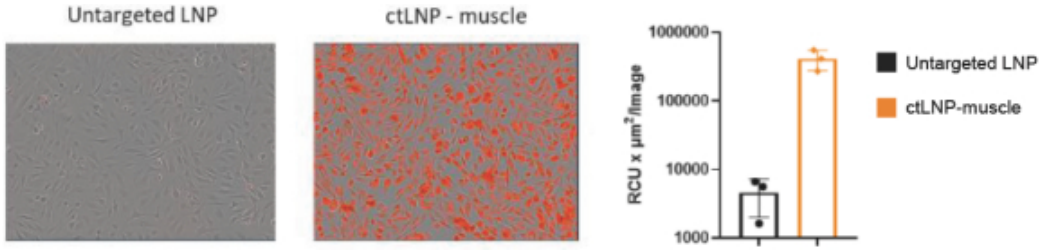
Skeletal muscle

We have identified a number of potential ligands for skeletal muscle and have been able to conjugate peptide-based ligands to ctLNP that have enhanced uptake into a differentiated skeletal muscle cell line, or myocyte, *in vitro*. These peptide-based ligands target known receptors, such as the transferrin receptor that is present on the surface of skeletal muscle. ctLNPs that include these peptide-based ligands on the surface of the particle show high levels of uptake in muscle cells in culture. We have observed this in *in vitro* studies in which we included a red dye in the ctLNP enabling quantification of uptake into these cells, as shown in the figure below. We are pursuing muscle-targeted ctLNPs for *in vivo*, systemic administration to target skeletal muscle and replace missing or defective genes, such as dystrophin in Duchenne Muscular Dystrophy.

ctLNP targeting skeletal muscle using peptide ligand



Enhanced uptake in c2c12 myocytes



LNPs are one of the most advanced non-viral delivery solutions for nucleic acid therapeutics. We have built on the attributes of the second generation of clinical LNPs, which include improved tolerability through utilization of biodegradable lipids. Specifically, we have engineered our ctLNP to allow for active targeting of specific cell types *in vivo*. Targeted delivery of DNA *in vivo* without incurring innate immune reactions has long been a challenge in the field. The profile of our ctLNP has led to further improvements in tolerability, increased delivery efficiency and application to tissues beyond liver and immune cells. Our ctLNP delivery system has shown proof of concept *in vivo* in liver and retina with *in vitro* proof of concept for skeletal muscle. We plan to continue to seek to optimize ctLNP for use in liver, retina and skeletal muscle and to expand its application across a range of tissues, including the CNS and tumors. We have filed numerous patent applications to solidify our leadership in this area, including ones covering fundamental LNP technology as well as methods to avoid or reduce immune response.

Established, scalable manufacturing

Since our founding, we have invested in internalizing core development capabilities to build our manufacturing processes and analytical testing as a point of strength. Our co-founder and Chief Operating Offer, Mark Angelino, has led successful development and manufacturing organizations across several novel modalities, including complex biologics, oligonucleotide and viral gene therapy for the past 15 years. He has recruited a seasoned team of development and manufacturing experts who have enabled more than 20 INDs and negotiated multiple product launches, including for both a cell and a gene therapy product.

In addition to this accumulated experience, we have built state-of-the-art development laboratories to create novel upstream and downstream processes as well as analytical methodologies that have shifted the product profile from early research efforts of approximately 10% pure ceDNA to one that is consistently greater than 99% pure ceDNA. Our current internal development efforts are focused on industrialization of the process to enable unit operations that are scalable using standard biological production equipment.

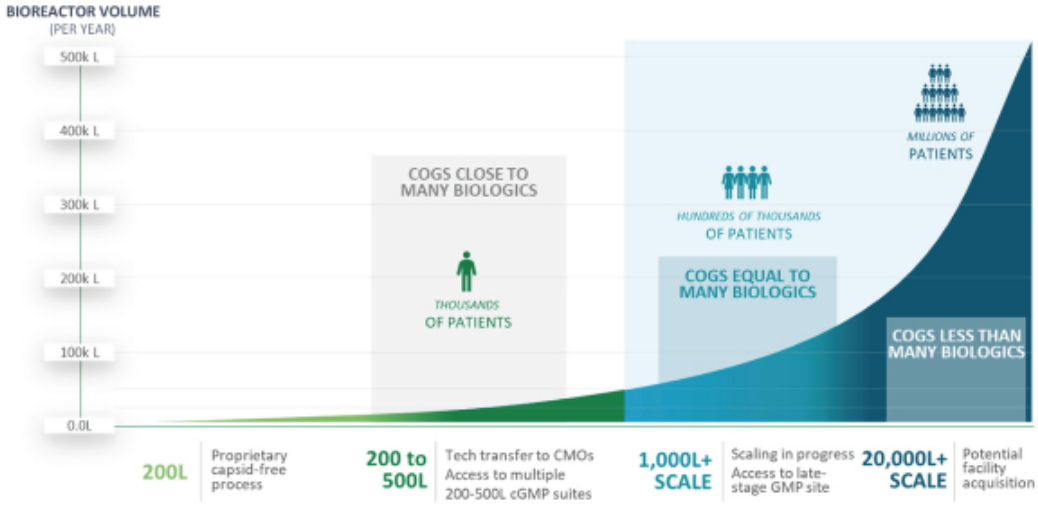
Our established, scalable manufacturing employs a proprietary, capsid-free process and utilizes standard biologics infrastructure, unlike traditional viral gene therapy manufacturing. Viral gene therapy relies on a protein capsid for therapeutic delivery of a viral vector, and as a result, the manufacturing process for viral gene therapies requires the production of protein capsids, which limit process scalability and consistency. Our capsid-free manufacturing process is an efficient and reproducible process that includes rigorous, industrial-scale purification that consistently yields greater than 99% pure ceDNA.

We have completed ceDNA drug substance and purification runs of one liter, 50 liters and 200 liters, with a consistent processing time in the manufacturing plant of three weeks per run, and greater than 99% purity ceDNA following the downstream purification process.

We produce material at 50-liter scale internally to support research studies, and our CDMOs have produced material at 200-liter scale, using our cGMP-ready process, to supply IND-enabling preclinical studies and early clinical trials. Additional development efforts have been initiated to further scale the process to thousands of liters.

The scalability and productivity of the manufacturing process is a significant driver of the cost-effectiveness of any therapeutic. We believe being able to produce ceDNA at a scale of thousands of liters per batch should enable a significant reduction in our overall cost of goods, and our goal over time is to be competitive with traditional biologics in scale and cost. We believe that our ability to conduct our manufacturing process at the 200-liter scale with high product quality suggests that further scaling to thousands of liters is feasible using standard biological production equipment and engineering methods.

Significant cost and scale advantage, eventually comparable to biologics



Our ongoing work in manufacturing technology has led to numerous innovations in production processes and analytics, some of which may have broader applications in related fields. We continue to seek to protect the full reach of these discoveries through both patent application filings and as trade secrets.

Summary

We believe our non-viral gene therapy platform represents a powerful product engine fueled by ceDNA, which in preclinical studies has provided durable episomal expression with large capacity, and our highly selective and modular ctLNP delivery system. We have designed the combination of these platform components with a goal of enabling a broad and expandable product portfolio that can be deployed against a range of tissues, including liver, retina, skeletal muscle, the CNS and tumors. These characteristics are supported by our established, scalable capsid-free manufacturing process, which supports the potential to extend the reach of gene therapy beyond rare diseases to prevalent diseases.

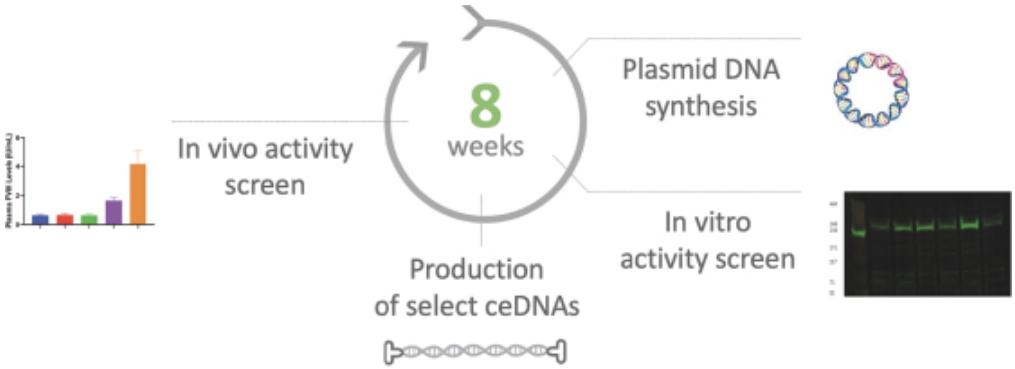
Our integrated research and development approach

Our development strategy is differentiated and informed by our extensive experience in rare disease drug development, regulatory engagement and commercialization. We are focused on diseases with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches. We are initially prioritizing rare monogenic diseases of the liver and retina that have well-established biomarkers and clear clinical and regulatory pathways. We plan to incorporate redosing in our first-in-human clinical trials, which may allow us to reach the desired therapeutic expression level in every patient, providing early and robust human proof concept.

In parallel, we are developing the constructs and manufacturing capacity for programs to address additional rare and prevalent diseases. We have established a highly efficient eight-week research cycle to rapidly design, produce and screen ceDNA constructs to enable new disease programs within a tissue once human proof of concept is established. By leveraging a common ctLNP for each tissue, we believe we can reduce the risk and accelerate the speed of development for subsequent indications.

Our research cycle, illustrated in the figure below, utilizes *in vitro* activity screens of novel plasmid DNA designs, followed by *in vivo* activity screens of select ceDNA constructs. We have iteratively employed this cycle to rapidly identify ceDNA constructs that achieve disease correction in animal models and have observed that learnings from our more mature programs accelerate our ability to identify effective ceDNA constructs for subsequent indications.

Our eight-week research cycle rapidly identifies ceDNA constructs for new programs

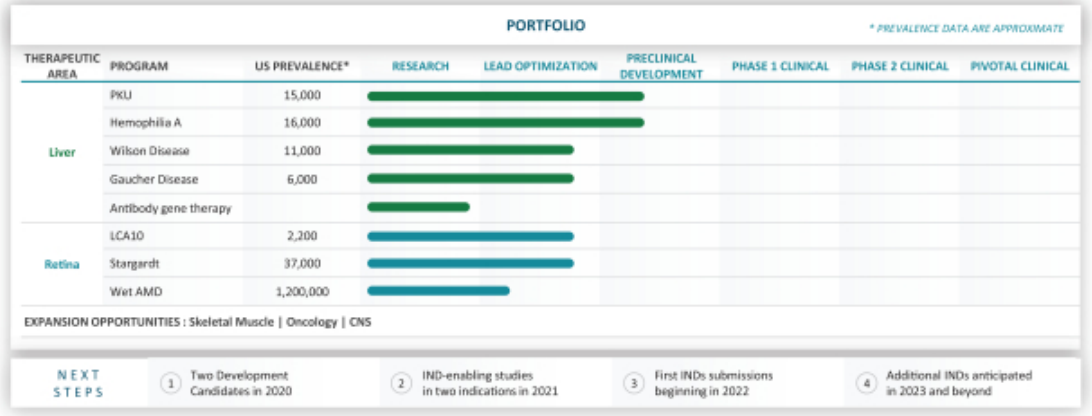


We plan to apply this integrated research and development strategy across liver, retina, skeletal muscle, oncology and the CNS.

Our portfolio

We are advancing a broad and expansive portfolio including eight programs for rare and prevalent diseases of the liver and retina. We are focused on diseases with significant unmet need for which our non-viral gene therapy platform may substantially improve clinical efficacy relative to current gene therapy approaches. We are initially prioritizing rare monogenic diseases of the liver and retina that have well-established biomarkers and clear clinical and regulatory pathways. We plan to expand our portfolio to include rare and prevalent diseases of the skeletal muscle, the CNS and oncology by developing discrete ctLNPs, each engineered to reach a different tissue. As shown in the figure below, our most advanced liver disease programs are in PKU and hemophilia A, which are in the preclinical stage of development, and our most advanced retina disease programs are in LCA10 and Stargardt disease, which are in the lead optimization stage of development.

In addition, we believe that our non-viral gene therapy platform may allow patients to produce antibody therapies from their own cells for years at a time from a single dose and plan to advance programs to deliver antibody genes, directing the body's own cells to express and secrete therapeutic antibodies. We believe the combination of the expected multi-year durability of a single dose of ceDNA, tissue-specific delivery and manufacturing capacity may provide dosing for millions of patients living with prevalent diseases.



Within the therapeutic area of the liver, we have established programs for inborn errors of metabolism in PKU and Wilson disease. We are also advancing programs for systemic disorders in which the liver can be utilized to secrete therapeutic proteins in hemophilia A, Gaucher disease and antibody gene therapy.

We plan to utilize our eight-week research cycle to rapidly design, produce and screen ceDNA constructs for other diseases within a tissue, so that we may rapidly expand clinical development efforts to include additional rare and prevalent diseases once human proof of concept is established in that tissue. For instance, if human proof of concept is established in PKU, we plan to rapidly expand our development efforts to include additional inborn errors of metabolism such as progressive familial intrahepatic cholestasis 2, or PFIC2, glycogen storage disease type 1a, or GSD1a, and ornithine transcarbamylase deficiency, or OTC. Similarly, if human proof of concept in hemophilia A is established, we plan to expand our programs in other diseases requiring secretion of therapeutic proteins such as Gaucher disease, Pompe disease, hereditary angioedema, or HAE, alpha1-antitrypsin deficiency, or A1AT, antibodies against Cov-2 and human immunodeficiency virus, or HIV.

We plan to apply this strategic approach of rapid expansion following initial human proof of concept in a therapeutic area across our portfolio.

Liver diseases

For the majority of our liver programs, we have designed and manufactured disease-modifying ceDNAs that have shown expression *in vitro* and/or disease correction *in vivo*. We have employed GalNAc as the targeting ligand in our ctLNP delivery system to selectively drive biodistribution to the liver. GalNAc binds to the ASGPr on hepatocytes, and the biology of this selective ligand-receptor pair for delivery to hepatocytes has been well validated in human clinical trials. For each liver program, we plan to formulate ceDNA within a ctLNP-GalNAc expressing the relevant gene of interest for intravenous delivery. GalNAc targeting has been demonstrated to efficiently deliver ceDNA to up to 100% of hepatocytes and we believe that broad biodistribution of ctLNP-GalNAc to hepatocytes will be a key strength of our pipeline programs since current gene therapy approaches deliver payload to 30% or fewer of hepatocytes with a single dose. Additionally, our potential to redose patients until they are in the therapeutic range of expression may enable early and robust human proof of concept in Phase 1/2 clinical trials and is a key differentiator from current gene therapy approaches.

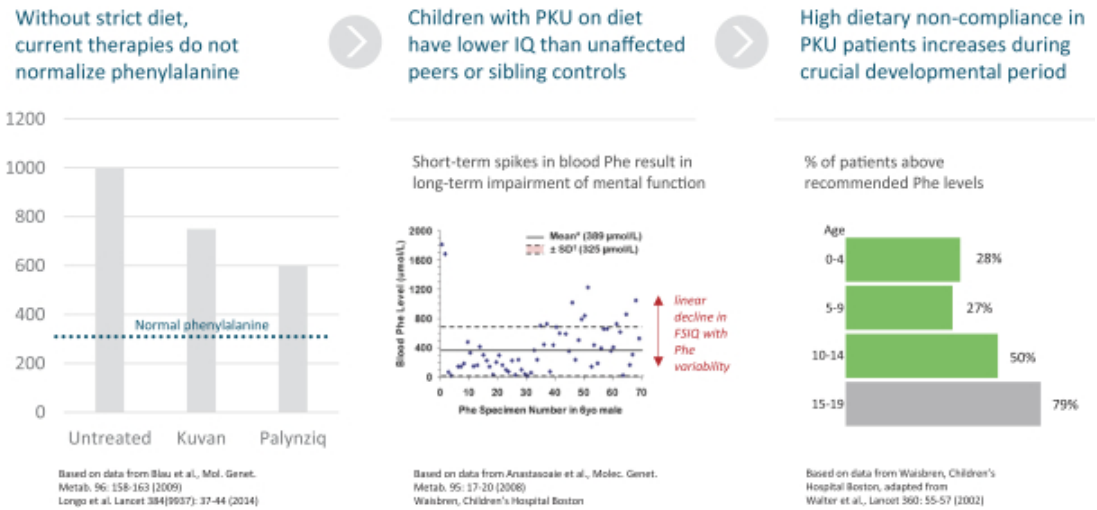
Phenylketonuria

Overview

Phenylketonuria, or PKU, is a rare autosomal recessive genetic disorder caused by deficiency of the hepatic enzyme phenylalanine hydroxylase, or PAH, that metabolizes the essential amino acid phenylalanine, or Phe, to tyrosine, or Tyr, an essential amino acid for CNS development and function. PAH deficiency leads to elevated levels of Phe in the blood and toxic Phe accumulation in the brain resulting in neurocognitive manifestations including failure to attain early developmental milestones and progressive impairment of cerebral function. Patients with uncontrolled severe PKU will develop profound neuropsychiatric disorders and irreversible intellectual disability.

There are approximately 15,000 patients with PKU in the United States and 41,000 patients in the European Union. PKU is usually diagnosed at birth through newborn screening, which provides the opportunity to introduce therapies that reduce Phe levels. However, as shown in the left figure below, without strict dietary control, current therapies do not normalize Phe levels. Attaining consistent levels of Phe in childhood is correlated with higher IQ levels and executive functioning in adults, and short-term spikes in Phe result in long-term impairment of neurocognitive function, as shown in the middle figure below. Even without optimal correction of Phe levels in childhood, control in adolescent and adult PKU patients has been shown to result in higher levels of executive function and attention and lower levels of depression and anxiety. As shown in the right figure below, adolescents are unable to maintain such a strict diet, with 50% of patients age 10-14 above the recommended Phe levels and almost 80% of patients outside the normal Phe range in the late teen years.

Early consistent Phe normalization key to neurocognitive outcome



Current approaches and limitations

The standard of care for PKU is strict, life-long dietary modification to control blood Phe levels to the recommended target range of 120 to 360 micromoles per liter. This requires PKU patients and caregivers to carefully monitor diet and severely restrict protein intake and other Phe-rich foods. Medical foods including formula and foods modified to be low in protein are also required.

Initiation of a Phe-restricted diet is recommended as early as possible in infancy to avoid irreversible neurocognitive decline due to elevated Phe levels. While this allows some patients to approach target Phe

levels, it is challenging to maintain as a life-long treatment. Even with full compliance of dietary therapy during childhood, many patients have episodic or chronic high Phe levels and suffer irreversible neurocognitive impairment as a result.

PALYNZIQ (pegvaliase) and KUVAN (sapropterin dihydrochloride), a biologic and a small molecule, respectively, are approved in the United States for patients with PKU and both have been shown to have modest benefits in a subset of patients. PALYNZIQ is approved only for adult PKU patients. KUVAN does not normalize Phe in most patients and has shown to be ineffective in patients with severe PKU. Despite treatment advances, including availability of a larger selection of medical and low protein foods and the approval of the two treatments, many patients still do not achieve the recommended daily Phe levels and are at risk of developing neurocognitive manifestations, including intellectual disability and neuropsychiatric disorders.

Several AAV gene therapy approaches are currently being tested in clinical trials in patients with PKU. However, following a single dose of AAV, antibodies are induced against the AAV capsid and thus, AAV gene therapy can only be administered once. The antibodies formed following a single dose of AAV prevent re-treatment to increase or extend efficacy for patients with inadequate initial response or declining levels of expression. Further, it precludes treatment of pediatric patients, whose organ growth and dividing cells would dilute expression over time, and therefore would require redosing. As a result, these therapies do not have the opportunity to correct PKU at or near the onset of disease, allowing for normal neurocognitive development.

Given the limitations of currently approved therapies and the AAV gene therapy approaches under development, there is a substantial unmet need for more effective therapies for PKU.

Our approach

Our non-viral gene therapy approach aims to:

- achieve stable correction of Phe levels in PKU patients of all ages upon initial dose or through individualized patient dose titration, allowing them to normalize their diet, eliminate the burden of ongoing treatment and stabilizing and/or preserving neurocognitive function;
- achieve the desired level of gene expression for each patient through our ability to redose;
- treat patients effectively for life by episodically monitoring serum Phe levels and redosing as needed, should expression wane over time;
- reverse attention, memory or executive function deficits in adults and adolescents; and
- preserve normal neurocognitive development in infants and children.

To establish benchmarks for full correction in PKU, we conducted a study utilizing the established mouse model of PKU, known as PAH^{enu2}, a mouse model in which the PAH gene is mutated, leading to dramatically elevated Phe, to assess how many copies of ceDNA, ceDNA-derived PAH RNA and ceDNA-derived PAH protein are required for full correction in this model. In this study, we administered a ceDNA-PAH construct by hydrodynamic injection into PAH^{enu2} mice. As shown in the figure below, we found that animals that had full correction of Phe, which is greater than 360 micromolar, or µM, had the following:

- ceDNA-PAH DNA copies in the liver of at least ~0.5 copies per diploid genome, or dg;
- ceDNA-PAH derived RNA transcripts at least 1 x 10^6 copies/µg; and
- ceDNA-PAH derived protein of at least 10% of normal levels.

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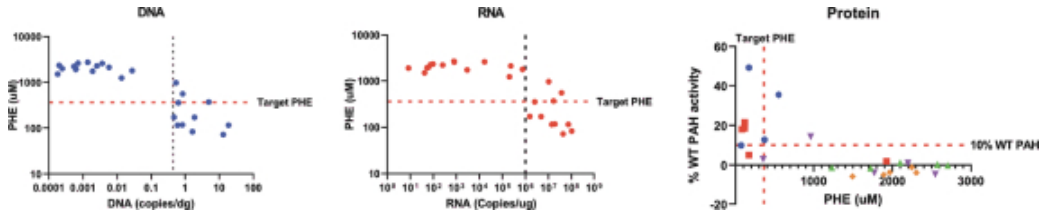
Threshold levels for ceDNA-PAH correction in PKU mice

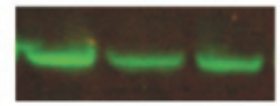


As shown in the left figure below, several ceDNA-PAH constructs express PAH protein at varying levels by Western Blot in cell culture.

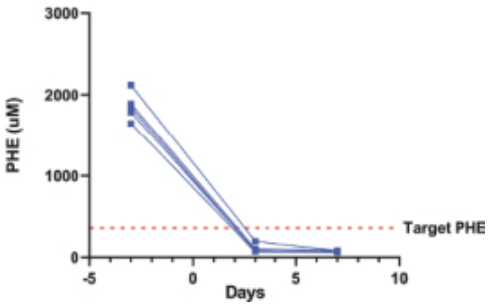
As shown in the right figure below, our most potent ceDNA-PAH construct, when administered hydrodynamically, has normalized Phe levels in PAH^{enu2} mice. The PAH^{enu2} mice serum samples at baseline exhibited very high Phe levels of greater than 1500µM, and dropped below target Phe levels (shown by the dashed red line) at three and seven days after IV administration of ceDNA-PAH.

Expression of ceDNA-PAH *in vitro* and correction of Phe after hydrodynamic injection of ceDNA-PAH *in vivo*

Expression of ceDNA-PAH by immunoblot



Phenylalanine normalization after hydrodynamic injection of ceDNA-PAH in PKU mice



Next steps

We expect to achieve murine preclinical proof of concept in 2020, defined as Phe normalization in PAH^{enu2} in mice after administration of ceDNA-PAH formulated in ctLNP. We plan to begin IND-enabling studies in 2021 and to submit an IND application for this program in 2022.

Hemophilia A

Overview

Hemophilia A is a rare X-linked hereditary bleeding disorder characterized by impaired blood coagulation as a result of deficiencies in the production or function of coagulation Factor VIII. There are approximately 16,000 hemophilia A patients in the United States and 320,000 patients worldwide. Because of the deficiency of coagulation Factor VIII, hemophilia A patients bleed in joints, muscles, soft tissues and within mucous membranes, which can be either spontaneous or due to internal or external trauma, depending on the severity

of the disease. The clinical presentation of hemophilia A can be mild, moderate or severe, depending on the residual level of circulating Factor VIII. The diagnosis of hemophilia A is often made at a young age, earlier than 36 months, based on persistent bleeding or internal hemorrhage.

Current approaches and limitations

Most patients with hemophilia A in the United States and the European Union are currently treated with clotting factors according to practice guidelines, which are relatively consistent around the world. Children are generally treated prophylactically, while adults may be treated either prophylactically or on demand, depending on the residual level of Factor VIII activity in the blood. Compliance with clotting factors is 50% to 80%, and up to 30% of patients with severe disease develop inhibitors to Factor VIII replacement. Approximately 75% of hemophilia A patients worldwide still receive inadequate treatment or have no access to treatment.

HEMLIBRA (emicizumab) is a bispecific Factor IXa- and Factor X-directed antibody indicated for routine adult and pediatric patients ages newborn and older with hemophilia A. However, this product has safety concerns as several cases of thrombotic microangiopathy/thrombosis have occurred, in some cases in the context of co-administration of activated prothrombin complex concentrate.

There are several AAV gene therapies currently in late-stage clinical trials, including Valrox (valoctocogene roxaparvovec), for which a biologics license application, or BLA, is under review by the FDA. Early data from these trials have shown variation in the amount of Factor VIII expressed from patient-to-patient with a substantial proportion of patients either becoming supratherapeutic or remaining subtherapeutic after Valrox administration. Many hemophilia A patients have pre-existing immunity to AAV and, therefore, are not candidates for this therapy. Mean Factor VIII levels decline over two to three years after treatment with Valrox, which means that it is possible that patients will become subtherapeutic over three to five years and cannot be redosed with AAV gene therapy. In addition, AAV gene therapy will not be available to children with hemophilia A since their livers are still growing and only one dose is possible.

There are no current or investigational therapies that have been shown to durably induce therapeutic Factor VIII levels in all patients of all ages, nor therapies that can be redosed when Factor VIII expression wanes through the life of the patient. Given the variable response to gene therapy in patients with hemophilia A, titration at onset of therapy is critical to ensure that all patients get within a therapeutic range. Since there are potential consequences to expressing too much Factor VIII, such as excess blood clotting, the ability to titrate the therapy will enable an optimal dosing regimen.

Our approach

Our gene therapy approach aims to do the following in hemophilia A:

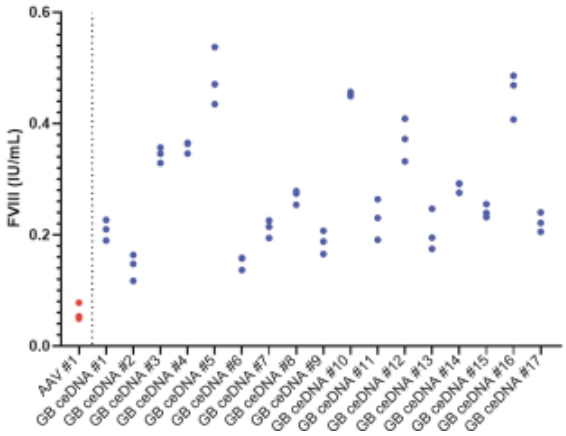
- achieve therapeutic Factor VIII levels in patients of all ages, resulting in normalization of bleeding risk;
- treat infants and children to prevent bleeds early in disease and prevent irreversible tissue and organ dysfunction;
- achieve the desired level of gene expression in a greater proportion of patients participating in our early clinical trials through our ability to redose;
- ensure that all patients achieve curative levels of Factor VIII of greater than 25% of normal activity levels with the ability to titrate expression to higher target levels for some patients as needed based on lifestyle and circumstances;

- deliver ceDNA-FVIII to a large percentage of hepatocytes resulting in a relatively low burden of expression for each hepatocyte, which may lead to more durable expression compared to other gene therapy modalities; and
- increase the safety index by achieving therapeutic Factor VIII levels at lower doses because of more potent ceDNA-FVIII constructs and greater hepatic biodistribution.

Our approach has the potential to titrate expression in each patient to reach target Factor VIII levels, avoiding supratherapeutic levels and minimizing the thrombotic, or clotting, risk to the patient. In addition, we can potentially treat patients for life by episodically following Factor VIII levels and redosing as needed, should expression wane over time. Redosing may also enable broader access for all patients with severe disease, and for children with mild to moderate disease severity who are currently managed through on-demand treatment, as shown in the right figure below.

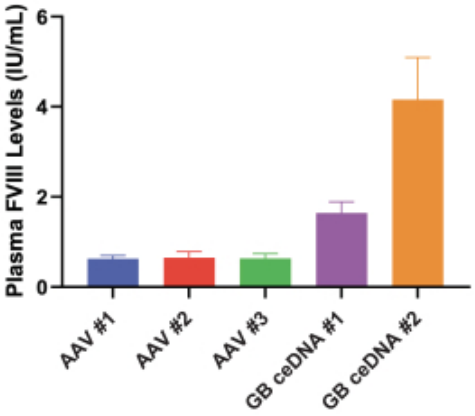
We have created multiple distinct ceDNA-FVIII constructs with different expression cassette elements, including promoter, intron, untranslated regions, or UTRs, and codon optimization sequences. *In vitro* screening of ceDNA-FVIII constructs revealed that several constructs express Factor VIII, as defined by functional activity measures, as shown in the figure below. All of our ceDNA constructs, labeled as GB ceDNA in the figure below, expressed greater activity of FVIII compared to a ceDNA construct with the expression cassette of an AAV-FVIII product candidate that is currently in clinical trials, AAV #1, with some expressing up to six-fold more Factor VIII activity.

Several ceDNA-FVIII demonstrated greater activity compared to AAV-FVIII



The enhanced potency of our ceDNA-FVIII constructs has also been confirmed *in vivo*. In an *in vivo* study, we measured serum levels of human Factor VIII after hydrodynamic injection of various ceDNA constructs into the tail vein of mice and assessed protein levels by enzyme-linked immunosorbent assay for human Factor VIII. As shown in the figure below, two ceDNA constructs listed as GB ceDNA #1 and GB ceDNA #2 demonstrated 1.0 and 6.0 IU/ml Factor VIII activity, or 100% and 600% of normal levels, respectively. In contrast, at the same dose, ceDNA constructs with the expression cassette of each of three AAV-FVIII product candidates currently in clinical development, demonstrated approximately 0.5 IU/ml Factor VIII activity, or 50% of normal levels in animals.

***In vivo* activity of ceDNA-FVIII constructs**



The direct relevance of having more potent ceDNA constructs is that the input dose required to have a therapeutic effect may be lower, thereby increasing the safety profile and lowering the metabolic requirements on individual hepatocytes to produce and secrete Factor VIII.

Next steps

We expect to achieve murine preclinical proof of concept in 2020, defined as demonstrating normal Factor VIII levels after administration of ceDNA-FVIII formulated in ctLNP. We also anticipate achieving proof of concept for biodistribution and durable expression in non-human primates using our ctLNP with a reporter protein such as Factor IX in 2020. We plan to begin IND-enabling studies in 2021, and to submit an IND application for this program in 2022.

Wilson disease

Overview

Wilson disease is a rare autosomal recessive disease due to a loss-of-function mutation in the ATB7B copper transporter. There are approximately 11,000 patients with Wilson disease in the United States and 17,000 patients in the European Union. Mutations in the ATP7B copper transporter prevent incorporation of copper into ceruloplasmin and diminishes biliary secretion of copper excess, resulting in toxic accumulation of copper in the liver and brain. Clinically, liver damage begins by six years of life and then progresses with inflammation, fibrosis and joint pain. Many patients also develop CNS manifestations of copper overload, including psychosis, tremors, dysarthria, or slurred speech and muscle stiffness.

Current approaches and limitations

There are no approved gene therapies for Wilson disease. Current treatment approaches include chelators promoting excretion of copper from the body and zinc salts that reduce copper absorption. These therapies have demonstrated limited effectiveness and safety issues, resulting in poor compliance in patients. The only curative option for acute liver failure related to Wilson disease today is a liver transplant, which cannot be offered to most patients due to lack of availability of matched donors. The average age of Wilson disease patients undergoing liver transplantation is 15 years old for those who have an available donor, indicating the need for intervention in childhood to prevent progression to this point.

There are no current gene therapy clinical trials for Wilson disease. The ATP7B gene is 4.4 kb, which means the size of the gene plus the remainder of the expression cassette cannot fit within an AAV. One preclinical AAV gene therapy program, known as VTX-801, is in development for Wilson disease utilizing a truncated ATP7B gene that may not have the full functionality of ATP7B.

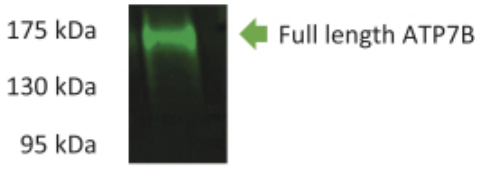
Our approach

Our gene therapy approach aims to do the following:

- enable full correction of copper metabolism by broadly transducing hepatocytes and utilizing full-length ATP7B gene and an optimized expression cassette;
- achieve full hepatic correction early in the disease, re-directing copper to be incorporated into ceruloplasmin and normalizing bile excretion, thereby avoiding hepatic and CNS tissue accumulation and irreversible liver fibrosis and neurocognitive decline;
- initiate treatment in children, early in the disease, to prevent the accumulation of liver damage and irreversible neurocognitive decline;
- maintain correction of hepatocytes by redosing to compensate for the effect of injury-driven cell division in the liver;
- achieve the appropriate therapeutic level of ATP7B needed for correction using serum biomarkers via individualized patient titration at the onset of therapy; and
- maintain copper and ceruloplasmin levels in the normal range throughout life with maintenance therapy, as needed.

We have generated Wilson disease plasmid constructs and demonstrated the expression and appropriate sub-cellular location of the expressed protein *in vitro*. We have induced cells to produce the full length ATP7B protein at 157 kilodaltons using Western Blot, as shown in the figure below. We have also demonstrated, by immunohistochemistry, appropriate localization of ATP7B in the golgi apparatus around the nucleus within cells, consistent with where native ATP7B localizes.

ATP7B plasmid constructs result in full length ATP7B protein production *in vitro*



Next steps

We plan to begin preclinical development in 2021 for this program.

Gaucher disease, Type 1

Overview

Gaucher disease is a rare inherited autosomal recessive disorder caused by the insufficient expression of lysosomal enzyme glucocerebrosidase, or GCase. Gaucher disease is the most common inherited lysosomal storage disease. There are approximately 6,000 patients with Gaucher disease in the United States and 9,000 patients in the European Union. Ninety percent of Gaucher patients are classified as Type 1, the most common form, which has no CNS involvement in the disease. Patients with Type 1 disease are typically diagnosed between 10 to 15 years of age.

Patients with Gaucher disease do not produce adequate levels of GCase, which causes glucosylceramide, a toxic lipid, to accumulate in macrophage lineage cells in visceral organs. This results in splenomegaly, hepatomegaly and cytopenia. Disease progression commonly involves loss of bone mass, either osteopenia or osteoporosis and can lead to painful bone crises and avascular necrosis, or death of bone tissue. We are specifically developing a gene therapy approach to address Type 1 Gaucher disease.

Current approaches and limitations

The current standard of care for Gaucher disease includes enzyme replacement therapy, or ERT, for patients of all ages or substrate reduction therapy, or SRT, for adults with Type 1. ERT is recommended as a potentially suitable treatment for all symptomatic Type 1 patients, though the required IV infusions every two weeks can lead to difficult treatment burden.

SRT treats Gaucher disease by inhibiting cellular production of glucosylceramide, rather than increasing the degradation of glucosylceramides through ERT. ZAVESCA (miglustat) and CERDELGA (eliglustat) effectively treat hepatosplenomegaly in a similar time course to ERT, though improvement in hematological aspects of the disease takes longer to materialize. SRT does not correct the fundamental lack of GCase and biochemical and tissue abnormalities persist.

Our approach

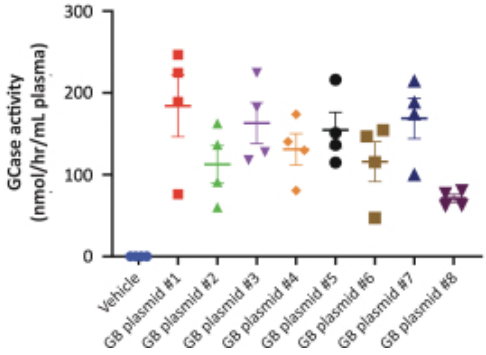
Our gene therapy approach aims to:

- provide continuous therapeutic levels of GCase in serum and tissues that can break down glucosylceramide, which may enhance tissue correction over episodic ERT;
- administer ceDNA-GCase early in disease before the onset of inflammation, fibrosis and irreversible tissue injury;
- achieve the appropriate GCase levels for potential disease modification using biomarkers such as glucosylsphingosine, or Lyso-Gb1, via individualized patient titration;
- treat patients for life by maintaining Lyso-Gb1 levels in the normal range through redosing as needed; and
- reduce immune reactions to GCase, which occur in 2% to 15% of Gaucher patients.

We have created multiple distinct GCase plasmid constructs and have tested them for activity *in vivo*. These constructs differ in various expression cassette elements, including promoter, intron, UTR and codon

optimization expression elements. We administered these plasmid GCase constructs hydrodynamically into mice and measured GCase enzymatic activity in the serum. As shown in the figure below, many of our GCase plasmid constructs have exhibited functional GCase activity in serum, indicating that hepatocytes are not only able to produce the GCase, but can also secrete it for uptake by other tissues that are affected in Gaucher.

Detection of GCase in plasma after hydrodynamic injection of plasmid constructs *in vivo*



Next steps

We plan to begin preclinical development in 2021 for this program.

Antibody gene therapy

Overview

We plan to advance product candidates to deliver antibody genes to direct the liver to express and secrete antibodies. Monoclonal antibodies, or mAbs, have demonstrated therapeutic benefit in many areas, including infectious diseases, rheumatology, hematology and oncology.

We believe that utilizing the patient's own cells to produce and secrete therapeutic mAbs, fragments or derivatives is a potentially transformative approach that can result in greater efficacy, produced at a larger scale and with lower cost of goods compared to the passive administration of some mAbs. This approach is called antibody gene therapy, or AGT.

Current approaches and limitations

The cost of goods, the burden of frequent administration and the manufacturing scale limitations of mAb therapy preclude their widespread utilization in many diseases.

Our approach

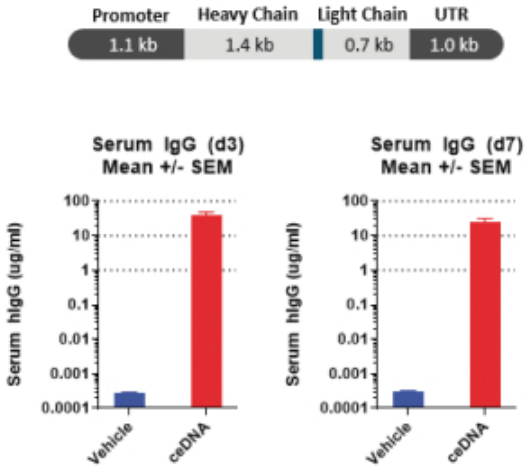
Our gene therapy approach aims to:

- enable a patient's own body to sustainably produce and secrete a therapeutic mAb from the liver by introducing ceDNA-AGT;
- enable continuous production of protein, resulting in a stable, effective levels of serum mAb, thereby avoiding toxicity due to off-target effects of pulsatile delivery and/or loss of efficacy often associated with rapid reduction in concentrations when delivered passively;

- rapidly induce a therapeutic effect due to liver production of the therapeutic mAb within days of administration;
- potentially eliminate compliance risk due to sustained expression after a single dose;
- encode multiple mAbs on a single ceDNA construct for broad therapeutic application;
- achieve the appropriate mAb levels in the blood via individualized patient titration; and
- induce rapid onset, durable immunity via expression of mAbs to prevent infection for large populations.

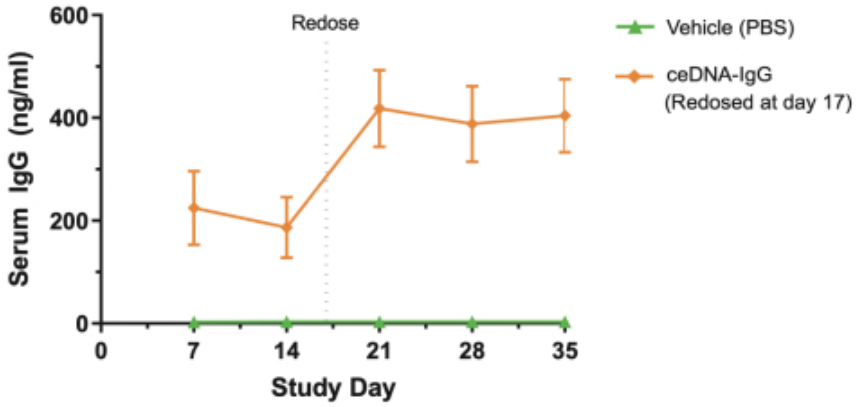
We have demonstrated hepatic expression of antibodies with ceDNA-AGT. As shown in the figure below, hydrodynamic injection of ceDNA-AGT resulted in serum mAb levels of greater than 40.0 µg/ml. Since many therapeutic mAbs are effective at serum concentrations of 1.0 to 5.0 µg/ml, we believe the level of mAb expression observed with our ceDNA-AGT is likely to be therapeutically relevant in humans.

Hydrodynamic injection of ceDNA-AGT results in serum levels up to 40.0µg/ml



We have also demonstrated stacking of mAb expression after repeat dosing via hydrodynamic injection, as shown in the figure below.

mAb expression increases after repeat dosing via hydrodynamic injection



Next steps

We are advancing our initial AGT program for the treatment of an infectious disease and we are evaluating ceDNA constructs that express neutralizing mAbs targeting a surface protein for a variety of infectious agents, including hepatitis B virus, or HBV, human immunodeficiency virus, or HIV, and respiratory syncytial virus, or RSV. Separately, we have established a research collaboration with Vir Biotechnology, Inc. to explore the potential for our non-viral gene therapy platform to extend the duration and reach of Vir's mAb therapies against the SARS-CoV-2 coronavirus.

Retinal diseases

Approximately 200 million individuals suffer from inherited retinal diseases, in which a gene mutation leads to degeneration of the retina. Many of these diseases are caused by genes too large to be enclosed within AAV, including LCA10 and Stargardt disease. Current AAV gene therapy approaches are not able to encode and deliver large genetic payloads and cannot provide the full gene required to treat LCA10 and Stargardt disease. We believe using ceDNA to deliver large gene payloads efficiently and specifically to relevant cell types in the retina, with the opportunity to optimize ctLNP for minimally invasive routes of delivery, represents an important therapeutic approach.

Lebers Congenital Amaurosis Type 10 (LCA10)

Overview

LCA10 is the most common genetic cause of childhood vision loss. There are approximately 2,200 patients with LCA10 in the United States and 3,400 patients in the European Union. It is a severe, autosomal recessive retinal dystrophy due to a mutation in the CEP290 protein that is expressed in and required for proper functioning of retinal photoreceptors. LCA10 causes blindness or severe vision loss, often from birth or within the first year of life.

Current approaches and limitations

There are no approved therapies for LCA10. Several therapeutic programs are in clinical development for LCA10, including a splicing oligonucleotide given episodically by intravitreal injection and a gene editing

approach. Both approaches address only a subset of LCA10 patients, specifically those with a CEP290 mutation amenable to splicing alteration, which makes up approximately 60% of the population. CEP290 is a large gene of 7.4 kb, which exceeds the 4.7 kb payload capacity of AAV. No single approach has been able to address the many mutations that cause LCA10.

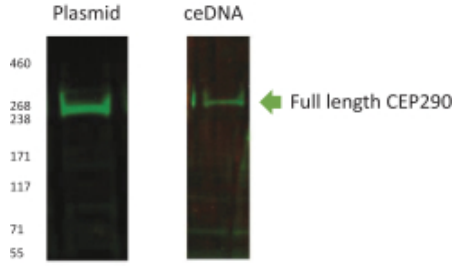
Our approach

Our gene therapy approach aims to:

- deliver directly to the retina;
- treat patients irrespective of their CEP290 mutation;
- utilize ctLNP to specifically deliver CEP290 to photoreceptors and not to retinal glial and immune cells, thereby potentially increasing the safety, tolerability and durability of transgene expression;
- enable single-dose therapy delivered subretinally, which may increase efficacy and compliance when compared, for example, to episodic intravitreal delivery; and
- treat infants and children to halt further decline of and restore vision.

We have created multiple plasmid and ceDNA constructs encoding the CEP290 gene and have demonstrated expression of full-length protein after transfection in cells in culture, as shown in the figure below.

Plasmid and CEP290 express full-length protein in HEK293 cells *in vitro*



Next steps

We plan to begin preclinical development in 2021 for this program.

Stargardt disease

Overview

Stargardt disease is the most common inherited macular dystrophy. There are approximately 37,000 patients with Stargardt disease in the United States and 66,000 patients in the European Union. Stargardt disease is an autosomal recessive disease due to mutation in the ABCA4 gene that is expressed in both the RPE and retinal photoreceptors. Loss of ABCA4 function disrupts normal processing of retinaldehyde, or Vitamin A, in both photoreceptors and RPE cells leading to accumulation of toxic bis-retinoid byproducts and photoreceptor death. Patients usually present in childhood with loss of visual acuity and exhibit progressive loss of RPE and photoreceptor cells.

Current approaches and limitations

There are currently no proven treatments for Stargardt disease. The ABCA4 gene is approximately 6.7 kb, too large to be delivered by AAV. There are currently no ongoing gene therapy trials for Stargardt disease. The goal of therapy in Stargardt disease is to preserve vision by correcting ABCA4 expression in enough photoreceptors and RPE cells to halt the progressive loss of these cells that would otherwise occur.

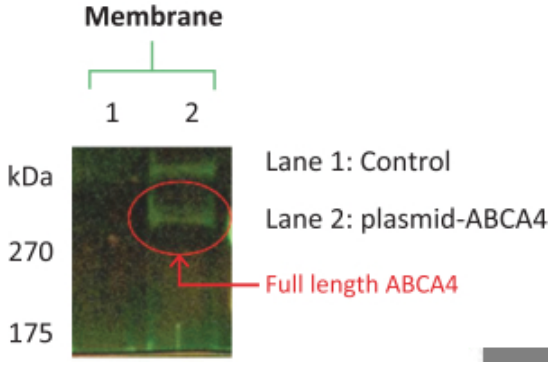
Our approach

Our gene therapy approach aims to:

- deliver to photoreceptors and RPE cells to halt progressive loss in cells and preserve vision;
- protect photoreceptors and RPE cells through expression of normal ABCA4, resulting in clearance of bis-retinoid byproducts;
- drive the appropriate level of ABCA4 expression in photoreceptors and RPE cells utilizing a native ABCA4 promoter and native regulation of expression;
- maintain normal macular vision and visual acuity when given to earlier-diagnosed patients; and
- deliver the entire ABCA4 gene in a single gene therapy vector, thereby increasing efficacy relative to dual AAV approaches.

We have generated plasmid constructs that express full length ABCA4. Further, as shown in the figure below, when we fractionate cellular lysates into cytosolic and membrane compartments, we see that plasmid ABCA4 expresses appropriately in the membrane bound subcellular compartment. This is important because ABCA4 is expressed in the cellular membrane of photoreceptors. Its cellular function requires that it be expressed and also appropriately trafficked to the correct intracellular compartment. The red circle in the figure below highlights the ABCA4 protein localized within cellular membrane.

Expression and appropriate subcellular localization of plasmid ABCA4 in vitro



Next steps

We plan to begin preclinical development in 2021 for this program.

Wet age-related macular degeneration (Wet AMD)

Overview

Age-related macular degeneration, or AMD, is the leading cause of irreversible vision loss occurring in approximately 10 million people in the United States. Wet AMD is the most severe form, characterized by neovascularization of the retina, leading to significant loss in visual acuity and rapid progression to blindness. There are approximately 1.2 million patients with wet AMD in the United States and over 2.5 million patients in the European Union. Wet AMD is most common in individuals over the age of 50, with increasing incidence every decade thereafter.

Current approaches and limitations

Passive administration of anti-vascular endothelial growth factor, or anti-VEGF, mAbs are an established therapy for patients with wet AMD. Anti-VEGF therapy, such as EYLEA (aflibercept), is effective in slowing the loss of visual acuity in patients with wet AMD. However, the frequency of intravitreal administration is a barrier to adherence and to widespread adoption.

AAV gene therapy to establish intra-ocular expression of anti-VEGF molecules is in early clinical development, either by subretinal or intravitreal delivery. It is unclear today if these therapies will generate sufficient expression of anti-VEGF in the retina. If successful, the scale limitations of AAV may present additional challenges to providing therapy for a substantial proportion of wet AMD patients.

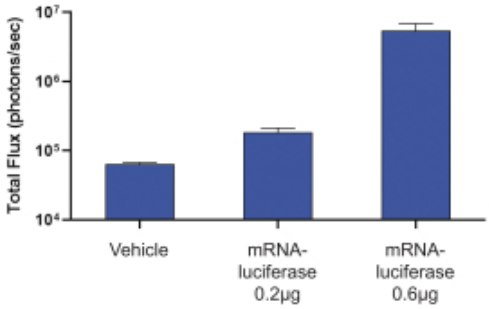
Our approach

Our gene therapy approach aims to:

- deliver intravitreally to enable retinal cells to express and secrete an anti-VEGF molecule;
- provide a durable and sustained level of expression of anti-VEGF, which may enhance regression of neovascularization and improve visual acuity and may enable administration only a few times over the life of a patient; and
- define when repeat therapy would be indicated to optimally preserve the retina.

In order to establish a baseline for the biodistribution of ctLNP in the eye, we administered mRNA-luciferase intravitreally at two doses of 0.2µg and 0.6µg using our ctLNP delivery system. As shown in the figure below, this resulted in luciferase expression in the retina.

Expression after intravitreal administration of mRNA-luciferase using ctLNP



We have generated several anti-VEGF mAb ceDNA constructs and have shown that these constructs result in high levels of anti-VEGF mAb levels in the blood after hydrodynamic intravenous delivery.

Next steps

We aim to combine these constructs with ctLNP to achieve intravitreal delivery of relevant antibody levels in the retina. We plan to begin preclinical development in 2021 for this program.

Expansion opportunities in other tissues

We plan to expand our portfolio by pursuing additional programs in rare and prevalent diseases of the skeletal muscle, oncology and the CNS by developing discrete ctLNPs, each engineered to reach a specific tissue.

Skeletal muscle

There are a variety of genetic muscle disorders, including muscular dystrophies, that may be treated by efficient and systemic gene therapy to skeletal muscle. We are currently developing a ctLNP utilizing a targeting ligand to deliver ceDNA specifically to skeletal muscle.

We believe this approach would have several benefits for rare monogenic diseases of the skeletal muscle, including:

- early treatment, near the onset of disease, before inflammation and fibrosis progressively replace muscle fibers;
- delivery of full-length of defective skeletal muscle genes, which are often very large as is the case, for example, for dystrophin, the gene responsible for Duchenne Muscular Dystrophy, or DMD, and genes that form the sarcoglycan complex, which are responsible for various forms of limb-girdle muscular dystrophy;
- efficient delivery of the gene of interest to enough muscle fibers to change the course of disease;
- sufficient expression within transduced muscle fibers to allow for normal constitution of the skeletal muscle fibers during growth and development; and
- keeping up with patients' needs over time through redosing.

We believe there are many diseases in the skeletal muscle with unmet need such as DMD, myotonic dystrophy, limb girdle dystrophies and fascioscapulohumeral dystrophies, which we may pursue in the future.

CNS

We plan to explore the use of ceDNA to correct disorders of the CNS. The work we are doing with local delivery in the retina to photoreceptors may inform expansion into the CNS, beginning for example with focal epilepsies, in which expression of a novel gene within a specific region of neurons may stop the abnormal seizures. One such example is Dravet syndrome, an epilepsy disorder that begins in infancy or early childhood usually caused by a loss-of-function mutation in the SCN1A gene. Another example is MPSII, or Hunter syndrome, which is caused by a deficiency in iduronate sulfatase resulting in both somatic (liver, bone and visceral organs) and CNS accumulation of toxic glycosaminoglycans.

Oncology

We plan to develop the use of ceDNA to treat a variety of cancer indications. We believe that we can use distinct targeting ligands to deliver ceDNA specifically and efficiently to tumors and can utilize ceDNA to express high

levels of relevant proteins within the tumor. For example, we believe after systemic delivery and efficient uptake by tumors, the expression of checkpoint inhibitors and particular cytokines encoded by the ceDNA may have both direct anti-tumor activity and may stimulate the immune system to respond to and attack tumor cells. Many of the genes that we can express within tumors have limited efficacy and substantial safety and tolerability issues when given systemically. The key attribute of this approach is the ability to drive efficient and selective uptake of ceDNA within tumors and then local, high concentrations of relevant anti-tumor agents.

Manufacturing

We have personnel with extensive technical, manufacturing, analytical and quality experience to oversee all internal and contracted manufacturing and testing activities. Relying on these personnel, we have built development laboratories to produce ceDNA (drug substance) and lipid nanoparticle-encapsulated ceDNA (drug product) for use in our research activities. We have produced ceDNA drug substance at up to 200 liters and converted these materials to drug product through our ctLNP manufacturing process to support our research studies. We plan to use third-party CDMOs to support our IND-enabling studies and to fully supply our clinical trials and commercial activities. As we scale manufacturing, we intend to continue to expand and strengthen our network of CDMOs, and we will also consider investing in internal cGMP manufacturing capabilities and infrastructure in the future if there is a technical need or a strategic or financial benefit.

Manufacturing is subject to extensive regulations that impose procedural and documentation requirements. These regulations govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our systems and contractors are required to comply with these regulations and are assessed through regular monitoring and formal audits.

Drug substance

We believe that the ceDNA drug substance requirements for our programs can be met by a variety of domestic and international contractors with standard biological manufacturing equipment. We have established a cGMP-ready process at the 200-liter scale, which we have transferred to our drug substance CDMOs to supply ceDNA drug substance for IND-enabling studies, clinical trials and early commercial activities. To ensure supply chain continuity, we have also established service agreements with additional suppliers to afford redundancy and flexibility in scaling. We have access rights to a biologics facility at one of our CDMOs that we believe could fully support multiple clinical programs if and when we advance our programs into clinical trials, as well as the early phases of commercialization.

We have invested in technical expertise and internal capabilities to optimize and develop the ceDNA drug substance process and to provide technical management and quality oversight for our process transfers to CDMOs.

Future ceDNA drug substance processes may require additional manufacturing capabilities, which may be addressed by either expanding our capabilities with existing contractors or establishing manufacturing supply relationships with new contract manufacturers. These changes in processes may also require new supply chain agreements with CDMOs that specialize in raw material manufacturing.

Drug product

Our drug product is ceDNA formulated with ctLNP. We believe that our drug product requirements can be met by a variety of domestic and international CDMOs. We have selected a subset of experienced organizations familiar with the specific operations that our current drug product processes require. We have established a service agreement with one of these CDMOs and have also engaged with suppliers for key components of our ctLNP delivery system.

We have invested in technical expertise and internal capabilities to optimize and develop the drug product process and to provide technical management and quality oversight for our process transfers to CDMOs. We have transitioned our drug product process from research-scale using microfluidics to standard clinical-scale equipment supporting cGMP operations for other established LNP-based modalities. These scaled systems have generated representative and well-characterized drug product that we have used in our preclinical studies. Additionally, as with our drug substance processes, progress on analytics has allowed us to leverage insights into our delivery system to upgrade and characterize purity and homogeneity. We plan to continue to implement process changes to improve purity and yield.

Intellectual property

We strive to protect our proprietary technology, inventions, improvements, platforms, product candidates and components thereof, their methods of use and processes for their manufacture that we believe are important to our business, including by obtaining, maintaining, defending and enforcing patent and other intellectual property rights for the foregoing in the United States and in certain foreign jurisdictions. We also rely on trade secrets and confidentiality agreements to protect our confidential information and know-how and other aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success depends in part on our ability to:

- obtain, maintain, enforce and defend patent and other intellectual property rights for our commercially important technology, inventions and improvements;
- preserve the confidentiality of our trade secrets and other confidential information;
- obtain and maintain licenses to use and exploit intellectual property owned or controlled by third parties;
- operate without infringing, misappropriating or otherwise violating any valid and enforceable patents and other intellectual property rights of third parties; and
- defend against challenges and assertions by third parties challenging the validity or enforceability of our intellectual property rights, or our rights in our intellectual property, or asserting that the operation of our business infringes, misappropriates or otherwise violates their intellectual property rights.

Patent portfolio

As of April 30, 2020, we own approximately 36 patent application families related to our business, including 13 pending Patent Cooperation Treaty, or PCT, patent applications (one of which is jointly owned with UMass) and two PCT applications that have entered the national stage in the United States and certain foreign jurisdictions, including Europe and Japan, and we exclusively license one patent application family, which has entered the national stage in the United States and certain foreign jurisdictions, including Europe and Japan. We also non-exclusively license one patent application family, which includes issued patents in each of the United States, Australia and Israel and national stage patent applications in several other jurisdictions, including Europe and Japan. In addition, we own approximately 24 U.S. provisional patent applications within the priority year. We do not currently own or exclusively license any issued patents covering any of our programs or technology, including the ceDNA platform, ctLNP delivery system and manufacturing processes. Our owned and licensed patent applications cover various aspects of our programs and technology, including our ceDNA construct, ctLNP delivery system and manufacturing process as further described below. Any U.S. or foreign patents issued from national stage filings of our owned or exclusively in-licensed PCT patent applications and any U.S. patents issued from non-provisional applications we may file in connection with our provisional patent applications would be scheduled to expire on various dates from 2037 through 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

ceDNA construct

As of April 30, 2020, we own approximately 26 patent application families, including eight pending PCT patent applications (one of which is jointly owned with UMass) and one PCT application that has entered the national stage in a number of jurisdictions outside the United States, and we exclusively license from UMass and Voyager one patent application family, which has entered the national stage in the United States and other jurisdictions, including Europe and Japan. These patent applications cover various aspects of our ceDNA construct, including ceDNA construct variants, certain disease-targeted ceDNA compositions and methods of use. We have also non-exclusively licensed one patent application family from the National Institutes of Health, or the NIH, and the Institut de Myologie, Universite Pierre et Marie Curie, Centre National de la Recherche Scientifique and Inserm Transfert SA, which we refer to as the French Institutions, which includes issued patents in each of the United States, Australia and Israel and national stage patent applications in other jurisdictions, including Europe and Japan, which cover our ceDNA construct, certain disease-targeted ceDNA compositions and methods of use. In addition, we own approximately 17 U.S. provisional patent applications within the priority year, which cover ceDNA construct variants, general applications of the ceDNA construct technology and certain properties of the construct, specific disease-targeted ceDNA compositions and methods of use. Any U.S. or foreign patents issued from the pending U.S. or foreign non-provisional patent applications or from non-provisional applications we may file in connection with the pending provisional patent applications would be scheduled to expire on various dates from 2038 through 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

ctLNP delivery system

As of April 30, 2020, we own approximately eight patent application families, including three pending PCT patent applications and one PCT application that has entered the national stage in the United States and a number of jurisdictions outside the United States, and approximately seven U.S. provisional patent applications within the priority year with respect to our ctLNP delivery system, including certain lipid and lipid nanoparticle compositions and combinations with ceDNA and/or targeting agents and methods of use. Any U.S. or foreign patents issued from the pending U.S. or foreign non-provisional patent applications or from any non-provisional applications we may file in connection with these provisional patent applications would be scheduled to expire on various dates from 2038 through 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

Manufacturing processes

As of April 30, 2020, we own approximately two patent application families, including two PCT patent applications, with respect to our ceDNA manufacturing processes. Any U.S. or foreign patents issued from the pending U.S. or foreign non-provisional patent applications or from any non-provisional applications we may file in connection with these provisional patent applications would be scheduled to expire on various dates from 2039 through 2040, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

Patent prosecution

A PCT patent application is not eligible to become an issued patent until, among other things, we file one or more national stage patent applications within 30 months, 31 months or 32 months of the PCT application’s priority date, depending on the jurisdiction, in the countries in which we seek patent protection. If we do not timely file any national stage patent applications, we may lose our priority date with respect to our PCT patent application and any potential patent protection on the inventions disclosed in such PCT patent application.

Moreover, a provisional patent application is not eligible to become an issued patent. A provisional patent application may serve as a priority filing for a non-provisional patent application we file within 12 months of such provisional patent application. If we do not timely file non-provisional patent applications, we may lose our priority date with respect to our existing provisional patent applications and any potential patent protection on the inventions disclosed in our provisional patent applications.

While we intend to timely file additional provisional patent applications and national stage and non-provisional patent applications relating to our PCT patent applications, we cannot predict whether any of our patent applications will result in the issuance of patents. If we do not successfully obtain patent protection, or if the scope of the patent protection we or our licensors obtain with respect to our product candidates or technology, including our ceDNA constructs, ctLNP delivery system or manufacturing processes is not sufficiently broad, we will be unable to prevent others from using our technology or from developing or commercializing technology and products similar or identical to ours or other similar competing products and technologies. Our ability to stop third parties from making, using, selling, offering to sell, importing or otherwise commercializing any of our technology, inventions and improvements, either directly or indirectly, will depend in part on our success in obtaining, maintaining, defending and enforcing patent claims that cover our technology, inventions and improvements.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. The protection afforded by a patent varies on a product-by-product basis, from jurisdiction-to-jurisdiction, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of patent term adjustments and regulatory-related patent term extensions, the availability of legal remedies in a particular jurisdiction and the validity and enforceability of the patent. No consistent policy regarding the scope of patent claims allowable in the field of genetic therapy has emerged in the United States. Moreover, patent laws and related enforcement in various jurisdictions outside of the United States are uncertain and may not protect our rights to the same extent as the laws of the United States. Changes in the patent laws and rules, whether by legislation, judicial decisions or regulatory interpretation, in the United States and other jurisdictions may diminish our ability to protect our inventions and obtain, maintain, defend and enforce our patent rights, and could therefore affect the value of our business.

The area of patent and other intellectual property rights in biotechnology is evolving and has many risks and uncertainties, and third parties may have blocking patents and other intellectual property that could be used to prevent us from commercializing our platforms and product candidates and practicing our proprietary technology. Our patent rights may be challenged, narrowed, circumvented, invalidated or ruled unenforceable, which could limit our ability to stop third parties from marketing and commercializing related platforms or product candidates or limit the term of patents that cover our platforms and product candidates. In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against third parties with similar technology, and third parties may independently develop similar technologies. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any competitive advantage provided by the patent. For this and other risks related to our proprietary technology, inventions, improvements, platforms and product candidates and intellectual property rights related to the foregoing, please see the section entitled “Risk factors—Risks related to our intellectual property.”

Patent term extensions

The term of individual patents depends upon the laws of the jurisdictions in which they are obtained. In most jurisdictions in which we file, the patent term is 20 years from the earliest date of filing of the first

non-provisional patent application to which the patent claims priority. However, the term of U.S. patents may be extended or adjusted for delays incurred due to compliance with FDA requirements or by delays encountered during prosecution that are caused by the United States Patent and Trademark Office, or the USPTO. For example, in the United States, a patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, for up to five years beyond the normal expiration date of the patent. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. For more information on patent term extensions, see "Business—Government regulation—Patent term restoration and extension". In the future, if and when any product candidates we may develop receive FDA approval, we expect to apply for patent term extensions on issued patents covering those product candidates. Moreover, we intend to seek patent term adjustments and extensions for any of our issued patents in any jurisdiction where such adjustments and extensions are available. However, there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such adjustments and extensions should be granted, and even if granted, the length of such adjustments and extensions.

Trade secrets

In addition to patent protection, we also rely on trade secrets, know-how, unpatented technology and other proprietary information to strengthen our competitive position. We take steps to protect and preserve our trade secrets and other confidential and proprietary information and prevent the unauthorized disclosure of the foregoing, including by entering into non-disclosure and invention assignment agreements with parties who have access to our trade secrets or other confidential and proprietary information, such as employees, consultants, outside scientific collaborators, contract research and manufacturing organizations, sponsored researchers and other advisors, at the commencement of their employment, consulting or other relationships with us. In addition, we take other appropriate precautions, such as maintaining physical security of our premises and physical and electronic security of our information technology systems, to guard against any misappropriation or unauthorized disclosure of our trade secrets and other confidential and proprietary information by third parties.

Despite these efforts, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or other confidential or proprietary information. In addition, we cannot provide any assurances that all of the foregoing non-disclosure and invention assignment agreements have been duly executed, and any of the counterparties to such agreements may breach them and disclose our trade secrets and other confidential and proprietary information. Although we have confidence in the measures we take to protect and preserve our trade secrets and other confidential and proprietary information, they may be inadequate, our agreements or security measures may be breached, and we may not have adequate remedies for such breaches. Moreover, to the extent that our employees, contractors, consultants, collaborators and advisors use intellectual property owned by others in their work for us, disputes may arise as to our rights in any know-how or inventions arising out of such work. For more information, please see the section entitled "Risk factors—Risks related to our intellectual property."

License agreements

We are a party to a number of license agreements under which we license patents, patent applications and other intellectual property from third parties. These licenses impose various diligence and financial payment

obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license agreements to be material to our business.

License agreement with the National Institutes of Health

In February 2017, we entered into a license agreement with the NIH, which was amended in July 2019 to include the French Institutions as licensors. Pursuant to the amended agreement, or the NIH Agreement, NIH and the French Institutions granted us a worldwide, non-exclusive license under a patent application family related to our ceDNA construct. This patent application family includes national stage patent applications in jurisdictions outside the United States, including Europe and Japan, and issued patents in each of the United States, Australia and Israel. The issued patents and any future patents issued from the pending patent applications would be scheduled to expire on various dates from March 2032 through October 2032, without taking into account any possible extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees. The non-exclusive license confers the right to make and have made, research and have researched, use and have used, sell and have sold, offer to sell and import products and to practice processes, in each case, covered by the licensed patents and patent applications, for the treatment, prevention or palliation of any human disease or condition.

Under the NIH Agreement, we are obligated to use reasonable commercial efforts to ensure that the licensed products and processes are utilized and made available to the public on reasonable terms, including pursuing commercially reasonable broad international patient accessibility for licensed gene therapy products for the treatment of rare diseases, in accordance with an agreed upon commercial development plan for gene therapy-based human therapeutics and certain performance milestone events. Unless terminated earlier, the NIH Agreement remains in effect until the last to expire of the licensed patent rights on a licensed product-by-licensed product and country-by-country basis. NIH and the French Institutions may terminate the NIH Agreement if we fail to perform our material obligations, including but not limited to our failure to meet the applicable performance milestones despite using commercially reasonable efforts, and have not remediated such deficiency within a specified time period. NIH and the French Institutions can terminate the NIH Agreement in the event we become insolvent, file a petition in bankruptcy, have such a petition filed against us, or determine to file a petition in bankruptcy. In addition, NIH and the French Institutions may terminate the NIH Agreement in the event of a material breach by us and failure to cure such breach within a certain period of time. We can voluntarily terminate the NIH Agreement with prior notice to NIH and the French Institutions.

As part of the NIH Agreement, we agreed to make milestone payments upon the achievement of certain milestones up to a maximum aggregate total of $350,000 for each licensed product, as well as a low single-digit royalty on net sales of licensed products. These royalty obligations last on a licensed product-by-licensed product and country-by-country basis until the expiration of the last licensed patent rights covering such licensed product in such country. In addition, if we sublicense rights under the NIH Agreement, we are required to pay a high single-digit percent of the sublicense revenue to NIH. Additionally, under the NIH Agreement, we may be required to reimburse the French Institutions for a portion of certain past and ongoing patent related expenses, including expenses associated with the preparation, filing, prosecution and maintenance of all patents and patent applications. As of March 31, 2020, there have been no invoiced expenses related to these reimbursable costs.

License Agreement with the University of Massachusetts

In June 2017, we entered into a license agreement with UMass pursuant to which UMass granted us an exclusive, worldwide license under a patent application family related to our ceDNA construct, which has pending national stage patent applications in the United States and certain foreign jurisdictions. In June 2020 Voyager became a joint owner with UMass of the licensed patent application family, and we entered into an

amendment to the UMass Agreement under which UMass, on behalf of Voyager, expanded the license granted to us to include an exclusive license to Voyager's rights in the licensed patent application family, subject to Voyager's retained non-exclusive rights to practice and exploit the licensed patent application family solely for its AAV gene therapy products. Any U.S. or foreign patents issued from the pending licensed U.S. or foreign patent applications would be scheduled to expire in March 2037, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees. The exclusive license confers the right to research, develop, manufacture, have manufactured, use, offer for sale, sell and import products and practice and have practiced processes, in each case, covered by the patent application family.

Unless terminated earlier, our license agreement with UMass, as amended, which we refer to as the UMass Agreement, will continue until the last-to-expire valid claim of the licensed patents. UMass may terminate the UMass Agreement if we fail to perform our material obligations, including but not limited to our failure to meet the applicable performance milestones despite using commercially reasonable efforts, and have not remediated such deficiency within a specified time period or negotiated a revised performance timeline. UMass can terminate the UMass Agreement if we fail to make any payments within a specified period after receiving written notice of such failure, or in the event of a material breach by us and failure to cure such breach within a certain period of time, provided that, if we fail to make payments due under the UMass Agreement more than a certain number of times, UMass may terminate the agreement immediately without any cure period. We can voluntarily terminate the UMass Agreement with prior notice to UMass.

Under the UMass Agreement, we agreed to use diligent efforts to develop the licensed products and introduce them into the commercial market and make them reasonably available to the public thereafter. Specifically, we agreed to achieve regulatory approval for and commercially launch at least one licensed product in the U.S. by certain specified dates.

As part of the UMass Agreement, we have issued to UMass 125,677 shares of our common stock. In addition, we may be obligated to make milestone payments up to $1,143,750 per licensed product that are contingent upon the achievement of certain regulatory and commercialization milestones, as well as low single-digit royalties on net sales of licensed products on a licensed product-by-licensed product and country-by-country basis. If we sublicense our rights under the UMass Agreement, we are required to pay a low-to-mid single-digit percentage of the license revenue to UMass, which will vary depending on when the sublicense agreement to a third party was executed. Royalty obligations under the UMass Agreement will continue until the expiration of the last valid claim of a licensed patent covering such licensed product in such country. As of March 31, 2020, we have recorded no royalty or milestone liabilities under the UMass Agreement.

Competition

The biotechnology and biopharmaceutical industries generally, and the genetic medicine field specifically, are characterized by rapid evolution of technologies, sharp competition and strong defense of intellectual property. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our technology, development experience and scientific knowledge in the field of gene therapy, nucleic acid delivery and manufacturing provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions.

There are numerous companies that are selling or developing genetic medicines, including in indications for which we may develop our non-viral gene therapies. These companies include viral gene therapy companies

such as BioMarin Pharmaceuticals, Inc., Homology Medicines, Inc., Adverum Biotechnologies, Inc. and Hoffmann La Roche Ltd.; gene editing companies such as CRISPR Therapeutics, AG and Intellia Therapeutics, Inc.; and mRNA companies such as Moderna, Inc.

Many of our competitors, either independently or with strategic partners, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than we are in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approval for treatments and achieving widespread market acceptance. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than products we may develop. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our products. In addition, our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of other drugs. The key competitive factors affecting the successful of all any products we may develop are likely to be their efficacy, safety, convenience, price and availability of reimbursement.

Government regulation

Government authorities in the United States, at the federal, state and local level and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, sales, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting and import and export of pharmaceutical products, including biological products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and regulation of biologics in the United States

In the United States, any product candidates we may develop would be regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations and guidance. The failure to comply with the applicable U.S. requirements at any time during the product development process, including preclinical testing, clinical testing, the approval process, or post-approval process, may subject an applicant to delays in the conduct of the study, regulatory review and approval and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA’s refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension, or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines and civil or criminal investigations and penalties brought by the FDA or the Department of Justice, or DOJ, and other governmental entities, including state agencies.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practices, or GLP regulations;
- completion of the manufacture, under cGMP conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current Good Clinical Practices, or GCP;
- preparation and submission to the FDA of a BLA for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labelling;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the preclinical studies and clinical trial sites to assure compliance with GLP, as applicable, and GCP, and the integrity of clinical data in support of the BLA;
- payment of user Prescription Drug User Fee Act, or PDUFA, securing FDA approval of the BLA and licensure of the new biologic product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and any post-approval studies or other post-marketing commitments required by the FDA.

Preclinical studies and investigational new drug application

Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In

that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin or recommence.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND review process, it may choose to impose a partial or complete clinical hold. Clinical holds are imposed by the FDA whenever there is concern for patient safety, may be a result of new data, findings, or developments in clinical, preclinical and/or chemistry, manufacturing and controls or where there is non-compliance with regulatory requirements. This order issued by the FDA would delay either a proposed clinical trial or cause suspension of an ongoing trial, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing our planned clinical trial or future clinical trials in a timely manner.

Additionally, gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH also are potentially subject to review by a committee within the NIH's Office of Science Policy called the Novel and Exceptional Technology and Research Advisory, or the NExTRAC. As of 2019, the charter of this review group has evolved to focus public review on clinical trials that cannot be evaluated by standard oversight bodies and pose unusual risks. With certain gene therapy protocols, FDA review of or clearance to allow the IND to proceed could be delayed if the NExTRAC decides that full public review of the protocol is warranted. The FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

Expanded access to an investigational drug for treatment use

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy publicly available. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and

biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 trial; or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act.

Human clinical trials in support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease or condition to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain regulatory requirements of the FDA in order to use the trial as support for an IND or application for marketing approval. Specifically, the FDA requires that such trials be conducted in accordance with GCP, including review and approval by an independent ethics committee and informed consent from participants. The GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign trials are conducted in a manner comparable to that required for clinical trials in the United States.

Further, each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, or DSMB. This group may recommend continuation of the trial as planned, changes in trial conduct, or cessation of the trial at designated check points based on certain available data from the trial to which only the DSMB has access. Finally, research activities involving infectious agents, hazardous chemicals, recombinant DNA and genetically altered organisms and agents may be subject to review and approval of an Institutional Biosafety Committee, or IBC, in accordance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.
- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.
- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are referred to as “pivotal.”

In some cases, the FDA may approve a BLA for a product but require the sponsor to conduct additional clinical trials to further assess the product’s safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement or to request a change in the product labeling. The failure to exercise due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA’s internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after FDA’s receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation

Act. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Information about applicable clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Special regulations and guidance governing gene therapy products

We expect that the procedures and standards applied to gene therapy products will be applied to any product candidates we may develop. The FDA has defined a gene therapy product as one that seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the OTAT and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The NIH, including the NExTRAC also advises the FDA on gene therapy issues and other issues related to emerging biotechnologies. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

The FDA has issued various guidance documents regarding gene therapies, including recent final guidance documents released in January 2020 relating to chemistry, manufacturing and controls information for gene therapy INDs, long-term follow-up after the administration of gene therapy products, gene therapies for rare diseases and gene therapies for retinal disorders. Although the FDA has indicated that these and other guidance documents it previously issued are not legally binding, compliance with them is likely necessary to gain approval for any gene therapy product candidate. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the chemistry, manufacturing and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe for potential delayed adverse effects in participants who have received investigational gene therapies with the duration of follow-up based on the potential for risk of such effects. For AAV vectors specifically, the FDA typically recommends that sponsors continue to monitor participants for potential gene therapy-related adverse events for up to a 5-year period.

Until 2019, most gene therapy clinical trials in the United States required pre-review by the predecessor of NExTRAC before being approved by the IRBs and any local biosafety boards or being allowed to proceed by FDA. In 2019, the NIH substantially eliminated the pre-review process and going forward, the review of gene therapy clinical trial protocols would be largely handled by local IRBs and IBCs, in addition to FDA. Furthermore, in 2019, the NIH removed from public access the Genetic Modification Clinical Research Information System database, which previously contained substantial amounts of safety and other participant information regarding human gene therapy trials performed up to that time.

Compliance with cGMP requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

Review and approval of a BLA

The results of product candidate development, preclinical testing and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2020 is $2,942,965 for an application requiring clinical data. The sponsor of a licensed BLA is also subject to an annual program fee, which for fiscal year 2020 is $325,424. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure and potent, and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure and potent. On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of preclinical and clinical trial sites to assure compliance with GCPs, 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. If the application is not approved, the FDA will issue a complete response letter, which will contain the conditions that must be met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by an applicant in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed.

The FDA may also refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

If the FDA approves a new product, it may limit the approved indication(s) for use of the product. It may also require that contraindications, warnings, or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's efficacy and/or safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast track, breakthrough therapy, priority review and regenerative medicine advanced therapy designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative medicine advanced therapy, or RMAT, designation. These designations are not mutually exclusive, and a product candidate may qualify for one or more of these programs. While these programs are intended to expedite product development and approval, they do not alter the standards for FDA approval.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough

therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner. Breakthrough designation may be rescinded if a product no longer meets the qualifying criteria.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months. Priority designation may be rescinded if a product no longer meets the qualifying criteria.

With passage of the Cures Act in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative medicine advanced therapies. A product is eligible for RMAT designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. In a recent guidance on expedited programs for regenerative medicine therapies for serious conditions, FDA specified that its interpretation of the definition of regenerative medicine advanced therapy products includes gene therapies that lead to a sustained effect on cells or tissues, such as *in vivo* AAV vectors delivered to non-dividing cells. The benefits of a regenerative medicine advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review, and accelerated approval based on surrogate or intermediate endpoints. RMAT designation may be rescinded if a product no longer meets the qualifying criteria.

Accelerated approval pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint

is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, confirm a clinical benefit during post-marketing studies or dissemination of false or misleading promotional materials would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Post-approval regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA have imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of 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 ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. 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 holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product recall, seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Although healthcare providers may prescribe products for uses not described in the drug's labeling, known as off-label uses, in their professional judgment, drug manufacturers are prohibited from soliciting, encouraging or promoting unapproved uses of a product. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such off-label uses because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Orphan drug designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for treatment of rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development

at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and the FDA has issued recent draft guidance suggesting that it would not consider two gene therapy products to be different drugs solely based on minor differences in the transgenes or vectors within a given vector class. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

Pediatric exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity that cover the product are extended by six months.

Biosimilars and exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. A biosimilar is a biological product that is highly similar to an existing FDA-licensed "reference product." As of January 1, 2020, the FDA has approved 26 biosimilar products for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by the FDA in the near term.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is “biosimilar to” or “interchangeable with” a previously approved biological product or “reference product.” In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their 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. Since the passage of the BPCIA, many states have passed laws or amendments to laws, including laws governing pharmacy practices, which are state-regulated, to regulate the use of biosimilars.

Federal and state data privacy and security laws

Under the federal Health Insurance Portability and Accountability Act of 1966, or HIPAA, the U.S. Department of Health and Human Services, or HHS, has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 or HITECH, and their regulations, including the omnibus final rule published on January 25, 2013, also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that are applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney’s fees and costs associated with pursuing federal civil actions. Accordingly, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA’s privacy and security rules. New laws and regulations governing privacy and security may be adopted in the future as well.

Additionally, California recently enacted legislation that has been dubbed the first “GDPR-like” law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. The CCPA could impact our business activities depending on how it is interpreted and exemplifies the

vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Patent term restoration and extension

In the United States, a patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which the extension is sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND involving human beings and the submission date of the BLA, plus the time between the submission date of the BLA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA.

FDA approval of companion diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion,

sales and distribution, export and import and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2020, the standard fee is $340,995 and the small business fee is $85,249.

Regulation and procedures governing approval of medicinal products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical trial approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, but it has not yet become effective. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications. As of January 1, 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME designation in the European Union

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated EMA contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies are appointed early in the PRIME scheme facilitating increased understanding of the product at the EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing authorization

To obtain a marketing authorization for a product under the European Union regulatory system, an applicant must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in European Union Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Manufacturers must demonstrate the quality, safety and efficacy of their products to the EMA, which provides an opinion regarding the MAA. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Specifically, the grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety and efficacy of their products to EMA which

provides an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Specialized procedures for gene therapies

The grant of marketing authorization in the European Union for gene therapy products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC includes specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety and efficacy of their products to the EMA, which provides an opinion regarding the MAA. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Regulatory data protection in the European Union

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Patent term extensions in the European Union and other jurisdictions

The European Union also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country

basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Periods of authorization and renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the European Union market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Regulatory requirements after marketing authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

Orphan drug designation and exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized European Union marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized

therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

Brexit and the regulatory framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020, which is extendable up to two years. Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the UK will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for any product candidates we may develop, which could significantly and materially harm our business.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that “implements” and complements the EU General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. During the period of “transition” (i.e., until December 31, 2020), EU law will continue to apply in the UK, including the GDPR, after which the GDPR will be converted into UK law. Beginning in 2021, the UK will be a “third country” under the GDPR. We may, however, incur liabilities, expenses, costs and other operational losses under GDPR and applicable European Union Member States and the United Kingdom privacy laws in connection with any measures we take to comply with them.

General Data Protection Regulation

The collection, use, disclosure, transfer or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may

increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payers to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates we may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payers, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payer will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payer will pay for the product once coverage is approved. Third-party payers are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payers may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payer not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payer's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a product does not assure that other payers will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payer to payer. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. In addition, any companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to any companion diagnostics.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

If we obtain approval in the future to market in the United States any product candidates we may develop, we may be required to provide discounts or rebates under government healthcare programs or to certain

government and private purchasers in order to obtain coverage under federal healthcare programs such as Medicaid. Participation in such programs may require us to track and report certain drug prices. We may be subject to fines and other penalties if we fail to report such prices accurately.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare law and regulation

Healthcare providers and third-party payers play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payers and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or

causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal civil monetary penalty and false statement laws and regulations relating to pricing and submission of pricing information for government programs, including penalties for knowingly and intentionally overcharging 340b eligible entities and the submission of false or fraudulent pricing information to government entities;
- HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, on certain covered healthcare providers, health plans and healthcare clearinghouses, as well as their respective business associates that perform services for them, that involve the use, or disclosure of, individually identifiable health information, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits 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;
- the Foreign Corrupt Practices Act, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, or PPACA, as amended by the Health Care Education Reconciliation Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payers, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. In addition, certain state and local laws require drug manufacturers to register pharmaceutical sales representatives. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations and the curtailment or restructuring of our operations.

Healthcare reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the PPACA, which, among other things, includes changes to the coverage and payment for products under government healthcare programs. Among the provisions of the PPACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- 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;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products. However, the IPAB implementation has been not been clearly defined. The PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a

targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to two percent per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, which was enacted in January 2013, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the PPACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the PPACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. One Executive Order directs federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the PPACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in PPACA risk corridor payments to third-party payers who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payers, the viability of the PPACA marketplace, providers and potentially our business, are not yet known.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the PPACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the PPACA is unconstitutional and it remanded the case to the district court for reconsideration of

the severability question and additional analysis of the provisions of the PPACA. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which are expected to occur in the fall. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending and drug price increases. On March 10, 2020, the current presidential administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for any product candidates we may develop or additional pricing pressures.

There have been, and likely will continue to be, additional legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Employees

As of April 30, 2020, we had more than 85 full-time employees, including a total of 32 employees with M.D. or Ph.D. degrees. Of these full-time employees, approximately 67 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

Our principal facilities consist of office and laboratory space. We occupy approximately 71,562 square feet of office space in Cambridge, Massachusetts under a lease that currently expires on April 30, 2029.

Legal proceedings

We are not currently subject to any material legal proceedings.

Management

Executive officers and directors

The following table sets forth the name, age and position of each of our executive officers and directors as of April 30, 2020.

Name	Age	Position
Executive Officers		
Geoff McDonough, M.D.	49	President and Chief Executive Officer, Director
Stephen DiPalma	61	Interim Chief Financial Officer
Matthew Stanton, Ph.D.	47	Chief Scientific Officer
Mark Angelino, Ph.D.	47	Chief Operating Officer
Douglas Kerr, M.D., Ph.D., M.B.A.	53	Chief Development Officer
Non-Employee Directors		
Jason Rhodes (2)(3)	50	Chairman of the Board of Directors
Catherine Stehman-Breen, M.D. (2)	57	Director
Gustav Christensen (1)	72	Director
Jeffrey Jonas, M.D. (3)	67	Director
Donald Nicholson, Ph.D. (2)	63	Director
Charles Rowland (1)	61	Director
Anthony Quinn, M.B. Ch.B., Ph.D. (1)(3)	58	Director

(1) Member of the Audit Committee.
(2) Member of the Talent Committee.
(3) Member of the Nominating and Corporate Governance Committee.

Executive officers

Geoff McDonough, M.D. has served as our president and chief executive officer and as a member of our board of directors since October 2017. Previously, Dr. McDonough served as president and chief executive officer of Swedish Orphan Biovitrum AB, or Sobi, a biopharmaceutical company, from August 2011 until May 2017. Dr. McDonough serves on the boards of directors of Surface Oncology, Inc., a biotechnology company, and Zafgen, Inc., a biopharmaceutical company. Dr. McDonough earned a Bachelor of Science in biology and a Bachelor of Arts in philosophy, both summa cum laude, from University of North Carolina at Chapel Hill. Dr. McDonough earned his M.D. at Harvard Medical School and completed his residency training in internal medicine and pediatrics at Massachusetts General Hospital and Boston Children's Hospital. We believe that Dr. McDonough's extensive leadership experience in the life sciences industry and his extensive knowledge of our company based on his role as our president and chief executive officer qualify him to serve as a member of our board of directors.

Stephen DiPalma, M.B.A. has served as our interim chief financial officer since September 2019, by agreement with Danforth Advisors, LLC, or Danforth, a financial consultancy firm specializing in working with life sciences companies. Mr. DiPalma has served as a Managing Director at Danforth since April 2014. Prior to and during his tenure at Danforth, Mr. DiPalma served as the chief financial officer and finance lead of eight public companies, and has served as chief financial officer, chief operating officer, chief executive officer or director of eight privately-held companies. Mr. DiPalma earned a Bachelor of Science from the University of Massachusetts-Lowell and an M.B.A. from Babson College.

Matthew Stanton, Ph.D. has served as our chief scientific officer since May 2019. Previously, Dr. Stanton served as our chief technology officer from October 2017 to May 2019. Prior to joining us, Dr. Stanton served as vice

president, head of chemistry and platform immunology at Moderna, Inc., a biotechnology company, from April 2014 until September 2017. Dr. Stanton earned a Bachelor of Science in chemistry from Virginia Tech, a Master of Science in chemistry and a doctorate in chemistry with a focus on physical organic chemistry and natural product synthesis from the University of North Carolina at Chapel Hill.

Mark Angelino, Ph.D. co-founded our company and has served as our chief operating officer since our inception in October 2016. Prior to co-founding our company, Dr. Angelino was senior vice president of development and manufacturing at bluebird bio Inc., a biotechnology company, from April 2012 until October 2016. Dr. Angelino earned a Bachelor of Science in chemical engineering from The Cooper Union, and both a M.Sc. in chemical engineering practice and a doctorate in chemical engineering from the Massachusetts Institute of Technology.

Douglas Kerr, M.D., Ph.D., M.B.A. has served as our chief development officer since May 2019. Previously, Dr. Kerr served as our chief scientific officer and executive vice president of research and development from August 2017 to May 2019. Prior to joining us, Dr. Kerr served as global development team lead and vice president for neurology at Shire plc, a biopharmaceutical company, from October 2015 to August 2017. Dr. Kerr earned a B.A. degree in biochemistry from Princeton University and, an M.B.A. with a specialization in entrepreneurship and finance from Northeastern University and an M.D. from Jefferson Medical College, as well as a doctorate in biochemistry and molecular biology.

Non-employee directors

Jason Rhodes has served as the chairman of our board of directors since October 2017 and served as our founding chief executive officer from October 2016 to October 2017. Mr. Rhodes has been a partner at Atlas Venture since 2014. From 2010 to 2014, Mr. Rhodes was at Epizyme, Inc., a biotechnology company, where he most recently served as President and Chief Financial Officer. Mr. Rhodes has been a member of the board of directors of Replimune Group, Inc. since September 2015. Mr. Rhodes earned a B.A. from Yale University and an M.B.A. from the Wharton School of the University of Pennsylvania. We believe Mr. Rhodes is qualified to serve on our Board based on his extensive knowledge of our company based on his role as the founding chief executive officer, as well as his extensive leadership experience, his biotechnology company board experience and his experience investing in life science companies.

Catherine Stehman-Breen, M.D. has served as a member of our board of directors since December 2017. Dr. Stehman-Breen has served as chief development officer of Obsidian Therapeutics, Inc., a biotechnology company, since July 2019. Previously, she served as an entrepreneur-in-residence at Atlas Ventures, serving as chief medical officer of both Dyne Therapeutics, Inc., a biotechnology company, from March 2018 to July 2019 and Disarm Therapeutics, Inc., a biotechnology company, from April 2018 to July 2019. Dr. Stehman-Breen also served as chief medical officer of Sarepta Therapeutics, Inc. from April 2017 to December 2017. Prior to that, Dr. Stehman-Breen served as vice president, clinical development and regulatory affairs at Regeneron Pharmaceuticals, Inc., a biotechnology company, initially as head, pain therapeutic area, and subsequently as head, clinical project management and operations from January 2015 to March 2017. Dr. Stehman-Breen earned a B.A. in biology and psychology from Colby College, a M.Sc. degree in epidemiology from the University of Washington, where she also conducted her residency and fellowship training, and a M.D. from the University of Chicago. We believe Dr. Stehman-Breen is qualified to serve on our Board based on her extensive leadership experience, her experience with clinical development and regulatory matters, and in the life science industry.

Gustav Christensen has served as a member of our board of directors since December 2017. Mr. Christensen has served as the chairman of the board of directors of Morphic Holding, Inc., since April 2016. Previously, Mr. Christensen served as the president and chief executive officer and director at Dyax Corp., a biopharmaceutical company, from April 2007 to February 2016. Mr. Christensen earned a M.Sc. in Economics from the University of Aarhus (Denmark) and his M.B.A. from Harvard Business School. We believe that

Mr. Christensen is qualified to serve on our board of directors due to his extensive leadership and business experience in the life sciences industry and in the commercialization of pharmaceutical products.

Jeffrey Jonas, M.D. has served as a member of our board of directors since May 2018. Dr. Jonas has served as the chief executive officer, president and a member of the board of directors of Sage Therapeutics, Inc., a biopharmaceutical company, since August 2013. Dr. Jonas has served on the board of directors of Karuna Pharmaceuticals, Inc. since October 2018. Dr. Jonas earned his B.A. from Amherst College and M.D. from Harvard Medical School. He completed a residency in psychiatry at Harvard Medical School, and he served as Chief Resident in psychopharmacology at McLean Hospital, Harvard Medical School. We believe Dr. Jonas' is qualified to serve on our Board based on his extensive leadership experience, his experience with clinical development and regulatory matters, and in the life science industry.

Donald Nicholson, Ph.D. has served as a member of our board of directors since December 2017. Previously, Dr. Nicholson served as chief executive officer of Nimbus Therapeutics, Inc., a biotechnology company, from August 2014 to October 2018. Prior to that, Dr. Nicholson spent 25 years at Merck & Co., Inc., in various leadership, strategic and operational roles. Dr. Nicholson earned his B.S. with honors in biochemistry and his doctorate in biochemistry from the University of Western Ontario and trained as a Medical Research Council postdoctoral fellow at the University of Munich in Germany. We believe Dr. Nicholson's extensive experience in both scientific and management roles in the life sciences industry qualifies him to serve on our board of directors.

Charles Rowland has served as a member of our board of directors since July 2018. Mr. Rowland served as chief executive officer and director of Aurinia Pharmaceuticals Inc., a biopharmaceutical company, from January 2014 to February 2017. Mr. Rowland currently serves as a member of the boards of directors of Orchard Therapeutics plc, since June 2018, Viking Therapeutics, Inc., since July 2016, Blueprint Medicines Corporation, since March 2015, and Nabriva Therapeutics plc, since January 2015. Mr. Rowland earned his B.S. from Saint Joseph's University and M.B.A. from Rutgers University. We believe that Mr. Rowland is qualified to serve as a director due to his extensive experience in pharmaceutical operations and as well as in finance and accounting.

Anthony Quinn, M.B. Ch.B., Ph.D. has served as a member of our board of directors since December 2017. Dr. Quinn has served as president and chief executive officer and as a director of Aeglea BioTherapeutics, Inc., a biotechnology company since July 2017. Prior to that, from October 2015 to July 2017 he worked as a private consultant for IDBioPharm Consulting LLC, a consulting firm. From August 2009 to June 2015, Dr. Quinn served in several roles at Synageva BioPharma Corp., a biotechnology company that was acquired by Alexion Pharmaceuticals, Inc. in June 2015, including most recently as head of research & development and chief medical officer. Following the acquisition, Dr. Quinn worked for Alexion Pharmaceuticals, Inc., a pharmaceutical company, from June 2015 to September 2015. Dr. Quinn has also served on the board of directors of Kaleido BioSciences, Inc., since February 2016. Dr. Quinn received his Bachelor of Medical Sciences in general pathology, his MB ChB (M.D.) from the University of Dundee, UK. and his Ph.D. in cancer research from the University of Newcastle in Tyne, UK. We believe Dr. Quinn is qualified to serve on our board of directors because of his medical and clinical experience in the biopharmaceutical industry, including experience in the development of therapeutics for rare diseases.

Board composition and election of directors

Board composition

Our board of directors currently consists of eight members. Our directors hold office until their successors have been elected and qualified or until the earlier of their death, resignation or removal.

Our certificate of incorporation and bylaws that will become effective upon the closing of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors. Our certificate of incorporation and bylaws will also provide that our directors may be removed only for cause by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

In accordance with the terms of our certificate of incorporation and bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be Geoff McDonough, Jeffrey Jonas and Donald Nicholson, and their term will expire at the annual meeting of stockholders to be held in 2021;
- the class II directors will be Anthony Quinn and Jason Rhodes, and their term will expire at the annual meeting of stockholders to be held in 2022; and
- the class III directors will be Gustav Christensen, Charles Rowland and Catherine Stehman-Breen, and their term will expire at the annual meeting of stockholders to be held in 2023.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

The classification of our board of directors may have the effect of delaying or preventing changes in our control or management. See “Description of capital stock—Delaware anti-takeover law and certain charter and bylaw provisions.”

Director independence

Applicable Nasdaq rules require a majority of a listed company’s board of directors to be comprised of independent directors within one year of listing. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company’s audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an “independent director” if, in the opinion of the listed company’s board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director’s ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In May 2020, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Dr. McDonough, is an “independent director” as defined under applicable Nasdaq rules, including, in the case of all the members of our audit committee, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all the members of our talent committee, which serves as our compensation committee, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. McDonough is not an independent director under these rules because he is our president and chief executive officer.

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

Role of the board in risk oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through the 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. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. The audit committee also monitors compliance with legal and regulatory requirements.

Board committees

Our board of directors has established an audit committee, a talent committee and a nominating and corporate governance committee, each of which operates under a charter that has been approved by our board.

Audit committee

The members of our audit committee are Charles Rowland, Gustav Christensen and Anthony Quinn, and Charles Rowland is the chair of the audit committee. Our audit committee’s responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;

- overseeing our internal audit function;
- overseeing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities and Exchange Commission, or SEC, rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Charles Rowland is an "audit committee financial expert" as defined by applicable SEC rules and that each of the members of our audit committee possesses the financial sophistication required for audit committee members under Nasdaq rules. We believe that the composition of our audit committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Talent committee

The members of our talent committee are Jason Rhodes, Donald Nicholson and Catherine Stehman-Breen, and Jason Rhodes is the chair of the talent committee. The talent committee serves as the compensation committee of our board. Our talent committee's responsibilities include:

- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and making recommendations to our board of directors with respect to management succession planning;
- reviewing and discussing annually with management our "Compensation discussion and analysis" disclosure if and to the extent required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

We believe that the composition of our talent committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Nominating and corporate governance committee

The members of our nominating and corporate governance committee are Jason Rhodes, Jeffrey Jonas and Anthony Quinn, and Jason Rhodes is the chair of the nominating and corporate governance committee. Our nominating and corporate governance committee's responsibilities include:

- recommending to our board of directors the persons to be nominated for election as directors and to each of our board's committees;

- reviewing and making recommendations to our board of directors with respect to our board leadership structure;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing a periodic evaluation of our board of directors.

We believe that the composition of our nominating and corporate governance committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Compensation committee interlocks and insider participation

No member of our talent committee is or has been a current or former officer or employee of our company. None of our executive officers serves, or in the past year has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our talent committee.

Code of ethics and code of conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions. We have posted a current copy of the code on our website, www.generationbio.com. In addition, we have posted on our website all disclosures that are required by law or Nasdaq listing standards concerning any amendments to, or waivers from, any provision of the code.

Executive compensation

The following discussion relates to the compensation of our president and chief executive officer, Geoff McDonough, our chief development officer, Douglas Kerr, and our former chief financial officer, Thomas Graney, for the fiscal year ended December 31, 2019. Dr. McDonough, Dr. Kerr and Mr. Graney are collectively referred to in this prospectus as our named executive officers.

In preparing to become a public company, we have begun a thorough review of all elements of our executive compensation program, including the function and design of our equity incentive programs. We have begun, and expect to continue in the coming months, to evaluate the need for revisions to our executive compensation program to ensure that our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

Summary compensation table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers during our fiscal year ended December 31, 2019.

Name and Principal Position	Year	Salary($)	Bonus($) (1)	Option awards($) (2)	Total($)
Geoff McDonough *President and Chief Executive Officer*	2019	423,500	169,400	—	592,900
Douglas Kerr *Chief Development Officer*	2019	396,069	138,624	—	534,693
Thomas Graney *Former Chief Financial Officer*	2019	313,060(3)	112,551	1,853,243	2,278,854

(1) The amounts reported in the “Bonus” column reflect discretionary annual cash bonuses earned by each of our named executive officers for their performance, as determined by the board of directors in its sole discretion.

(2) The amounts reported in the “Option awards” column reflect the aggregate grant-date fair value of stock options awarded in 2019, calculated in accordance with the provisions of the Financial Accounting Standard Board Accounting Standards Codification Topic 718. See Note 8 to our consolidated financial statements appearing elsewhere this prospectus regarding assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(3) Mr. Graney’s salary was prorated to reflect the portion of the calendar year during which he was employed with us, taking into account the portion of the year in which Mr. Graney was a full-time employee. His salary also includes $50,000 paid under a consulting agreement before the commencement of his employment with us.

Narrative to summary compensation table

Base salary. During 2019, the annualized base salaries for Dr. McDonough, Dr. Kerr and Mr. Graney were $423,500, $396,069 and $375,000, respectively. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Annual bonus. Our board of directors may, in its discretion, award bonuses to our named executive officers from time to time. We typically establish annual bonus targets based on specified corporate goals and individual performance and conduct annual performance reviews to assess individual performance. Each of our named executive officers was eligible to receive an annual bonus for 2019, with the target amount of such

bonus for each named executive officer set forth in his employment or letter agreement with us. For 2019, the target bonus amounts, expressed as a percentage of base salary, for each of Dr. McDonough, Dr. Kerr and Mr. Graney were as follows: 40%, 35% and 35%, respectively.

With respect to 2019, our board of directors awarded bonuses of $169,400, $138,624 and $112,551 to Dr. McDonough, Dr. Kerr and Mr. Graney, respectively, with the bonus for Mr. Graney pro-rated to reflect the portion of the calendar year during which he was employed by us.

Equity incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executive officers with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executive officers and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our executive officers, including our named executive officers, and from time to time may grant equity incentive awards to them in the form of stock options.

We granted an option to purchase 435,937 shares of our common stock to Mr. Graney in February 2019 in connection with him joining the company as chief financial officer. This option vested as to 25% of the shares underlying the option January 5, 2020, and then an additional 6.25% of the shares underlying the option in quarterly installments thereafter, subject to continuous service. When Mr. Graney's employment with us ended on April 10, 2020, 25% of the unvested portion of his option vested and the remainder was cancelled.

Prior to this offering, our executive officers were eligible to participate in our 2017 Stock Incentive Plan, as amended, or the 2017 Plan. All stock options were granted pursuant to the 2017 Plan. We did not grant any restricted stock awards during 2019. Following this offering, our employees and executive officers will be eligible to receive stock options and other equity awards pursuant to our 2020 Stock Incentive Plan, or the 2020 Plan.

We have used stock options to compensate our executive officers in the form of initial grants in connection with the commencement of employment. Prior to this offering, awards of stock options and restricted stock to our executive officers have been made by our board of directors. The options and restricted stock that we have granted to our executive officers are typically subject to time-based vesting, generally over four years following the vesting commencement date. Upon certain terminations of employment in connection with a change of control, vesting is fully accelerated; upon other involuntary terminations, 25% of the unvested portion of each grant will vest as of the date of the termination. Prior to the exercise of a stock option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

We have historically awarded stock options with exercise prices that are equal to the fair market value of our common stock on the date of grant as determined by our board of directors.

Outstanding equity awards at fiscal year-end

The following table sets forth information regarding all outstanding equity awards for each of our named executive officers as of December 31, 2019:

	Option awards				Stock awards	
Name	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price ($)	Option expiration date	Number of shares of stock that have not vested (#)	Market value of shares of stock that have not vested ($)(1)
Geoff McDonough	—	—	—	—	807,969(2)	15,351,411
Douglas Kerr	46,409	77,351(3)	4.60	4/2/2028	155,382(4)	2,952,258
Thomas Graney	—	435,937(5)	4.60	(6)	—	—

(1) The market price of our common stock is based on the initial public offering price of $19.00 per share.

(2) Dr. McDonough's restricted stock award for 1,592,311 shares vests over four years, with 25% of the shares vesting on October 16, 2017, and the remainder vesting in equal quarterly installments thereafter, subject to continuous service. The vesting of this restricted stock award will accelerate upon a qualifying termination of Dr. McDonough's employment.

(3) Dr. Kerr's option award for 123,760 shares vests over four years, with 25% of the shares vesting on April 2, 2019, and the remainder vesting in equal quarterly installments thereafter, subject to continuous service. The vesting of this option award will accelerate upon a qualifying termination of Dr. Kerr's employment.

(4) Dr. Kerr's restricted stock awards vest over four years, (i) with respect to the award for 226,462 shares, 25% of the shares vested on August 14, 2018, and (ii) with respect to the award for 100,096 shares, 25% of the shares vested on January 4, 2019, with each of (i) and (ii) vesting in equal quarterly installments thereafter, subject to continuous service. The vesting of these restricted stock awards will accelerate upon a qualifying termination of Dr. Kerr's employment.

(5) Mr. Graney's option award for 435,937 shares vested as to 25% of the shares underlying the option on January 5, 2020, and vested as to an additional 6.25% of the shares underlying the option in quarterly installments thereafter, subject to continuous service. When Mr. Graney's employment with us ended on April 10, 2020, an additional 25% of the unvested portion of his option award vested and the remainder was cancelled.

(6) In connection with the termination of Mr. Graney's employment, his option expiration date was extended to the earlier of (i) 18 months after Mr. Graney's separation on April 10, 2020 or (ii) 30 days after the closing of our initial public offering.

Agreements with our named executive officers

Offer Letters

Geoff McDonough

In October 2017, in connection with our appointment of Dr. McDonough as our Chief Executive Officer, we entered into an offer letter with Dr. McDonough. The offer letter established Dr. McDonough's title, his base salary, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally and also provided for certain benefits upon termination of his employment under specified conditions. Dr. McDonough's employment is at will. Pursuant to the offer letter, we granted Dr. McDonough a restricted stock award for 1,592,311 shares of our common stock, which is subject to service-based vesting, and agreed to grant to him additional restricted stock awards or stock options to maintain his ownership percentage in the company until such time as we had sold equity having an aggregate purchase price of $50,000,000. Effective upon the closing of this offering, Dr. McDonough's base salary will be set at $566,500 and his target bonus percentage for 2020 will be 55%.

Douglas Kerr

In June 2017, in connection with our appointment of Dr. Kerr as our Chief Scientific Officer, we entered into an offer letter with Dr. Kerr. The offer letter established Dr. Kerr's title, his base salary, his eligibility for an annual

bonus, and his eligibility for benefits made available to employees generally and also provided for certain benefits upon termination of his employment under specified conditions. Dr. Kerr's employment is at will. Pursuant to the offer letter, we granted Dr. Kerr a restricted stock award for 226,462 shares of our common stock, which is subject to service-based vesting, and agreed to grant to him additional restricted stock awards or stock options to maintain his ownership percentage in the company until such time as we had sold equity having an aggregate purchase price of $10,000,000. Subsequently in May 2019, we entered into a promotion letter agreement with Dr. Kerr to establish his title as Chief Development Officer. Effective upon the closing of this offering, Dr. Kerr's base salary will be set at $408,400 and his target bonus percentage for 2020 will be 40%.

Thomas Graney

In December 2018, we entered into an offer letter with Mr. Graney, which provided for the appointment of Mr. Graney as our Chief Financial Officer as of February 2019. The offer letter established Mr. Graney's title, his base salary, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally and also provided for certain benefits upon termination of his employment under specified conditions. Mr. Graney's employment was at will. Pursuant to the offer letter, we granted Mr. Graney a stock option award for 435,937 shares of our common stock.

In January 2019, we entered into a Consulting Agreement with Mr. Graney, pursuant to which Mr. Graney served as a consultant to the Company until his appointment as Chief Financial Officer in February 2019.

In January 2020, we entered into a separation letter with Mr. Graney under which Mr. Graney took a short-term disability leave and subsequently resigned as Chief Financial Officer of the Company in April 2020. Pursuant to the separation letter, at the time of Mr. Graney's resignation, and subject to his execution of a general release of potential claims against us, we agreed to continue to pay Mr. Graney's then-current base salary for a period of six months and to pay premiums for continuation of health coverage under COBRA for up to six months. In addition, we agreed to accelerate the vesting of any outstanding equity grants by 25% of the then unvested portion of those grants, and to provide an extended exercise window for such vested and outstanding options.

Severance upon termination of employment; change in control

In May 2020, we entered into a severance plan benefits agreement with certain of our executive officers, including Dr. McDonough and Dr. Kerr. The separation benefits provided in the severance benefits plan agreement superseded the separation benefits provided under the terms of each executive officer's offer letter. Under the terms of the severance benefits agreement, if the executive officer's employment is terminated by us without cause or by the executive officer for good reason prior to or more than 12 months following a change in control, each as defined in the agreement, and subject to the executive officer's execution of a general release of potential claims against us, we have agreed to continue to pay his then-current base salary for a period of 12 months, in the case of our chief executive officer, or nine months, in the case of our other executive officers, and to pay premiums for continuation of health coverage under COBRA for up to 12 months, in the case of our chief executive officer, or nine months, in the case of our other executive officers. In addition, we have agreed that we may pay such executive officer a bonus for the year in which his employment is terminated determined by reference to the officer's target annual incentive bonus for the year in which his termination of employment occurs and based on our and the executive officer's performance for such year, as determined by our board of directors in its sole discretion, and prorated based on the number of days the executive officer was actually employed by us for the year in which his termination occurs, and that we will accelerate the vesting of any then-outstanding equity grants held by the executive officer by 25% of the then unvested portion of those grants. Alternatively, if the executive officer's employment is terminated by us without cause or by the executive officer

for good reason within one year following a change in control, and subject to the executive officer's execution of a general release of potential claims against us, we have agreed, in the case of our chief executive officer, to continue to pay his then-current base salary for a period of 18 months and, in the case of our other executive officers, to pay the executive officer a lump sum amount equal to 12 months of his then-current base salary; to pay premiums for continuation of health coverage under COBRA for up to 18 months, in the case of our chief executive officer, or 12 months, in the case of our other executive officers; and to pay a lump sum bonus equal to 150%, in the case of our chief executive officer, or 100%, in the case of our other executive officers, of the executive officer's target annual incentive bonus for the year in which his employment is terminated and accelerate the vesting of any outstanding equity grants in full.

We have also entered into employee confidentiality, inventions, non-solicitation and non-competition agreements with each of our named executive officers. Under the employee confidentiality, inventions, non-solicitation and non-competition agreements, each named executive officer has agreed (1) not to compete with us during his employment and for a period of one year after the termination of his employment, (2) not to solicit our employees during his employment and for a period of one year after the termination of his employment, (3) to protect our confidential and proprietary information and (4) to assign to us related intellectual property developed during the course of his employment.

Stock option and other compensation plans

In this section we describe our 2017 Plan, our 2020 Plan and our Employee Stock Purchase Plan, or 2020 ESPP. Prior to this offering, we granted awards to eligible participants under the 2017 Plan. We expect to grant awards to eligible participants from time to time only under the 2020 Plan.

2017 Stock incentive plan

The 2017 Plan was initially approved by our board of directors and our stockholders in October 2017, and was subsequently amended in October 2017, November 2017, February 2018, December 2018 and January 2020, in each case solely to increase the total number of shares reserved for issuance under the 2017 Plan. The 2017 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2017 Plan; however, incentive stock options may only be granted to our employees. The type of award granted under the 2017 Plan and the terms of such award are set forth in the applicable award agreement. Pursuant to the terms of the 2017 Plan, our board of directors (or a committee delegated by our board of directors) administers the plan and, subject to any limitations in the plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to, and the terms and conditions of, any stock appreciation rights, awards of restricted stock, restricted stock units or other stock-based awards, including conditions for repurchase or cancellation, measurement price, issue price and repurchase price, if any

(though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years) and any performance conditions.

The maximum number of shares of common stock authorized for issuance under the 2017 Plan is 10,275,717 shares. Our board of directors may amend, suspend or terminate the 2017 Plan at any time, except that stockholder approval may be required to comply with applicable law.

Effect of certain changes in capitalization

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, we are required by the 2017 Plan to make equitable adjustments (or make substitute awards, if applicable), in the manner determined by our board of directors, to:

- the number and class of securities available under the 2017 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding award of restricted stock; and
- the share and per-share related provisions and purchase price, if any, of each outstanding restricted stock unit award and each other stock-based award.

Effect of certain corporate transactions

Upon the occurrence of a merger or other reorganization event (as defined in the 2017 Plan), our board of directors may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2017 Plan as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation);
- upon written notice to a participant, provide that all of the participant's unexercised and/or unvested awards will terminate immediately prior to the consummation of such transaction unless exercised, to the extent exercisable, by the participant within a specified period following the date of such notice;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;
- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;

- provide that, in connection with our liquidation or dissolution, awards convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

In taking any of the foregoing actions, our board of directors is not obligated by the 2017 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, our repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the succeeding company and will, unless our board of directors determines otherwise, apply to the cash, securities or other property which our common stock was converted into or exchanged for pursuant to the reorganization event in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award. However, our board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between a participant and us, either initially or by amendment, or provide for forfeiture of such restricted stock if issued at no cost. Upon the occurrence of a reorganization event involving our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the participant and us, all restrictions and conditions on all outstanding restricted stock awards will automatically be deemed terminated or satisfied.

Our board of directors may at any time provide that any award under the 2017 Plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

As of April 30, 2020, there were options to purchase an aggregate of 4,805,609 shares of common stock outstanding under the 2017 Plan at a weighted-average exercise price of $4.92 per share, options to purchase 1,172,297 shares of common stock were available for future issuance under the 2017 Plan and 1,233,488 shares of unvested restricted common stock were outstanding under the 2017 Plan. No further awards will be made under the 2017 Plan on or after the effective date of the 2020 Plan described below; however, awards outstanding under the 2017 Plan will continue to be governed by their existing terms.

2020 Stock incentive plan

In May 2020 our board of directors adopted, and in June 2020 our stockholders approved, the 2020 Plan, which became effective immediately prior to the effectiveness of the registration statement for this offering. The 2020 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares of our common stock reserved for issuance under the 2020 Plan is the sum of (1) 2,547,698 shares; plus (2) the number of shares (up to a maximum of 7,173,014 shares) as is equal to the sum of (x) the number of shares of our common stock reserved for issuance under the 2017 Plan that remained available for grant under the 2017 Plan immediately prior to the effectiveness of the registration statement for this offering and (y) the number of shares of our common stock subject to outstanding awards granted under the 2017 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing until, and including, the

fiscal year ending December 31, 2030, equal to the lesser of (i) 4% of the number of shares of our common stock outstanding on such date, and (ii) an amount determined by our board of directors. Up to 16,984,657 of the shares of Common Stock available for issuance under the 2020 Plan may be issued as Incentive Stock Options.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2020 Plan; however, incentive stock options may only be granted to our employees. In connection with the effectiveness of the registration statement of which this prospectus forms a part, we have granted options to purchase an aggregate of approximately 648,481 shares of our common stock at an exercise price equal to the initial public offering price in this offering to certain of our directors, employees and consultants.

Pursuant to the terms of the 2020 Plan, our board of directors (or a committee delegated by our board of directors) will administer the 2020 Plan and, subject to any limitations set forth in the 2020 Plan, will select the recipients of awards and determine:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the exercise price of options, which price must be at least equal to the fair market value of our common stock on the date of grant;
- the duration of options, which may not be in excess of ten years;
- the methods of payment of the exercise price of options; and
- the number of shares of our common stock subject to and the terms and conditions of any stock appreciation rights, awards of restricted stock, restricted stock units or other stock-based awards, including conditions for repurchase, measurement price, issue price and repurchase price, if any (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years) and any performance conditions.

If our board of directors delegates authority to one or more of our officers to grant awards under the 2020 Plan, the officer will have the power to make awards to all of our employees, except officers and executive officers (as such terms are defined in the 2020 Plan). Our board of directors will fix the terms of the awards to be granted by any such officer, the maximum number of shares subject to awards that any such officer may grant, and the time period in which such awards may be granted.

The 2020 Plan contains limits on the compensation that may be paid to our non-employee directors. The maximum amount of cash and value (calculated based on grant-date fair value for financial reporting purposes) of awards granted under the plan in any calendar year to any individual non-employee director in his or her capacity as a non-employee director may not exceed $750,000, or in the case of a new director during his or her first year of service, $1,000,000; provided, however, that fees paid by us on behalf of any non-employee director in connection with regulatory compliance and any amounts paid to a non-employee director as reimbursement of an expense shall not count against the foregoing limit. However, our board of directors may make additional exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the board of directors may determine in its discretion, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation. For the avoidance of doubt, the maximum amount set forth above will not apply to cash or awards granted under the 2020 Plan to a non-employee director in his or her capacity as a consultant or advisor.

Effect of certain changes in capitalization

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, we are required by the 2020 Plan to make equitable adjustments (or make substitute awards, if applicable), in the manner determined by our board of directors, to:

- the number and class of securities available under the 2020 Plan;
- the share counting rules of the 2020 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding award of restricted stock; and
- the share and per-share related provisions and purchase price, if any, of each outstanding restricted stock unit award and each other stock-based award.

Effect of certain corporate transactions

Upon the occurrence of a merger or other reorganization event (as defined in the 2020 Plan), our board of directors may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2020 Plan as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation);
- upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited immediately prior to the consummation of the reorganization event and/or vested but unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised, to the extent exercisable, by the participant within a specified period following the date of such notice;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;
- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with our liquidation or dissolution, awards convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or

- any combination of the foregoing.

In taking any of the foregoing actions, our board of directors is not obligated by the 2020 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, our repurchase and other rights with respect to each outstanding award of restricted stock will continue for the benefit of the succeeding company and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock is converted into or exchanged for pursuant to the reorganization event in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award. However, our board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or in any other agreement between a participant and us, either initially or by amendment. Upon the occurrence of a reorganization event involving our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the participant and us, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied.

Our board of directors may, at any time, provide that any award under the 2020 Plan will become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to certain actions requiring stockholder approval under the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, or Nasdaq Stock Market rules, our board of directors may amend, modify or terminate any outstanding award under the 2020 Plan, including but not limited to, substituting for the award another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a nonstatutory stock option, subject to certain participant consent requirements. However, unless our stockholders approve such action, the 2020 Plan provides that we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2020 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding stock option or stock appreciation right (whether or not granted under the 2020 Plan) and grant a new award under the 2020 Plan in substitution for the cancelled award (other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock (valued in the manner determined by (or in the manner approved by) our board of directors); or
- take any other action that constitutes a “repricing” within the meaning of Nasdaq Stock Market rules or rules of any other exchange or marketplace on which our common stock is listed or traded.

No award may be granted under the 2020 Plan on or after the date that is ten years from the effectiveness of the 2020 Plan. Our board of directors may amend, suspend or terminate the 2020 Plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

2020 Employee stock purchase plan

In May 2020 our board of directors adopted, and in June 2020 our stockholders approved, the 2020 ESPP, which became effective immediately prior to the effectiveness of the registration statement for this offering. The 2020 ESPP is administered by our board of directors or by a committee appointed by our board of directors. The 2020 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 481,231 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2020 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2021 and continuing for each fiscal year until, and including the fiscal year commencing on, January 1, 2030, in an amount equal to the lowest of (1) 1,302,157 shares of our common stock, (2) 1% of the number of shares of our common stock outstanding on such date, and (3) an amount determined by our board of directors.

All of our employees and employees of any designated subsidiary, as defined in the 2020 ESPP, are eligible to participate in the 2020 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least three months prior to enrolling in the 2020 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2020 ESPP.

We retain the discretion to determine which eligible employees may participate in an offering under applicable regulations.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2020 ESPP beginning at such time and on such dates as our board of directors may determine, or on the first business day thereafter. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors or a committee designated by the board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On each offering commencement date, each participant will be granted an option to purchase, on the last business day of the offering period, up to a number of shares of our common stock determined by multiplying $2,083 by the number of full months in the offering period and dividing that product by the closing price of our common stock on the first day of the offering period. No employee may be granted an option under the 2020 ESPP that permits the employee's rights to purchase shares under the 2020 ESPP and any other employee stock purchase plan of ours or of any of our subsidiaries to accrue at a rate that exceeds $25,000 of the fair market value of our common stock (determined as of the first day of each offering period) for each calendar year in which the option is outstanding. In addition, no employee may purchase shares of our common stock under the 2020 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

Each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2020 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2020 ESPP, the purchase price will be determined by our board of directors or the committee for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors or the committee does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may at any time prior to the close of business on the fifteenth business day (or such other number of days as is determined by us) prior to the end of the offering period, and for any reason, permanently withdraw from participating in the offering and permanently withdraw the balance accumulated in the employee's account. Partial withdrawals are not permitted. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be taken and the balance in the employee's account will be paid to the employee.

We will be required to make equitable adjustments to the extent determined by our board of directors or a committee thereof to the number and class of securities available under the 2020 ESPP, the share limitations under the 2020 ESPP, and the purchase price for an offering period under the 2020 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2020 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2020 ESPP on such terms as our board of directors or committee thereof determines:

- provide that options will be assumed, or substantially equivalent options will be substituted, by the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by the board of directors or committee thereof in such notice, which date will not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the cash payment for each share surrendered in the reorganization event is treated as

the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2020 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or

- provide that, in connection with our liquidation or dissolution, options convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2020 ESPP or any portion of the 2020 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board of directors may not make any amendment that would cause the 2020 ESPP to fail to comply with Section 423 of the Code. The 2020 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) plan

We maintain a defined contribution employee retirement plan for our employees, including our named executive officers. The plan is intended to qualify as a tax-qualified 401(k) plan so that contributions to the 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan (except in the case of contributions under the 401(k) plan designated as Roth contributions). Under the 401(k) plan, each employee is fully vested in his or her deferred salary contributions and our discretionary match after one year of employment with us. Employee contributions are held and invested by the plan's trustee as directed by participants. The 401(k) plan provides us with the discretion to match employee contributions, but to date we have not provided any employer matching contributions.

Limitation of liability and indemnification

Our certificate of incorporation, which will become effective upon the closing of this offering, limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law, or the DGCL, and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the DGCL is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our certificate of incorporation, which will become effective upon the closing of this offering, provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we

intend to enter into indemnification agreements with all of our executive officers and directors prior to the completion of this offering. These indemnification agreements may require us, among other things, to indemnify each such executive officer or director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our executive officers or directors.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, or the Securities Act, may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. It also is possible that the director or officer could amend the plan in certain circumstances when not in possession of material, nonpublic information or terminate the plan. In addition, our directors and executive officers may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director compensation

The table below shows all compensation to our non-employee directors during the year ended December 31, 2019.

Name	Fees earned or paid in cash($)	Stock awards($) (1)	Option awards($) (2)	Total($)
Jason Rhodes	—	—	—	—
Gustav Christensen	32,500(3)	—	—	32,500
Donald Nicholson, Ph.D.	32,500(3)	—	—	32,500
Catherine Stehman-Breen, M.D.	25,000	—	—	25,000
Anthony Quinn, M.D. Ch.B., Ph.D.	25,000	—	—	25,000
Jeffrey Jonas, M.D.	25,000	—	—	25,000
Charles Rowland	40,000(3)(4)	—	—	40,000

(1) As of December 31, 2019, the aggregate number of shares of our common stock held pursuant to restricted stock awards by each non-employee director was as follows: Mr. Rhodes, 0 shares; Mr. Christensen, 42,461 shares; Dr. Nicholson, 42,461 shares; Dr. Stehman-Breen, 42,461 shares; Dr. Quinn, 42,461 shares; Dr. Jonas, 0 shares; and Mr. Rowland 0 shares.

(2) As of December 31, 2019, the aggregate number of shares of our common stock subject to outstanding option awards for each non-employee director was as follows: Mr. Rhodes, 0 shares; Mr. Christensen, 0 shares; Dr. Nicholson, 0 shares; Dr. Stehman-Breen, 0 shares; Dr. Quinn, 0 shares; Dr. Jonas, 42,461 shares; and Mr. Rowland 42,461 shares.

(3) Mr. Christensen, Dr. Nicholson, and Mr. Rowland received an additional $7,500 as a committee retainer fee for their service on our audit committee.

(4) Mr. Rowland received an additional $7,500 as a chairmanship fee for his service as chair of our audit committee.

Prior to this offering, we granted restricted stock awards for 42,461 shares of our common stock or options to purchase 42,461 shares of our common stock to our non-employee directors upon their initial election to the Board and paid annual cash fees our non-employee directors for their service on our board of directors. However, we did not have a formal non-employee director compensation policy. In 2019, we did not grant any

equity awards to any of our directors. We have historically reimbursed our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings. We do not pay any compensation to our President and Chief Executive Officer in connection with his service on our board of directors.

In May 2020, our board of directors approved a director compensation program that will become effective on the effective date of the registration statement of which this prospectus is a part. Under this director compensation program, we will pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chair of the board and of each committee will receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors and no fee will be payable in respect of any period prior to the completion of this offering. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Member Annual Fee	Chair Annual Fee
Board of Directors	$ 35,000	$ 30,000
Audit Committee	$ 7,500	$ 7,500
Talent Committee	$ 7,500	$ 7,500
Nominating and Corporate Governance Committee	$ 4,000	$ 4,000

We also will continue to reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

In addition, under our director compensation program, each of our current non-employee directors received, on the effective date of the registration statement of which this prospectus is a part, an option to purchase 52,000 shares of our common stock under the 2020 Plan, and each non-employee director elected after the effective date of the registration statement of which this prospectus is a part will receive, upon his or her initial election or appointment to our board of directors, an option to purchase 52,000 shares of our common stock under the 2020 Plan. Each of these options will vest as to 25% of the shares of our common stock underlying such option on the first anniversary of the grant, with the remainder vesting in equal quarterly installments until the fourth anniversary of the date of grant, subject to the non-employee director's continued service as a director. Further, on the date of each annual meeting of stockholders, each non-employee director that has served on our board of directors for at least six months will receive, under the 2020 Plan, an option to purchase 26,000 shares of our common stock under the 2020 Plan. Each of these options will vest as to 25% of the shares of our common stock underlying such option on the first anniversary of the grant, with the remainder vesting in equal quarterly installments until the fourth anniversary of the grant, subject to the non-employee director's continued service as a director. All options issued to our non-employee directors under our director compensation program will be issued at exercise prices equal to the fair market value of our common stock on the date of grant (with the options granted to our current non-employee directors on the effective date of the registration statement of which this prospectus is a part having an exercise price equal to the public offering price) and will have a term of ten years.

Transactions with related persons

Since January 1, 2017, we have engaged in the following transactions in which the amounts involved exceeded $120,000 and any of our directors, executive officers or holders of more than 5% of our voting securities, or any member of the immediate family of, or person sharing the household with, the foregoing persons, had or will have a direct or indirect material interest. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unrelated third parties.

Convertible promissory notes and SAFEs

From November 2016 to February 2017, we issued convertible promissory notes in an aggregate principal amount of $1,000,000 to Atlas Venture Fund X, L.P. These notes, which we refer to as the Atlas notes, accrued interest at a rate of 6% per annum. On November 20, 2017, all principal and accrued but unpaid interest under the notes were converted into 1,051,020 shares of our Series A preferred stock.

Between April and September 2017, we issued Simple Agreements for Future Equity, or SAFEs, in an aggregate principal amount of $6,000,000 to Atlas Venture Fund X, L.P. On November 20, 2017, these agreements, which we refer to as the Atlas SAFEs, were converted into 6,000,000 shares of our Series A preferred stock.

Series A preferred stock financing

From November to December 2017, we issued and sold (1) 8,400,000 shares of our Series A preferred stock at a price per share of $1.00 in cash, for an aggregate purchase price of $8,400,000, (2) 1,051,020 shares of our Series A preferred stock upon conversion of the Atlas notes, and (3) 6,000,000 shares of our Series A preferred stock upon conversion of the Atlas SAFEs. The following table sets forth the aggregate number of shares of our Series A preferred stock that we issued and sold to our directors, officers and 5% stockholders and their affiliates in this transaction and the aggregate amount of consideration for such shares:

Purchaser(1)	Shares of Series A preferred stock	Cash purchase price
Atlas Venture Fund X, L.P.	8,000,000	$ 8,000,000
Geoff McDonough	200,000	$ 200,000

(1) See “Principal stockholders” for additional information about shares held by these entities.

Series B preferred stock financing

In February 2018, we issued and sold an aggregate of 10,974,644 shares of our Series B preferred stock at a price per share of $9.1457 in cash, for an aggregate purchase price of $100,370,801.68. The following table sets forth the aggregate number of shares of our Series B preferred stock that we issued and sold to our directors, officers and 5% stockholders and their affiliates in this transaction and the aggregate amount of consideration for such shares:

Purchaser(1)	Shares of Series B preferred stock	Cash purchase price
Entities affiliated with Fidelity Investment	5,731,743	$ 52,420,802
Entities affiliated with Invus Public Equities, L.P.	2,186,820	$ 20,000,000

(1) See “Principal stockholders” for additional information about shares held by these entities.

Series C preferred stock financing

In January 2020, we issued and sold an aggregate of 19,936,296 shares of our Series C preferred stock at a price per share of $5.5914 in cash, for an aggregate purchase price of $111,471,805.56. The following table sets forth the aggregate number of shares of our Series C preferred stock that we issued and sold to our directors, officers and 5% stockholders and their affiliates in this transaction and the aggregate amount of consideration for such shares:

Purchaser(1)	Shares of Series C preferred stock	Cash purchase price
Entities affiliated with Atlas Venture Fund X, L.P.	2,682,691	$ 14,999,998
Entities affiliated with Fidelity Investment	2,457,000	$ 13,738,070
Invus Public Equities, L.P.	1,073,076	$ 5,999,997
Certain funds and accounts advised or subadvised by T. Rowe Price	5,365,382	$ 29,999,997
Gustav Christensen	44,711	$ 249,997
Anthony Quinn	53,654	$ 300,001
Charles Rowland	89,423	$ 500,000

(1) See “Principal stockholders” for additional information about shares held by these entities.

Registration rights

We are a party to an investors’ rights agreement with the holders of our preferred stock, including our 5% stockholders and their affiliates and certain of our directors and officers. This investors’ rights agreement provides these stockholders the right, subject to certain conditions, beginning six months following the completion of this offering, to demand that we file a registration statement or to request that their shares be covered by a registration statement that we are otherwise filing.

See “Description of capital stock—Registration rights” for additional information regarding these registration rights.

Indemnification agreements

Our certificate of incorporation, which will become effective upon the closing of this offering, provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we intend to enter into new indemnification agreements with all of our directors and executive officers prior to the completion of this offering. These indemnification agreements may require us, among other things, to indemnify each such director or executive officer for some expenses, including attorneys’ fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers.

Policies and procedures for related person transactions

Our board of directors adopted in May 2020 written policies and procedures for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds $120,000, and one of our executive officers, directors, director nominees or 5% stockholders (or their immediate family members), each of whom we refer to as a “related person,” has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a “related person transaction,” the related person must report the proposed related person transaction to our Chief Legal Officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the audit committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chair of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between audit committee meetings, subject to ratification by the audit committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person’s interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person’s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person’s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the Securities and Exchange Commission’s related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person’s position as an executive officer of another entity, whether or not the person is also a director of such entity, that is a participant in the transaction, where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction, and the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our talent committee in the manner specified in the talent committee’s charter.

We did not have a written policy regarding the review and approval of related person transactions prior to this offering. Nevertheless, with respect to such transactions, it has been the practice of our board of directors to consider the nature of and business reasons for such transactions, how the terms of such transactions compared to those which might be obtained from unaffiliated third parties and whether such transactions were otherwise fair to and in the best interests of, or not contrary to, our best interests.

Principal stockholders

The following table sets forth information with respect to the beneficial ownership of our common stock, as of April 30, 2020 by:

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

The column entitled “Percentage of shares beneficially owned—Before offering” is based on a total of 34,108,104 shares of our common stock outstanding as of April 30, 2020, assuming the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 27,094,085 shares of our common stock upon the closing of this offering. The column entitled “Percentage of shares beneficially owned—After offering” is based on 44,634,420 shares of our common stock to be outstanding after this offering, including the shares of our common stock that we are selling in this offering and 1,233,488 shares of unvested restricted stock subject to repurchase by us, but not including any additional shares issuable upon exercise of outstanding options.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock that an individual has a right to acquire within 60 days after April 30, 2020 are considered outstanding and beneficially owned by the person holding such right for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Unless otherwise indicated, the address of each beneficial owner is c/o Generation Bio Co. 301 Binney Street, Cambridge, MA 02142.

		Percentage of shares beneficially owned	
Name of beneficial owner	**Number of shares beneficially owned**	**Before offering(%)**	**After offering(%)**
5% Stockholders			
Entities affiliated with Atlas Venture Fund X, L.P.(1)	12,630,758	37.03%	28.30%
Entities affiliated with Fidelity Investment(2)	5,077,956	14.89%	11.38%
Certain funds and accounts advised or subadvised by T. Rowe Price(3)	3,037,629	8.91%	6.81%
Entities affiliated with Invus Public Equities, L.P.(4)	2,014,191	5.91%	4.51%
Named Executive Officers and Directors			
Jason Rhodes(1)	12,630,758	37.03%	28.30%
Geoff McDonough, M.D.(5)	1,705,542	5.00%	3.82%
Douglas Kerr, M.D., Ph.D., M.B.A.(6)	388,438	1.14%	*
Thomas Graney(7)	211,156	*	*
Gustav Christensen(8)	131,423	*	*
Donald Nicholson, Ph.D.(9)	99,076	*	*
Anthony Quinn, M.B. Ch.B., Ph.D.(10)	72,837	*	*
Charles Rowland(11)	69,203	*	*
Catherine Stehman-Breen, M.D.(12)	47,523	*	*
Jeffrey Jonas, M.D.(13)	21,230	*	*
All current executive officers and directors as a group (12 persons)(14)	16,045,785	46.59%	35.69%

* Less than one percent.

(1) Consists of (i) 8,521,213 shares of common stock underlying shares of Series A convertible preferred stock held by Atlas Venture Fund X, L.P., or Atlas Fund X, (ii) 2,590,726 shares of common stock held by Atlas Fund X and (iii) 1,518,819 shares of common stock underlying shares of Series C convertible preferred stock held by Atlas Venture Opportunity Fund I, L.P., or Atlas Fund I. Atlas Venture Associates X, L.P. is the general partner of Atlas Fund X, and Atlas Venture Associates X, LLC is the general partner of Atlas Venture Associates X, L.P. Bruce Booth, Jean-Francois Formela, David Grayzel, Jason Rhodes and Kevin Bitterman are the members of Atlas Venture Associates X, LLC and collectively make investment decisions on behalf of Atlas Venture Fund X, LLC. Each of Atlas Fund X, Atlas Venture Associates X, L.P., and Atlas Venture Associates X, LLC may be deemed to beneficially own the shares held by Atlas Fund X. Atlas Fund I is managed by Atlas Venture Associates Opportunity I, L.P., which is managed by Atlas Venture Associates Opportunity I, LLC, or AVAO, LLC. Bruce Booth, Jean-Francois Formela, David Grayzel, Jason Rhodes, and Kevin Bitterman are the members of AVAO LLC and collectively make investment decisions on behalf of Atlas Fund I. Jason Rhodes is also a member of our board of directors. Mr. Rhodes disclaims beneficial ownership of the shares listed. The mailing address of Atlas Fund X and Atlas Fund I is 400 Technology Square, 10th Floor, Cambridge, MA 02139.

(2) Consists of (i) 668,380 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Mag & Co fbo Fidelity Growth Company Commingled Pool, (ii) 934,248 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Powhatan & Co., LLC fbo Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund, (iii) 565,648 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by M Gardiner & Co fbo Fidelity Securities Fund: Fidelity Blue Chip Growth Fund, (iv) 18,624 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Mag & Co fbo Fidelity Blue Chip Growth Commingled Pool, (v) 56,155 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by FLAPPER CO fbo FIAM Target Date Blue Chip Growth Commingled Pool, (vi) 39,319 shares of common stock underlying

shares of Series B convertible preferred stock and Series C convertible preferred stock held by Booth & Co FBO Fidelity Securities Fund: Fidelity Blue Chip Growth K6 Fund, (vii) 123,522 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by WAVECHART + CO fbo Fidelity Securities Fund: Fidelity Series Blue Chip Growth Fund, (viii) 453 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Booth & Co fbo Fidelity Securities Fund: Fidelity Flex Large Cap Growth Fund, (ix) 238,322 shares of common stock underlying shares of Series B convertible preferred stock held by M Gardiner & Co fbo Fidelity Puritan Trust: Fidelity Puritan Fund, (x) 59,945 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by M Gardiner & Co fbo Fidelity Central Investment Portfolios LLC: Fidelity Health Care Central Fund, (xi) 17,158 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by M Gardiner & Co fbo Variable Insurance Products Fund IV: Health Care Portfolio, (xii) 154,622 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Mag & Co fbo Fidelity Select Portfolios: Health Care Portfolio, (xiii) 74,620 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by M Gardiner & Co fbo Fidelity Advisor Series VII: Fidelity Advisor Health Care Fund, (xiv) 1,563,474 shares of common stock underlying shares of Series B convertible preferred held by Mag & Co fbo Fidelity Contrafund: Fidelity Contrafund, (xv) 30,875 shares of common stock underlying shares of Series B convertible preferred stock held by Booth & Co FBO Fidelity Contrafund: Fidelity Contrafund K6, (xvi) 259,549 shares of common stock underlying shares of Series B convertible preferred stock held by Mag & Co fbo Fidelity Contrafund Commingled Pool, (xvii) 243,660 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Mag & Co. fbo Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund, (xviii) 7,473 shares of common stock underlying shares of Series C convertible preferred stock held by Mag & Co fbo Fidelity Select Portfolios: Pharmaceuticals Portfolio, (xix) 1,188 shares of common stock underlying shares of Series C convertible preferred stock held by Fidelity Blue Chip Growth Institutional Trust, and (xx) 20,721 shares of common stock underlying shares of Series C convertible preferred stock held by Fidelity Mt. Vernon Street Trust: Fidelity Growth Company K6 Fund. Fidelity Management & Research Company, or Fidelity, 82 Devonshire Street, Boston, Massachusetts 02109, a wholly owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of such shares of common stock as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Edward C. Johnson 3d and FMR LLC, through its control of Fidelity and the Fidelity Funds, each has sole power to dispose of the shares owned by the Fidelity Funds. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Fidelity Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees.

(3) Consists of shares of common stock underlying shares of Series C convertible preferred stock held by each of the following funds and accounts: (i) 809,669 shares of Series C convertible preferred stock held by T. Rowe Price Health Sciences Fund, Inc., (ii) 49,684 shares of Series C convertible preferred stock held by TD Mutual Funds – TD Health Sciences Fund, (iii) 48,484 shares of Series C convertible preferred stock held by VALIC Company I—Health Sciences Fund, (iv) 37,224 shares of Series C convertible preferred stock held by T. Rowe Price Health Sciences Portfolio, (v) 1,108,915 shares of Series C convertible preferred stock held by T. Rowe Price New Horizons Fund, Inc., (vi) 157,210 shares of Series C convertible preferred held by T. Rowe Price New Horizons Trust, (vii) 8,991 shares of Series C convertible preferred stock held by T. Rowe Price U.S. Equities Trust, (viii) 9,567 shares of Series C convertible preferred stock held by MassMutual Select Funds -MassMutual Select T. Rowe Price Small and Mid Cap Blend Fund, (ix) 407,349 shares of Series C convertible preferred stock held by T. Rowe Price Small-Cap Stock Fund, Inc., (x) 223,149 shares of Series C convertible preferred stock held by T. Rowe Price Institutional Small-Cap Stock Fund, (xi) 3,498 shares of Series C convertible preferred stock held by T. Rowe Price Spectrum Conservative Allocation Fund, (xii) 5,889 shares of Series C convertible preferred stock held by T. Rowe Price Spectrum Moderate Allocation Fund, (xiii) 9,493 shares of Series C convertible preferred stock held by T. Rowe Price Spectrum Moderate Growth Allocation Fund, (xiv) 428 shares of Series C convertible preferred stock held by T. Rowe Price Moderate Allocation Portfolio, (xv) 18,849 shares of Series C convertible preferred stock held by U.S. Small-Cap Stock Trust, (xvi) 4,245 shares of Series C convertible preferred stock held by VALIC Company I—Small Cap Fund, (xvii) 15,979 shares of Series C convertible preferred stock held by TD Mutual Funds—TD U.S. Small-Cap Equity Fund, (xviii) 95,055 shares of Series C convertible preferred stock held by T. Rowe Price U.S. Small-Cap Core Equity Trust, (xix) 4,634 shares of Series C convertible preferred stock held by Minnesota Life Insurance Company, and (xx) 19,317 shares of Series C convertible preferred stock held by Costco 401(k) Retirement Plan. The foregoing accounts are advised or sub-advised by T. Rowe Price Associates, Inc., or "T. Rowe Price", a registered investment adviser. T. Rowe Price serves as investment adviser or subadviser, as applicable, with power to direct investments and/or sole power to vote the securities owned by the accounts (with the exception of one subadvisory fund that retains its own voting authority). Although T. Rowe Price may be deemed to be the beneficial owner of all the shares listed, T. Rowe Price expressly disclaims beneficial ownership of such securities. T. Rowe Price Investment Services, Inc., or TRPIS, a registered broker-dealer (and FINRA member), is a subsidiary of T. Rowe Price Associates, Inc., the investment adviser or subadviser, as applicable, to the accounts listed above. TRPIS was formed primarily for the limited purpose of acting as the principal underwriter and distributor of shares of the funds in the T. Rowe Price mutual fund family. TRPIS does not engage in underwriting or market-making activities involving individual securities. T. Rowe Price Associates, Inc. is the wholly owned subsidiary of T. Rowe Price Group, Inc., which is a publicly traded financial services holding company. The principal address for T. Rowe Price is 100 East Pratt Street, Baltimore, Maryland 21202.

(4) Consists of 2,014,191 shares of common stock underlying shares of Series B convertible preferred stock and Series C convertible preferred stock held by Invus Public Equities, L.P. Invus Public Equities Advisors, LLC, as the general partner of Invus Public Equities, L.P., controls Invus Public Equities, L.P. and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. Artal Treasury Ltd., as the managing member of Invus Public Equities Advisors, LLC, controls Invus Public Equities Advisors, LLC and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. The Geneva branch of Artal International S.C.A. is the sole stockholder of Artal Treasury Ltd. and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. Artal International Management S.A., as the managing partner of Artal International S.C.A., controls Artal International S.C.A. and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. Artal Group, S.A., as the parent company of Artal International Management, S.A.,

controls Artal International Management S.A. and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. Westend, S.A., as the parent company of Artal Group S.A. controls Artal Group S.A., and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. Stichting Administratiekantoor Westend, as the parent company of Westend S.A., controls Westend S.A. and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. Mr. Pascal Minne, as the sole member of the board of Stichting Administratiekantoor Westend, controls Stichting Administratiekantoor Westend and, accordingly, may be deemed to beneficially own the shares held by Invus Public Equities, L.P. The address for Invus Public Equities, L.P. is 750 Lexington Avenue, 30th Floor, New York, NY 10022.

(5) Consists of (i) 113,231 shares of common stock underlying shares of Series A convertible preferred stock and 1,365,849 shares of common stock owned by Geoff McDonough, M.D. and (ii) 226,462 shares of common stock owned by McDonough Family 2018 Irrevocable Trust, or the Trust. Dr. McDonough is the settlor of the Trust, Allison L. McDonough and David S. Grayzel are trustees for the Trust and the Trust is for the benefit of Graeme and Owen McDonough. Dr. McDonough may be deemed to beneficially own the shares of common stock owned by the Trust.

(6) Consists of 326,558 shares of common stock and 61,880 shares of common stock issuable upon the exercise of options that are exercisable as of April 30, 2020 or will become exercisable within 60 days of such date.

(7) Consists of 211,156 shares of common stock issuable upon the exercise of options that are exercisable as of April 30, 2020 or will become exercisable within 60 days of such date.

(8) Consists of 88,962 shares of common stock underlying shares of Series A convertible preferred stock, Series B convertible preferred stock, and Series C convertible preferred stock and 42,461 shares of common stock.

(9) Consists of (i) 56,615 shares of common stock underlying shares of Series A convertible preferred stock and (ii) 42,461 shares of common stock.

(10) Consists of 30,376 shares of common stock underlying shares of Series C convertible preferred stock and 42,461 shares of common stock.

(11) Consists of 50,627 shares of common stock underlying shares of Series C convertible preferred stock and 18,576 shares of common stock issuable upon the exercise of options that are exercisable as of April 30, 2020 or will become exercisable within 60 days of such date.

(12) Consists of 5,062 shares of common stock underlying shares of Series C convertible preferred stock and 42,461 shares of common stock.

(13) Consists of 21,230 shares of common stock issuable upon the exercise of options that are exercisable as of April 30, 2020 or will become exercisable within 60 days of such date.

(14) Consists of 10,384,905 shares of common stock underlying shares of preferred stock, 5,330,516 shares of common stock and 330,364 shares of common stock issuable upon the exercise of options that are exercisable as of April 30, 2020 or will become exercisable within 60 days after such date.

Description of capital stock

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to the certificate of incorporation and bylaws that will become effective upon the closing of this offering. We will file copies of these documents with the SEC as exhibits to our registration statement of which this prospectus forms a part. The description of our common stock reflects changes to our capital structure that will occur upon the closing of this offering.

Upon the closing of this offering, our authorized capital stock will consist of 150,000,000 shares of our common stock, par value $0.0001 per share, and 5,000,000 shares of our preferred stock, par value $0.0001 per share, all of which preferred stock will be undesignated.

As of April 30, 2020, we had issued and outstanding:

- 7,014,019 shares of our common stock held by 38 stockholders of record;
- 15,451,020 shares of our Series A preferred stock held by four stockholders of record;
- 10,974,644 shares of our Series B preferred stock held by 26 stockholders of record; and
- 19,936,296 shares of our Series C preferred stock held by 54 stockholders of record.

Upon the closing of this offering, all of the outstanding shares of our preferred stock will automatically convert into an aggregate of 27,094,085 shares of our common stock.

Common stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of our outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of 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 and issue in the future.

Preferred stock

As of April 30, 2020, we had issued and outstanding 15,451,020 shares of Series A preferred stock, 10,974,644 shares of Series B preferred stock and 19,936,296 shares of Series C preferred stock. Upon the closing of this offering, our Series A preferred stock and Series C preferred stock is automatically convertible into shares of our common stock on a 1.7663-to-one basis, and our Series B preferred stock is automatically convertible into shares of our common stock on a 1.5546-to-one basis (when rounded to the nearest ten-thousandth). Upon the

closing of this offering, all of the outstanding shares of our preferred stock will automatically convert into an aggregate of 27,094,085 shares of our common stock. Under the terms of our certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options and unvested restricted common stock

As of April 30, 2020, options to purchase an aggregate of 4,805,609 shares of our common stock were outstanding, at a weighted average exercise price of $4.92 per share, and 1,233,488 shares of unvested restricted common stock were outstanding.

Registration rights

We have entered into an amended and restated investors' rights agreement dated as of January 9, 2020, or the investors' rights agreement, with holders of our preferred stock. Beginning six months following the closing of this offering, holders of a total of 31,887,648 shares of our common stock will have the right to require us to register these shares under the Securities Act upon demand and in connection with any registration statement that we plan to file, as described below under "—Demand registration rights" and "—Incidental registration rights." We refer to the shares with these registration rights as registrable securities. After registration pursuant to these rights, the registrable securities will become freely tradable without restriction under the Securities Act.

Demand registration rights

Beginning 180 days after the effective date of the registration statement of which this prospectus is a part, subject to specified limitations set forth in the investors' rights agreement, at any time, the holders of a majority of the then outstanding registrable securities may demand that we register at least 40% of the registrable securities then outstanding under the Securities Act for purposes of a public offering.

In addition, subject to specified limitations set forth in the investors' rights agreement, at any time after we become eligible to file a registration statement on Form S-3, certain holders of at least 20% of the registrable securities then outstanding may request that we register their registrable securities on Form S-3 for purposes of a public offering for which the anticipated aggregate offering price to the public would exceed, net of selling expenses, $5.0 million.

We shall use our commercially reasonable efforts to cause such registration statements to become effective.

Incidental registration rights

If, at any time after the closing of this offering, we propose to register for our own account any of our securities under the Securities Act, the holders of registrable securities will be entitled to notice of the registration and,

subject to specified exceptions, have the right to require us to register all or a portion of the registrable securities then held by them in that registration. We have the right to terminate or withdraw any registration initiated by us before the effective date of such registration.

In the event that any registration in which the holders of registrable securities participate pursuant to our investors' rights agreement is an underwritten public offering, we have agreed to enter into an underwriting agreement in usual and customary form.

Expenses

Pursuant to the investors' rights agreement, we are required to pay all registration expenses, including all registration, filing and qualification fees; printing and accounting fees; reasonable fees and disbursements not to exceed $25,000 of one counsel representing the selling stockholders or, in the event of an initial public offering, of one counsel representing the investors; but excluding underwriting discounts, selling commissions and stock transfer taxes applicable to the sale of registrable securities and the fees and expenses of the selling stockholders' own counsel (other than the counsel selected to represent all selling stockholders).

The investors' rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us or any violation or alleged violation whether by action or inaction by us under the Securities Act, the Exchange Act, any state securities or Blue Sky law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities or Blue Sky law in connection with such registration statement or the qualification or compliance of the offering, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Delaware anti-takeover law and certain charter and bylaw provisions

Delaware law

We are subject to Section 203 of the Delaware General Corporation Law, or DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that will own 15% or more of our outstanding voting stock upon the closing of this offering.

Staggered board; removal of directors

Our certificate of incorporation and our bylaws to be effective upon the closing of this offering divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws to be effective upon the closing of this offering provide that directors may be removed only for cause and only by the affirmative vote of the holders of at least 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and our bylaws to be effective upon the closing of this offering, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Furthermore, our certificate of incorporation to be effective upon the closing of this offering provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Super-majority voting

The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws to be effective upon the closing of this offering may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Stockholder action; special meeting of stockholders; advance notice requirements for stockholder proposals and director nominations

Our certificate of incorporation and our bylaws to be effective upon the closing of this offering provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws to be effective upon the closing of this offering also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our board of directors. In addition, our bylaws to be effective upon the closing of this offering establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock because even if the third party acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Exclusive forum provision

Our certificate of incorporation to be effective upon the closing of this offering provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for the following types of proceedings: (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware or as to which the General Corporation Law of the State of Delaware confers jurisdiction on the Court

of Chancery of the State of Delaware, or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction. Furthermore, our certificate of incorporation that will become effective upon the closing of this offering provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. Although our certificate of incorporation contains the choice of forum provisions described above, it is possible that a court could rule that such provisions are inapplicable for a particular claim or action or that such provisions are unenforceable.

Transfer agent and registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Nasdaq Global Select Market

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol “GBIO.”

Shares eligible for future sale

Prior to this offering, there has been no public market for our common stock, and a liquid trading market for our common stock may not develop or be sustained after this offering. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the anticipation of these sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of equity securities.

Upon the closing of this offering, we will have outstanding 44,634,420 shares of our common stock, based on the 7,014,019 shares of our common stock that were outstanding on April 30, 2020, including 1,233,488 shares of unvested restricted stock subject to repurchase by us, and after giving effect to the issuance of 10,526,316 shares of our common stock in this offering, assuming no exercise by the underwriters of their option to purchase additional shares of our common stock and the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 27,094,085 shares of our common stock upon the closing of this offering. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless purchased by our “affiliates,” as that term is defined in Rule 144 under the Securities Act.

The remaining 34,108,104 shares of our common stock will be “restricted securities” under Rule 144, and we expect that substantially all of these restricted securities will be subject to the 180-day lock-up period under the lock-up agreements as described below. These restricted securities may be sold in the public market upon release or waiver of any applicable lock-up agreements and only if registered or pursuant to an exemption from registration, such as Rule 144 or Rule 701 under the Securities Act.

Lock-up agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding securities have agreed that, without the prior written consent of J.P. Morgan Securities LLC and Jefferies LLC, on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 180 days after the date of this prospectus, subject to extension in specified circumstances:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock, or make any public announcement of an intention to do any of the foregoing; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock, whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

These agreements are subject to certain exceptions, as described in the section of this prospectus entitled “Underwriting.”

Rule 144

In general, under Rule 144 of the Securities Act, beginning 90 days after the date of this prospectus, any person who is not our affiliate and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell those shares without restriction, subject to the availability of current public information about us. In addition, under Rule 144, any person who is not our affiliate and has not been our affiliate at any time during the preceding three months and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares immediately upon the closing of this offering without regard to whether current public information about us is available.

Beginning 90 days after the date of this prospectus, a person who is our affiliate or who was our affiliate at any time during the preceding three months and who has beneficially owned restricted securities for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 446,344 shares immediately after this offering; and
- the average weekly trading volume in our common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the date of filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Upon waiver or expiration of the 180-day lock-up period described below, approximately 25,462,319 shares of our common stock will be eligible for sale under Rule 144. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

Rule 701

In general, under Rule 701 of the Securities Act, any of our employees, consultants or advisors, other than our affiliates, who purchased shares from us in connection with a qualified compensatory stock plan or other

written agreement is eligible to resell these shares 90 days after the date of this prospectus in reliance on Rule 144, but without compliance with the various restrictions, including the availability of public information about us, holding period and volume limitations, contained in Rule 144. Subject to the 180-day lock-up period described above, approximately 9,105,492 shares of our common stock, based on shares outstanding as of April 30, 2020, will be eligible for sale in accordance with Rule 701.

Stock options and form S-8 registration statement

We expect to file one or more registration statements on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding awards and reserved for future issuance under the 2017 Plan, the 2020 Plan and the 2020 ESPP. See “Executive compensation—Stock option and other compensation plans” for additional information regarding these plans. Accordingly, shares of our common stock registered under the registration statements will be available for sale in the open market, subject to Rule 144 volume limitations applicable to affiliates, and subject to any vesting restrictions and lock-up agreements applicable to these shares.

Registration rights

Upon the closing of this offering, the holders of 31,887,645 shares of common stock will have rights, subject to certain 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. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. See “Description of capital stock—Registration rights” for additional information regarding these registration rights.

Material U.S. tax considerations for non-U.S. holders of common stock

The following is a discussion of material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term “non-U.S. holder” means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or 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 taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, as in effect as of the date of this prospectus, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change or different interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, there can be no assurance that the Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described in this prospectus.

This discussion addresses only non-U.S. holders that hold shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder’s individual circumstances nor does it address the alternative minimum tax, the Medicare tax on net investment income or any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other entities that are pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the purchase, ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.

Dividends

If we pay distributions on our common stock, those distributions generally 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. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such non-U.S. holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "—Gain on disposition of common stock."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such non-U.S. holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income is taxed on a net income basis at the same U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence.

Gain on disposition of common stock

A non-U.S. holder generally will not be subject to U.S. federal income tax on gain recognized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the same U.S. federal income tax rates applicable to United States persons (as

defined in the Code), and if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty, may also apply;

- the non-U.S. holder is a nonresident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S.-source capital losses of the non-U.S. holder, if any; or
- we are, or have been at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter), a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

Information reporting and backup withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the non-U.S. holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate, with respect to dividends on our common stock. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8) or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading "—Dividends," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the non-U.S. holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and gross proceeds from the sale or other disposition of, our common stock if paid to a foreign entity unless (1) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (2) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, or (3) the foreign entity is otherwise excepted under FATCA.

Withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA may apply to payments of gross proceeds from a sale or other disposition of our common stock, under recently proposed U.S. Treasury Regulations, withholding on payments of gross proceeds is not required. Although such regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

If withholding under FATCA is required on any payment related to our common stock, investors not otherwise subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) on such payment may be able to seek a refund or credit from the IRS. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock.

Federal estate tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for prospective investors' information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Jefferies LLC and Cowen and Company, LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	4,315,790
Jefferies LLC	3,052,632
Cowen and Company, LLC	2,315,790
Wedbush Securities Inc.	842,104
Total	10,526,316

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.7980 per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to $0.2660 per share from the initial public offering price. After the initial offering of the shares to the public, if all of the common shares are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of any shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 1,578,947 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $1.33 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	$ 1.33	$ 1.33
Total	$ 14,000,000.30	$ 16,099,999.80

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $3,000,000. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $40,000.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, or submit to, or file with, the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exercisable or exchangeable for any shares of our common stock, or publicly disclose the intention to undertake any of the foregoing, or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of the ownership of any shares of common stock or any such other securities (whether any such transaction described in clause (1) or (2) above is to be settled by delivery of shares of common stock or such other securities, in cash or otherwise), without the prior written consent of J.P. Morgan Securities LLC and Jefferies LLC for a period of 180 days after the date of this prospectus, other than the shares of our common stock to be sold in this offering.

The restrictions on our actions, as described above, do not apply to certain transactions, including (1) the issuance of shares of common stock or securities convertible into or exercisable for shares of our common stock pursuant to the conversion or exchange of convertible or exchangeable securities or the exercise of warrants or options (including net exercise) or the settlement of RSUs (including net settlement), in each case outstanding on the date of the underwriting agreement and described in this prospectus; (2) grants of stock options, stock awards, restricted stock, RSUs or other equity awards and the issuance of shares of our common stock or securities convertible into or exercisable or exchangeable for shares of our common stock (whether upon the exercise of stock options or otherwise) to our employees, officers, directors, advisors or consultants pursuant to the terms of an equity compensation plan in effect as of the closing of this offering and described in this prospectus, provided that such recipients enter into a lock-up agreement with the underwriters; (3) our filing of any registration statement on Form S-8 relating to securities granted or to be granted pursuant to any plan in effect on the date of the underwriting agreement and described in this prospectus or any assumed benefit plan pursuant to an acquisition or similar strategic transaction; or (4) shares of our common stock or other securities issued in connection with a transaction with an unaffiliated third party that includes a debt financing or a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or acquisition of not less than a majority or controlling portion of the equity of another entity, provided that (A) the aggregate number of shares issued pursuant to this clause (4) shall not exceed five percent of the total number of outstanding shares of our common stock immediately following the issuance and sale of the shares in this offering and (B) any recipients of such shares enter into a lock-up agreement with the underwriters.

Our directors and executive officers, and substantially all of our shareholders, which we refer to as the lock-up parties, have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 180 days after the date of this prospectus, or the restricted period, may not (and may not cause any of their direct or indirect affiliates to),
without the prior written consent of J.P. Morgan Securities LLC and Jefferies LLC, (1) offer, pledge, sell, contract

to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such lock-up parties in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant (collectively with the common stock, the "lock-up securities")), (2) enter into any hedging, swap or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of ownership of the lock-up securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of lock-up securities, in cash or otherwise, (3) make any demand for, or exercise any right with respect to, the registration of any lock-up securities, or (4) publicly disclose the intention to do any of the foregoing. Such persons or entities have further acknowledged that these undertakings preclude them from engaging in any hedging or other transactions or arrangements (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined) designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition or transfer (by any person or entity, whether or not a signatory to such agreement) of any economic consequences of ownership, in whole or in part, directly or indirectly, of any lock-up securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of lock-up securities, in cash or otherwise.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and the lock-up parties do not apply, subject in certain cases to various conditions, to certain transactions, including (a) transfers or dispositions of lock-up securities: (1) as bona fide gifts, or for bona fide estate planning purposes, (2) by will, other testamentary document or intestate succession, (3) to any trust for the direct or indirect benefit of the lock-up party or any immediate family member, (4) to a corporation, partnership, limited liability company, trust or other entity of which the lock-up party and/or one or more members of its immediate family members are the legal and beneficial owner of all of the outstanding equity securities or similar interests, (5) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (1) through (4), (6) in the case of a corporation, partnership, limited liability company, trust or other entity, (A) to another corporation, partnership, limited liability company, trust or other entity that is an affiliate of the lock-up party, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the lock-up party or its affiliates or (B) as part of a distribution or other transfer or distribution to general or limited partners, members or stockholders of, or other holders of equity interests in, the lock-up party, (7) by operation of law, (8) to us from an employee or other service provider upon death, disability or termination of employment of such employee or service provider, (9) as part of a sale of lock-up securities acquired in this offering (other than, in the case of one of our officers or directors, any securities such officer or director may purchase in this offering) or in open market transactions after the completion of this offering, (10) to us in connection with the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of our common stock (including "net" or "cashless" exercise), including for the payment of exercise price and tax and remittance payments, (11) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all shareholders involving a change in control, provided that if such transaction is not completed, all such lock-up securities would remain subject to the restrictions in the immediately preceding paragraph, or (12) prior to the first public filing of the registration statement filed in connection with this prospectus; (b) exercise of the options, settlement of RSUs or other equity awards, or the exercise of warrants granted pursuant to plans or other equity compensation arrangements described in in this prospectus, provided that any lock-up securities received upon such exercise, vesting or settlement would be subject to restrictions similar to those in the immediately preceding paragraph; (c) exercise outstanding warrants and convert

outstanding convertible securities of our or any securities received upon any such exercise or conversion, provided that any common stock or warrant received upon such exercise or conversion would be subject to restrictions similar to those in the immediately preceding paragraph; and (d) the establishment by lock-up parties of one or more trading plans under Rule 10b5-1 under the Exchange Act, provided that (1) such plan does not provide for the transfer or disposition of lock-up securities during the restricted period and (2) no filing by any party under the Exchange Act or other public announcement is required or made voluntarily in connection with such trading plan.

J.P. Morgan Securities LLC and Jefferies LLC, in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol “GBIO.”

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. 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 that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Notice to prospective investors in Canada

The shares may be sold 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 shares must be made in accordance with an exemption from, 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.

Notice to prospective investors in the European Economic Area and United Kingdom

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

(a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares 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 and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a "qualified investor" within the meaning of Article 2(e) of the Prospectus Regulation. In the case of any shares being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

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

Notice to prospective investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Regulation) (1) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (2) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as

"relevant persons") or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to prospective investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to prospective investors in Japan

The shares have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any "resident" of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to prospective investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong), or the SFO, of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong), or the CO, or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, 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 of 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" as defined in the SFO and any rules made thereunder.

Notice to prospective investors in Singapore

Each representative has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each representative has represented and agreed that it has not offered or sold any shares or caused the shares to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares or cause the shares to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale or invitation for subscription or purchase, of the shares, whether directly or indirectly, to any person in Singapore other than:

(a) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time, or the SFA) pursuant to Section 274 of the SFA;

(b) 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

(c) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) 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; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

   (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

   (ii) where no consideration is or will be given for the transfer;

   (iii) where the transfer is by operation of law;

   (iv) as specified in Section 276(7) of the SFA; or

   (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Notice to prospective investors in the United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Legal matters

The validity of the shares of common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Davis Polk & Wardwell LLP, New York, New York, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

Experts

The consolidated financial statements of Generation Bio Co. at December 31, 2018 and 2019, and for each of the two years in the period ended December 31, 2019, appearing in this prospectus and registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

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 common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement or the exhibits, schedules and amendments to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document are not necessarily complete, and in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference to such contract, agreement or document.

Upon completion of this offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. We also maintain a website at www.generationbio.com and upon completion of the offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Index to consolidated financial statements

Report of independent registered public accounting firm

To the Stockholders and the Board of Directors of Generation Bio Co.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Generation Bio Co. (the Company) as of December 31, 2018 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

Boston, Massachusetts
April 9, 2020, except for Note 13(d), as to which the date is June 8, 2020

Generation Bio Co.
Consolidated balance sheets

(in thousands, except share and per share amounts)	December 31, 2018	December 31, 2019	March 31, 2020 (unaudited)	Pro forma March 31, 2020 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	$ 7,305	$ 15,076	$ 104,473	$ 104,473
Marketable securities	67,565	—	—	—
Tenant receivable	1,288	448	32	32
Prepaid expenses and other current assets	714	2,577	2,787	2,787
Restricted cash	54	55	—	—
Total current assets	76,926	18,156	107,292	107,292
Property and equipment, net	4,486	21,845	22,617	22,617
Restricted cash, noncurrent	2,107	2,052	2,052	2,052
Deferred offering costs	—	87	658	658
Other noncurrent assets	—	—	17	17
Total assets	$ 83,519	$ 42,140	$ 132,636	$ 132,636
Liabilities, convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	$ 1,681	$ 2,251	$ 464	$ 464
Accrued expenses and other current liabilities	4,874	6,907	6,629	6,629
Total current liabilities	6,555	9,158	7,093	7,093
Deferred rent, net of current portion	2,962	15,981	15,769	15,769
Total liabilities	9,517	25,139	22,862	22,862
Commitments and contingencies (Note 11)				
Convertible preferred stock (Series A, B, and C), $0.0001 par value; 26,425,664 shares authorized at December 31, 2018 and 2019 and 46,361,960 shares authorized at March 31, 2020 (unaudited); 26,425,664 shares issued and outstanding at December 31, 2018 and 2019 and 46,361,960 shares issued and outstanding at March 31, 2020 (unaudited); liquidation preference of $115,822 at December 31, 2019 and $227,294 at March 31, 2020 (unaudited); no shares issued or outstanding, pro forma at March 31, 2020 (unaudited)	115,593	115,593	224,425	—

(in thousands, except share and per share amounts)	December 31, 2018	December 31, 2019	March 31, 2020 (unaudited)	Pro forma March 31, 2020 (unaudited)
Stockholders' equity (deficit):				
Common stock, $0.0001 par value; 46,750,000 shares authorized at December 31, 2018 and 2019 and 75,000,000 shares authorized at March 31, 2020 (unaudited); 6,874,424 and 6,976,077 shares issued at December 31, 2018 and 2019, respectively, and 7,010,906 shares issued at March 31, 2020 (unaudited); 4,054,475 and 5,270,889 shares outstanding at December 31, 2018 and 2019, respectively, and 5,570,652 shares outstanding at March 31, 2020 (unaudited); 34,104,991 shares issued and 32,664,737 shares outstanding, pro forma at March 31, 2020 (unaudited)	1	1	1	3
Additional paid-in capital	5,552	9,859	11,517	235,940
Accumulated other comprehensive loss	(9)	—	—	—
Accumulated deficit	(47,135)	(108,452)	(126,169)	(126,169)
Total stockholders' equity (deficit)	(41,591)	(98,592)	(114,651)	109,774
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 83,519	$ 42,140	$ 132,636	$ 132,636

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

Generation Bio Co.
Consolidated statements of operations and comprehensive loss

(in thousands, except share and per share amounts)	Year ended December 31, 2018	Year ended December 31, 2019	Three months ended March 31, 2019 (unaudited)	Three months ended March 31, 2020 (unaudited)
Revenue	$ 36	$ —	$—	$ —
Operating expenses:				
Research and development	28,152	50,134	11,719	13,394
General and administrative	9,178	12,168	2,757	4,642
Total operating expenses	37,330	62,302	14,476	18,036
Loss from operations	(37,294)	(62,302)	(14,476)	(18,036)
Other income (expense):				
Interest income and other income (expense), net	1,491	985	382	319
Net loss and net loss attributable to common stockholders	$ (35,803)	$ (61,317)	$(14,094)	$ (17,717)
Net loss per share attributable to common stockholders, basic and diluted	$ (10.69)	$ (12.96)	$(3.29)	$ (3.22)
Weighted average common shares outstanding, basic and diluted	3,350,537	4,731,519	4,284,174	5,495,013
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (3.11)		$ (0.56)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)		19,692,546		31,389,125
Comprehensive loss:				
Net loss	$ (35,803)	$ (61,317)	$(14,094)	$ (17,717)
Other comprehensive income (loss):				
Unrealized gains (losses) on marketable securities	(9)	9	14	—
Comprehensive loss	$ (35,812)	$ (61,308)	$(14,080)	$ (17,717)

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

Generation Bio Co.
Consolidated statements of convertible preferred stock and stockholders' equity (deficit)

(in thousands, except share amounts)	Series A, B and C convertible preferred stock		Common stock		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount				
Balances at December 31, 2017	**15,451,020**	**$ 15,404**	**2,917,665**	**$ 1**	**$ 2,064**	**$ —**	**$ (11,332)**	**$ (9,267)**
Issuance of Series B convertible preferred stock, net of issuance costs of $181	10,974,644	100,189	—	—	—	—	—	—
Vesting of restricted common stock	—	—	1,136,810	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	3,488	—	—	3,488
Unrealized losses on marketable securities	—	—	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	—		(35,803)	(35,803)
Balances at December 31, 2018	**26,425,664**	**115,593**	**4,054,475**	**1**	**5,552**	**(9)**	**(47,135)**	**(41,591)**
Issuance of common stock for license	—	—	125,677	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	34,740	—	100	—	—	100
Vesting of restricted common stock	—	—	1,055,997	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	4,207	—	—	4,207
Unrealized gains on marketable securities	—	—	—	—	—	9	—	9
Net loss	—	—	—	—	—	—	(61,317)	(61,317)
Balances at December 31, 2019	**26,425,664**	**115,593**	**5,270,889**	**1**	**9,859**	**—**	**(108,452)**	**(98,592)**
Issuance of Series C convertible preferred stock, net of issuance costs of $2,640 (unaudited)	19,936,296	108,832	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options (unaudited)	—	—	34,829	—	154	—	—	154
Vesting of restricted common stock (unaudited)	—	—	264,934	—	—	—	—	—
Stock-based compensation expense (unaudited)	—	—	—	—	1,504	—	—	1,504
Net loss (unaudited)	—	—	—	—	—	—	(17,717)	(17,717)
Balances at March 31, 2020 (unaudited)	**46,361,960**	**224,425**	**5,570,652**	**1**	**11,517**	**—**	**(126,169)**	**(114,651)**
Conversion of convertible preferred stock into common stock (unaudited)	(46,361,960)	(224,425)	27,094,085	2	224,423	—	—	224,425
Pro Forma Balances at March 31, 2020 (unaudited)	**—**	**$ —**	**32,664,737**	**$ 3**	**$ 235,940**	**$ —**	**$ (126,169)**	**$ 109,774**

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

Generation Bio Co.
Consolidated statements of convertible preferred stock and stockholders' equity (deficit)

	Series A and B convertible preferred stock		Common stock		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' deficit
	Shares	Amount	Shares	Amount				
Balances at December 31, 2018	**26,425,664**	**$115,593**	**4,054,475**	**$ 1**	**$ 5,552**	**$ (9)**	**$ (47,135)**	**$ (41,591)**
Issuance of common stock upon exercise of stock options (unaudited)	—	—	14,861	—	9	—	—	9
Vesting of restricted common Stock (unaudited)	—	—	286,335	—	—	—	—	—
Stock-based compensation expense (unaudited)	—	—	—	—	993	—	—	993
Unrealized gains on marketable securities (unaudited)	—	—	—	—	—	14	—	14
Net loss (unaudited)	—	—	—	—	—	—	(14,094)	(14,094)
Balances at March 31, 2019 (unaudited)	**26,425,664**	**$115,593**	**4,355,671**	**$ 1**	**$ 6,554**	**$ 5**	**$ (61,229)**	**$ (54,669)**

Generation Bio Co.
Consolidated statements of cash flows

(in thousands)	Year ended December 31, 2018	Year ended December 31, 2019	Three months ended March 31, 2019 (unaudited)	Three months ended March 31, 2020 (unaudited)
Cash flows from operating activities:				
Net loss	$ (35,803)	$ (61,317)	$ (14,094)	$ (17,717)
Adjustments to reconcile net loss to net cash used in operating activities:				
Stock-based compensation expense	3,488	4,207	993	1,504
Depreciation and amortization expense	347	1,864	170	677
Accretion of discount on marketable securities	(834)	(317)	(145)	—
Gain on sale of property and equipment	—	(10)	—	—
Changes in operating assets and liabilities:				
Tenant receivable	(1,288)	840	(3,807)	416
Prepaid expenses and other current assets	(498)	(1,863)	(961)	(210)
Other noncurrent assets	17	—	—	(17)
Accounts payable	223	761	(647)	(1,304)
Accrued expenses and other current liabilities	3,263	2,470	329	(917)
Deferred rent	2,966	13,019	6,068	(212)
Net cash used in operating activities	(28,119)	(40,346)	(12,094)	(17,780)
Cash flows from investing activities:				
Purchases of property and equipment	(3,021)	(19,986)	(5,844)	(2,011)
Proceeds from sale of property and equipment	—	80	—	—
Purchases of marketable securities	(109,940)	(20,789)	(20,789)	—
Sales and maturities of marketable securities	43,200	88,680	42,080	—
Net cash provided by (used in) investing activities	(69,761)	47,985	15,447	(2,011)
Cash flows from financing activities:				
Proceeds from issuance of convertible preferred stock, net of issuance costs	100,189	—	—	109,044
Proceeds from exercise of stock options	—	100	9	154
Payments of deferred offering costs	—	(22)	—	(65)
Net cash provided by financing activities	100,189	78	9	109,133
Net increase in cash, cash equivalents and restricted cash	2,309	7,717	3,362	89,342
Cash, cash equivalents and restricted cash at beginning of period	7,157	9,466	9,466	17,183
Cash, cash equivalents and restricted cash at end of period	$ 9,466	$ 17,183	$ 12,828	$ 106,525
Supplemental disclosure of noncash investing and financing information:				
Purchases of property and equipment included in accounts payable and accrued expenses	$ 1,337	$ 644	$ 2,887	$ 82
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ —	$ —	$ 658
Preferred stock issuance costs included in accrued expenses	$ —	$ 65	$ —	$ 125

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

Generation Bio Co.
Notes to consolidated financial statements

1. Nature of the business and basis of presentation

The Company was incorporated on October 21, 2016 as Torus Therapeutics, Inc. and subsequently changed its name to Generation Bio Co. (the “Company” or “Generation Bio”). The Company is an innovative genetic medicines company creating a new class of gene therapy utilizing its proprietary non-viral gene therapy platform to provide durable, redosable treatments for millions of patients living with rare and prevalent diseases. The Company’s non-viral gene therapy platform incorporates its high-capacity DNA construct called closed-ended DNA (“ceDNA”), its cell-targeted lipid nanoparticle delivery system (“ctLNP”) and its established, scalable capsid-free manufacturing process. Using its approach, the Company is developing novel gene therapies to provide targeted delivery of genetic payloads that include large and multiple genes to a range of tissues across a broad array of diseases. The Company is also engineering its gene therapies to be redosable, which may enable individualized patient titration to reach the desired therapeutic expression and to maintain efficacy throughout a patient’s life. The Company is headquartered in Cambridge, Massachusetts.

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, dependence on key personnel, protection of proprietary technology, compliance with government regulations, the ability to establish clinical- and commercial-scale manufacturing processes and the ability to secure additional capital to fund operations. Programs currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization of a product. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company’s development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The accompanying consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Through December 31, 2019, the Company has funded its operations with the proceeds from instruments convertible into convertible preferred stock (which converted into convertible preferred stock in 2017) and the sale of convertible preferred stock. Since inception, the Company has incurred recurring losses, including net losses of $61.3 million for the year ended December 31, 2019 and $17.7 million for the three months ended March 31, 2020 (unaudited). As of December 31, 2019 and March 31, 2020 (unaudited), the Company had an accumulated deficit of $108.5 million and $126.2 million, respectively. The Company expects to continue to generate operating losses in the foreseeable future. As of April 9, 2020, the issuance date of the annual consolidated financial statements for the year ended December 31, 2019, the Company expected that its cash and cash equivalents, including gross proceeds of $111.5 million it received in January 2020 from the sale of Series C convertible preferred stock (see Note 13), would be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the issuance date of the annual consolidated financial statements.

As of May 12, 2020 (unaudited), the issuance date of the interim condensed consolidated financial statements for the three months ended March 31, 2020, the Company expects that its cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months.

The Company is seeking to complete an initial public offering (“IPO”) of its common stock. Upon the completion of a qualified public offering on specified terms, the Company’s outstanding convertible preferred stock will automatically convert into shares of common stock (see Note 6).

The Company will need to obtain additional funding through public or private equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborative or strategic alliances or licensing arrangements. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. Arrangements with collaborators or others may require the Company to relinquish rights to certain of its technologies or programs. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, pipeline expansion or commercialization efforts, which could adversely affect its business prospects.

Although management will continue to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations when needed or at all.

The accompanying consolidated financial statements reflect the operations of the Company and the Company's wholly owned subsidiary, Generation Bio Securities Corporation. Intercompany balances and transactions have been eliminated in consolidation. The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles ("GAAP") in the United States of America. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

2. Summary of significant accounting policies

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual of research and development expenses and stock-based compensation expense. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates, as there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results may differ from those estimates or assumptions.

Unaudited interim financial information

The accompanying consolidated balance sheet as of March 31, 2020, the condensed consolidated statements of operations and comprehensive loss and cash flows for the three months ended March 31, 2019 and 2020, and the condensed consolidated statements of convertible preferred stock and stockholders' equity (deficit) for the three months ended March 31, 2019 and 2020 are unaudited. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited annual consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of March 31, 2020 and the results of its operations and its cash flows for the three months ended March 31, 2019 and 2020. The financial data and other information disclosed in these notes related to the three months ended March 31, 2019 and 2020 are also unaudited. The results for the three months ended March 31, 2020 are not necessarily indicative of results to be expected for the year ending December 31, 2020, any other interim periods, or any future year or period.

Unaudited pro forma information

The accompanying unaudited pro forma consolidated balance sheet and consolidated statement of convertible preferred stock and stockholders' equity (deficit) as of March 31, 2020 have been prepared to give effect, upon a qualified IPO, to the automatic conversion of all shares of convertible preferred stock outstanding into 27,094,085 shares of common stock as if the proposed IPO had occurred on March 31, 2020.

In the accompanying consolidated statements of operations and comprehensive loss, the unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2019 and the three months ended March 31, 2020 have been prepared to give effect, upon a qualified IPO, to the automatic conversion of all shares of convertible preferred stock outstanding into shares of common stock as if the proposed IPO had occurred on the later of the beginning of the period presented or the issuance date of the convertible preferred stock. The unaudited pro forma basic and diluted net loss per share attributable to common stockholders gives effect to the issuance of shares of Series C convertible preferred stock and the resulting adjustment to the Series B convertible preferred stock conversion ratio on the date the transaction occurred in January 2020 (see Notes 6 and 13).

Concentrations of credit risk and of significant suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company has not experienced any other-than-temporary losses with respect to its cash and cash equivalents and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on a small number of third-party suppliers for its drug substance and drug product. In particular, the Company relies, and expects to continue to rely, on third-party suppliers for certain materials and components required for the production of any product candidates it may develop for its programs. These programs could be adversely affected by a significant interruption in the supply process.

Deferred offering costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the carrying value of the preferred stock or, for issuances of common stock, in stockholder's equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. As of December 31, 2019, the Company recorded $0.1 million of deferred offering costs related to its Series C convertible preferred stock financing (see Note 13). Upon the issuance of the Series C convertible preferred stock in January 2020 (unaudited), the deferred offering costs were reclassified as a reduction to the carrying value of the preferred stock. As of March 31, 2020 (unaudited), the Company recorded $0.7 million of deferred offering costs related to its planned IPO.

Cash equivalents

The Company considers all highly liquid investments with a remaining maturity when purchased of three months or less to be cash equivalents.

Restricted cash

Amounts included in restricted cash represent amounts pledged as collateral for letters of credit required for security deposits on the Company's leased facilities. These amounts are classified as restricted cash (current and noncurrent) on the Company's consolidated balance sheets.

Marketable securities

The Company's marketable securities, which consisted of debt securities as of December 31, 2018, are classified as available-for-sale and are reported at fair value. Unrealized gains and losses on available-for-sale debt securities are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity (deficit). Realized gains and losses and declines in value determined to be other than temporary are based on the specific identification method and are included as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss.

The Company evaluates its marketable securities with unrealized losses for other-than-temporary impairment. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company reduces the investment to fair value through a charge to the statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Fair value measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and financial liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents and marketable securities are carried at fair value, determined according to the fair value hierarchy described above (see Note 3). The carrying values of the Company's tenant receivable, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

Deferred rent

Payment escalations, rent holidays and other lease incentives that may be included in lease agreements are accrued or deferred as appropriate such that rent expense for each lease is recognized on a straight-line basis over the respective lease term. Adjustments for such items are recorded as deferred rent and amortized over the respective lease terms.

Property and equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	Estimated useful life
Laboratory equipment	5 years
Computer equipment and software	3 years
Furniture and fixtures	5 years
Leasehold improvements	Shorter of remaining life of lease or useful life

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance which do not improve or extend the life of the respective assets are charged to expense as incurred.

Impairment of long-lived assets

Long-lived assets consist of property and equipment. The Company evaluates the recoverability of its long-lived assets when circumstances indicate that an event of impairment may have occurred. The Company recognizes an impairment loss only if the carrying amount of a long-lived asset is not recoverable based on its undiscounted future cash flows. Impairment is measured based on the difference between the carrying value of the related assets and the fair value of such assets. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2018 or 2019 or the three months ended March 31, 2019 or 2020 (unaudited).

Classification and accretion of convertible preferred stock

The Company's convertible preferred stock is classified outside of stockholders' equity (deficit) on the consolidated balance sheets because the holders of such shares have redemption rights in the event of a deemed liquidation that, in certain situations, is not solely within the control of the Company and would require the redemption of the then-outstanding convertible preferred stock. A deemed liquidation includes Liquidation Events as that term is defined in Note 6. The Company's Series A and Series B convertible preferred stock are not redeemable, except in the event of a deemed liquidation (see Note 6). Because the occurrence of a deemed liquidation event is not currently probable, the carrying values of the convertible preferred stock are not being accreted to their redemption values. If a deemed liquidation event became probable, the carrying values of the convertible preferred stock would be accreted to redemption values.

Segment information

The Company has determined that its chief executive officer is the chief operating decision maker ("CODM"). The CODM reviews financial information presented on a consolidated basis. Resource allocation decisions are made by the CODM based on consolidated results. There are no segment managers who are held accountable by the CODM for operations, operating results, and planning for levels or components below the consolidated unit level. As such, the Company has concluded that it operates as one segment. All long-lived assets are located in the United States.

Revenue recognition

To date, the Company has derived its revenue by providing services to pharmaceutical and life sciences companies. On January 1, 2019, the Company adopted ASU 2014-09, discussed below under the heading “Recently Adopted Accounting Pronouncements”, which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition across all industries. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of the new revenue standard, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation.

The Company only applies the five-step model to contracts when collectability of the consideration to which the Company is entitled in exchange for the goods or services it transfers to the customer is determined to be probable. Amounts are recorded as accounts receivable when the Company’s right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. The Company recognizes revenue when it satisfies its performance obligations by delivering the services to its customers in an amount that reflects the consideration to which it expects to be entitled in exchange for those services.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue on the accompanying balance sheets. Amounts expected to be recognized as revenue within 12 months of the balance sheet date are classified as current deferred revenue. The Company had no deferred revenue as of December 31, 2019, or March 31, 2020 (unaudited). The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that would have been recognized is one year or less or the amount is immaterial. As of December 31, 2019 and March 31, 2020 (unaudited), the Company had not capitalized any costs to obtain contracts.

Research and development costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries and bonuses, stock-based compensation, employee benefits, facilities costs, laboratory supplies, depreciation and amortization, manufacturing expenses and external costs of vendors engaged to conduct preclinical development activities as well as the cost of licensing technology.

Upfront payments and milestone payments made for the licensing of technology are expensed as research and development expenses in the period in which they are incurred. Advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Research and manufacturing contract costs and accruals

The Company has entered into various research and development and manufacturing contracts. These agreements are generally cancelable, and related payments are recorded as the corresponding expenses are incurred. The Company records accruals for estimated ongoing costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the research studies and manufacturing activities, including the phase or completion of events, invoices received and contracted costs. Significant judgments and

estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-based compensation

The Company measures stock options with service-based vesting or performance-based vesting granted to employees, non-employees and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. The Company measures restricted common stock awards using the difference between the purchase price per share of the award, if any, and the fair value of the Company's common stock at the date of grant. The Company's board of directors values the Company's common stock, taking into consideration its most recently available valuation of common stock performed by third parties as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

Compensation expense for awards with service-based vesting is generally recognized over the vesting period of the award using the straight-line method to record the expense. The Company uses the graded-vesting method to record the expense of awards with both service-based and performance-based vesting conditions, commencing once achievement of the performance condition becomes probable. The Company accounts for forfeitures of share-based awards as they occur. The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Prior to the adoption of ASU 2018-07 on January 1, 2019 discussed below, the Company measured the fair value of stock-based awards granted to non-employees on the date that the related service was complete, which was generally the vesting date of the award. Prior to the service completion date, compensation expense was recognized over the period during which services were rendered by such non-employees. At the end of each financial reporting period prior to the service completion date, the fair value of the unvested awards was remeasured using the then-current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model for options or the then-current fair value of the Company's common stock for restricted common stock awards.

Comprehensive loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2018 and 2019, and the three months ended March 31, 2019 (unaudited) the Company's only element of other comprehensive loss was unrealized gains (losses) on marketable securities. The Company did not record other comprehensive loss during the three months ended March 31, 2020 (unaudited).

Income taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and

liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties. The Company's policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company had accrued no amounts for interest and penalties on its consolidated balance sheets at December 31, 2018 and 2019 and March 31, 2020 (unaudited).

Net loss per share

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (loss) available to common stockholders for the period to be allocated between common stock and participating securities based upon their respective rights to share in the earnings as if all income (loss) for the period had been distributed.

Basic net income (loss) per share attributable to common stockholders is computed by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net income (loss) per share attributable to common stockholders is computed by adjusting net income (loss) attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares.

The Company's participating securities contractually entitle the holders of such shares to participate in dividends but do not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2018 and 2019 and the three months ended March 31, 2019 and 2020 (unaudited).

Recently adopted accounting pronouncements

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the Company expects to receive for those goods or services. The FASB has subsequently issued several amendments to ASU 2014-09 that have the same effective date and transition date. For public entities, the guidance was effective for annual reporting periods beginning after December 15, 2017 and for interim periods within that reporting period. For nonpublic entities, the guidance is effective for annual reporting periods beginning after December 15, 2018. The Company adopted ASU 2014-09 on January 1, 2019 using the modified retrospective transition method. The adoption did not have an impact on its consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07, Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The new standard largely aligns the accounting for share-based payment awards issued to employees and nonemployees by expanding the scope of ASC 718 to apply to nonemployee share-based transactions, as long as the transaction is not effectively a form of financing. For public entities, ASU 2018-07 was required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. For non-public entities, ASU 2018-07 is effective for annual periods beginning after December 15, 2019. Early adoption is permitted for all entities but no earlier than the Company's adoption of ASU 2014-09. The Company early adopted ASU 2018-07 on January 1, 2019 and the adoption did not have a material impact on the Company's consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820): Disclosure Requirements for Fair Value Measurement. The new standard added, modified or removed disclosure requirements under Topic 820 for clarity and consistency. ASU 2018-13 is effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The Company adopted ASU 2018-03 on January 1, 2020 and the adoption did not have a material impact on its consolidated financial statements.

Recently issued accounting pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that the Company adopts as of the specified effective date. The Company qualifies as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 and has elected not to "opt out" of the extended transition related to complying with new or revised accounting standards, which means that when a standard is issued or revised and it has different application dates for public and nonpublic companies, the Company can adopt the new or revised standard at the time nonpublic companies adopt the new or revised standard and can do so until such time that the Company either (i) irrevocably elects to "opt out" of such extended transition period or (ii) no longer qualifies as an emerging growth company.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). The new standard requires that all lessees recognize the assets and liabilities that arise from leases on the balance sheet and disclose qualitative and quantitative information about its leasing arrangements. In July 2018, the FASB issued ASU 2018-11, which provides entities with an additional transition method to adopt Topic 842. Under the new transition method, an entity initially applies the new lease requirements at the adoption date, not the earliest period presented, and recognizes a cumulative effect adjustment to the opening balance of retained earnings in the period of adoption. For public entities, the guidance was effective for annual reporting periods beginning after December 15, 2018 and for interim periods within those fiscal years. For nonpublic entities, the guidance was effective for annual reporting periods beginning after December 15, 2019. Early adoption is permitted for all entities. In November 2019, the FASB issued ASU 2019-10, which deferred the effective date for nonpublic

entities to annual reporting periods beginning after December 15, 2020, and interim periods within fiscal years beginning after December 15, 2021. Early adoption continues to be allowed. The Company will adopt ASU 2016-02 on January 1, 2021 using the modified retrospective approach transition method as of the date of adoption such that prior periods will not be restated. The Company will also elect a package of practical expedients, under which an entity need not reassess whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases, or initial direct costs for any existing leases. The adoption of the new standard is expected to result in the recognition of material liabilities and right-of-use assets, however, the Company has not completed its assessment.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments – Credit Losses (Topic 326). The new standard adjusts the accounting for assets held at amortized costs basis, including marketable securities accounted for as available-for-sale. The standard eliminates the probable initial recognition threshold and requires an entity to reflect its current estimate of all expected credit losses. The allowance for credit losses is a valuation account that is deducted from the amortized cost basis of the financial assets to present the net amount expected to be collected. For public entities, the guidance is effective for annual reporting periods beginning after December 15, 2019 and for interim periods within those fiscal years. For nonpublic entities, the guidance was effective for annual reporting periods beginning after December 15, 2020. Early adoption is permitted for all entities. In November 2019, the FASB issued ASU 2019-10, which deferred the effective date for nonpublic entities to annual reporting periods beginning after December 15, 2022, including interim periods within those fiscal years. The Company is currently evaluating when to adopt the guidance and the impact the guidance will have on its consolidated financial statements.

3. Marketable securities and fair value measurements

Marketable securities by security type consisted of the following:

	December 31, 2018			
(in thousands)	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair value
U.S. treasury bills and notes	$ 67,574	$ —	$ (9)	$67,565
	$ 67,574	$ —	$ (9)	$67,565

The Company did not have marketable securities as of December 31, 2019 or March 31, 2020 (unaudited).

The following tables present the Company's assets that are measured at fair value on a recurring basis and indicate the level within the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value, which is described further within Note 2, Summary of Significant Accounting Policies:

	Fair value measurements at December 31, 2018 using:			
(in thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 7,244	$ —	$ —	$ 7,244
Marketable securities				
U.S. treasury bills and notes	—	67,565	—	67,565
Totals	$ 7,244	$67,565	$ —	$74,809

(in thousands)	Fair value measurements at December 31, 2019 using: Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$15,076	$ —	$ —	$15,076
Totals	$15,076	$ —	$ —	$15,076

(in thousands)	Fair value measurements at March 31, 2020 (unaudited) using: Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$104,473	$ —	$ —	$104,473
Totals	$104,473	$ —	$ —	$104,473

U.S. government money market funds were valued by the Company based on quoted market prices, which represent a Level 1 measurement within the fair value hierarchy. U.S. treasury bills and notes were valued by the Company using quoted prices in active markets for similar securities, which represent a Level 2 measurement within the fair value hierarchy. During the years ended December 31, 2018 and 2019, there were no transfers between Level 1, Level 2 and Level 3.

4. Property and equipment, net

Property and equipment, net consisted of the following:

(in thousands)	December 31, 2018	2019	March 31, 2020 (unaudited)
Laboratory equipment	$3,053	$ 5,029	$ 5,658
Computer equipment and software	261	740	740
Furniture and fixtures	—	826	826
Leasehold improvements	1,561	12,993	12,855
Construction in progress	—	4,487	5,445
	4,875	24,075	25,524
Less: Accumulated depreciation and amortization	(389)	(2,230)	(2,907)
	$4,486	$21,845	$ 22,617

Depreciation and amortization expense for the years ended December 31, 2018 and 2019 was $0.3 million and $1.9 million, respectively. Depreciation and amortization expense for the three months ended March 31, 2019 and 2020 (unaudited) was $0.2 million and $0.7 million, respectively. At December 31, 2019 and March 31, 2020 (unaudited), construction in progress was related to the build-out of leasehold improvements in the Company's new facility.

5. Accrued expenses

Accrued expenses consisted of the following:

(in thousands)	December 31, 2018	December 31, 2019	March 31, 2020 (unaudited)
Accrued employee compensation and benefits	$2,572	$3,255	$ 1,779
Accrued external research and development expenses	1,284	1,344	1,412
Accrued professional fees	102	619	1,626
Deferred rent	4	1,370	1,370
Other	912	319	442
	$4,874	$6,907	$ 6,629

6. Convertible preferred stock

The Company has issued Series A convertible preferred stock (the “Series A”), Series B convertible preferred stock (the “Series B”) and Series C convertible preferred stock (the “Series C”). Collectively the Series A, Series B and Series C are referred to as the Preferred Stock. On February 22, 2018, the Company issued and sold 10,974,644 shares of Series B at a price of $9.1457 per share for gross proceeds of $100.4 million. The Company incurred issuance costs in connection with this transaction of $0.2 million.

On January 9, 2020 (unaudited), the Company issued and sold 19,936,296 shares of Series C at a price of $5.5914 per share for gross proceeds of $111.5 million. The Company incurred issuance costs in connection with this transaction of $2.6 million.

Upon issuance of each class of Preferred Stock, the Company assessed the embedded conversion and liquidation features of the shares and determined that such features did not require the Company to separately account for these features. The Company also concluded that no beneficial conversion feature existed on the issuance date of each class of Preferred Stock.

Preferred Stock consisted of the following at December 31, 2018 and 2019:

(in thousands except share amounts)	Preferred stock authorized	Preferred stock issued and outstanding	Carrying value	Liquidation preference	Common stock issuable upon conversion
Series A Preferred Stock	15,451,020	15,451,020	$ 15,404	$ 15,451	8,747,675
Series B Preferred Stock	10,974,644	10,974,644	100,189	100,371	6,213,352(1)
	26,425,664	26,425,664	$ 115,593	$ 115,822	14,961,027(1)

(1) Upon issuance and sale of the Series C in January 2020 (see Note 13), the 10,974,644 outstanding shares of Series B became convertible into 7,059,406 shares of common stock and the 26,425,664 outstanding shares of Preferred Stock became convertible into 15,807,081 shares of common stock.

Preferred Stock consisted of the following at March 31, 2020 (unaudited):

(in thousands except share amounts)	Preferred stock authorized	Preferred stock issued and outstanding	Carrying value	Liquidation preference	Common stock issuable upon conversion
Series A Preferred Stock	15,451,020	15,451,020	$ 15,404	$ 15,451	8,747,675
Series B Preferred Stock	10,974,644	10,974,644	100,189	100,371	7,059,406
Series C Preferred Stock	19,936,296	19,936,296	108,832	111,472	11,287,004
	46,361,960	46,361,960	$ 224,425	$ 227,294	27,094,085

The holders of Preferred Stock have the following rights and preferences after considering the issuance of the Series C in January 2020 (unaudited):

Voting

The holders of Preferred Stock are entitled to vote, together with the holders of common stock, on matters submitted to stockholders for a vote. The holders of Preferred Stock are entitled to the number of votes equal to the number of shares of common stock into which each such share of Preferred Stock could convert. In addition, the holders of Series A, voting exclusively and as a separate class, are entitled to elect two directors of the Company. The holders of Series B, voting exclusively and as a separate class, are entitled to elect one director of the Company.

Conversion

Each share of Preferred Stock is convertible at the option of the holder at any time after the date of issuance. Each share of Preferred Stock will be automatically converted into shares of common stock at the applicable conversion ratio then in effect upon the closing of a firm commitment public offering of common stock with a price of at least $8.0496 per share and at least $40.0 million of gross proceeds to the Company. Shares of Series A will be automatically converted into shares of common stock at the applicable conversion ratio then in effect upon written consent of the holders of at least a majority of the then-outstanding shares of Series A. Shares of Series B will be automatically converted into shares of common stock at the applicable conversion ratio then in effect upon written consent of the holders of at least 57% of the then-outstanding shares of Series B. Shares of Series C will be automatically converted into shares of common stock at the applicable conversion ratio then in effect upon written consent of the holders of at least a majority of the then-outstanding shares of Series C.

The conversion ratio of each series of Preferred Stock is determined by dividing the Original Issue Price of each series by the Conversion Price of each series. The Original Issue Price is $1.00 per share for Series A and $9.1457 per share for Series B. The Conversion Price at issuance was $1.7663 per share for Series A and $16.1540 per share (when rounded to the nearest ten-thousandth) for Series B, subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization and other adjustments as set forth in the Company's certificate of incorporation, as amended and restated. As a result, as of December 31, 2018 and 2019, each outstanding share of Series A and Series B was convertible into common stock on a 1.7663-for-one basis. The Original Issue Price is $5.5914 per share for Series C and the Conversion Price of the Series C is $9.8761 per share (when rounded to the nearest ten-thousandth), subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization and other adjustments as set forth in the Company's certificate of incorporation, as amended and restated. As a result, each outstanding share of Series C is convertible into common stock on a 1.7663-for-one basis.

Upon the issuance and sale of Series C in January 2020 at the Original Issue Price of $5.5914 per share, the Conversion Price of the Series B was adjusted to $14.2180 per share (when rounded to the nearest ten-thousandth) (see Note 13).

Dividends

The holders of Preferred Stock are entitled to receive noncumulative dividends if and when declared by the Company's board of directors at a rate of 6.0% of the Original Issuance Price per share of each series of Preferred Stock (subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization with respect to such shares) per annum. The Company may not declare, pay or set aside any dividends on shares of any other series of capital stock of the Company, other than dividends on common stock payable in common stock, unless the holders of the Preferred Stock first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock in an amount equal to the greater of (i) 6.0% of the Original Issuance Price of each series of Preferred Stock (subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization with respect to such shares) per annum from the date of issuance of such shares, and (ii) (A) in the case of a dividend on common stock or any class or series of stock that is convertible into common stock, that dividend per share of Preferred Stock as would equal the product of (1) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (2) the number of shares of common stock issuable upon conversion of each share of Preferred Stock, or (B) in the case of a dividend on any class or series that is not convertible into common stock, at a rate per share of Preferred Stock determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the Original Issue Price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination of or other similar recapitalization affecting such shares) and (2) multiplying such fraction by an amount equal to the Original Issue Price of each series of Preferred Stock. If the Company declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Company, the dividend payable to the holders of the Preferred Stock shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest Preferred Stock dividend. No dividends were declared or paid during the years ended December 31, 2018 or 2019 or the three months ended March 31, 2020 (unaudited).

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Company or Liquidating Event (as described below), the holders of shares of Preferred Stock will receive, in preference to the common stockholders, an amount equal to the greater of (i) the Original Issue Price per share of the respective share of Preferred Stock, plus all dividends declared but unpaid on such shares, or (ii) the amount the holders would receive if the Preferred Stock were converted into common stock prior to such liquidation event. In the event that the assets available for distribution to the Company's stockholders are not sufficient to permit payment to the holders of Preferred Stock in the full amount to which they are entitled, the assets available for distribution will be distributed on a pro rata basis among the holders of the Preferred Stock. After the payment of all preferential amounts to the holders of the Preferred Stock then, to the extent available, the remaining assets available for distribution shall be distributed among the holders of the common stock ratably based on the number of shares of common stock held by each holder.

Unless the holders of (i) at least a majority of the then-outstanding shares of Preferred Stock, voting together as a single class on an as-converted basis, (ii) at least 57% of the then-outstanding shares of Series B, voting together as a separate series on an as-converted basis, and (iii) at least a majority of the then-outstanding shares of Series C, voting together as a separate series on an as-converted basis, elect otherwise, a Liquidating Event shall include a merger or consolidation (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

7. Common stock

The voting, dividend and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth above. Each share of common stock entitles the holder to one vote, together with the holders of the Preferred Stock, on all matters submitted to the stockholders for a vote.

8. Stock-based compensation

2017 Stock Incentive Plan

The Company's 2017 Stock Incentive Plan (the "2017 Plan") provides for the Company to grant incentive stock options or nonstatutory stock options, restricted stock, restricted stock units and other equity awards to employees, directors and consultants of the Company. The 2017 Plan is administered by the board of directors or, at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting and other restrictions on any award under the 2017 Plan are determined at the discretion of the board of directors, or its committee if so delegated.

Stock options granted under the 2017 Plan with service-based vesting conditions generally vest over four years and expire after ten years. The exercise price for stock options granted is not less than the fair value of common stock as determined by the board of directors as of the date of grant.

The total number of shares of common stock that may be issued under the 2017 Plan was 8,407,405 shares as of December 31, 2019, of which 773,652 shares remained available for future issuance. During the three months ended March 31, 2020 (unaudited), the Company increased the number of shares of common stock authorized for issuance under the 2017 Plan from 8,407,405 shares to 10,275,717 shares. As of March 31, 2020 (unaudited), 946,809 shares remained available for future issuance under the 2017 Plan. Shares that are expired, terminated, surrendered or canceled without having been fully exercised will be available for future awards under the 2017 Plan.

Stock option valuation

The fair value of stock option grants is estimated using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the fair value of stock options granted:

Stock options

	Year ended December 31,		Three months ended March 31,	
	2018	2019	2019	2020
			(unaudited)	(unaudited)
Risk-free interest rate	2.70%	2.00%	2.54%	0.73%
Expected volatility	76.0%	75.7%	74.1%	78.9%
Expected dividend yield	—	—	—	—
Expected term (in years)	6.1	6.0	6.0	6.0

The following table summarizes the Company's stock option activity since December 31, 2018:

	Number of shares	Weighted average exercise price	Weighted average contractual term (in years)	Aggregate intrinsic value (in thousands)
Outstanding as of December 31, 2018	2,784,581	$ 4.05	9.4	$ 1,403
Granted	1,200,954	5.92		
Exercised	(34,740)	2.88		
Forfeited	(576,911)	3.89		
Outstanding as of December 31, 2019	3,373,884	$ 4.76	8.79	$ 8,492
Granted (unaudited)	1,728,443	5.16		
Exercised (unaudited)	(34,829)	4.42		
Forfeited (unaudited)	(33,288)	4.63		
Outstanding as of March 31, 2020 (unaudited)	5,034,210	$ 4.89	9.03	$ 1,797
Vested and expected to vest as of December 31, 2019	3,373,884	$ 4.76	8.79	$ 8,492
Vested and expected to vest as of March 31, 2020 (unaudited)	5,034,210	$ 4.89	9.03	$ 1,797
Options exercisable as of December 31, 2019	852,647	$ 4.05	8.38	$ 2,735
Options exercisable as of March 31, 2020 (unaudited)	1,077,849	$ 4.16	8.25	$ 1,171

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had strike prices lower than the fair value of the Company's common stock.

The weighted average grant-date fair value of awards granted during the years ended December 31, 2018 and 2019 was $3.59 per share and $4.46 per share, respectively. The weighted average grant-date fair value of awards granted during the three months ended March 31, 2019 and 2020 (unaudited) was $4.26 per share and $3.46 per share, respectively.

There were no stock options exercised during the year ended December 31, 2018. The total intrinsic value of stock options exercised during the year ended December 31, 2019 was $0.1 million. The aggregate intrinsic value of stock options exercised during the three months ended March 31, 2019 and 2020 (unaudited) was $0.1 million and $0.1 million, respectively.

Restricted common stock

The Company issued 394,213 shares of service-based restricted common stock awards during the year ended December 31, 2018. The Company did not issue any restricted common stock awards during the year ended December 31, 2019 or the three months ended March 31, 2020 (unaudited).

The following table summarizes the Company's restricted common stock activity since December 31, 2018:

	Shares	Weighted average grant date fair value
Unvested restricted common stock as of December 31, 2018	2,819,949	$ 1.24
Issued	—	—
Vested	(1,055,997)	1.30
Forfeited	(58,764)	0.73
Unvested restricted common stock as of December 31, 2019	1,705,188	$ 1.22
Issued (unaudited)	—	—
Vested (unaudited)	(264,934)	1.16
Forfeited (unaudited)	—	—
Unvested restricted common stock as of March 31, 2020 (unaudited)	1,440,254	$ 1.24

The total fair value of restricted common stock vested during the years ended December 31, 2018 and 2019 was approximately $1.2 million and $7.0 million, respectively. The total fair value of restricted common stock vested during the three months ended March 31, 2019 and 2020 (unaudited) was approximately $1.8 million and $1.5 million, respectively.

Stock-Based Compensation

The Company records compensation cost for all share-based payment arrangements, including employee, director and consultant stock options and restricted common stock. The Company recorded stock-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss:

	Year ended December 31,		Three months ended March 31,	
(in thousands)	2018	2019	2019	2020
			(unaudited)	(unaudited)
Research and development expenses	$2,093	$2,753	$ 676	$ 827
General and administrative expenses	1,395	1,454	317	677
	$3,488	$4,207	$ 993	$ 1,504

As of December 31, 2019, total unrecognized compensation cost related to unvested stock-based awards was $10.9 million, which is expected to be recognized over a weighted average period of 2.4 years. As of March 31, 2020 (unaudited), total unrecognized compensation cost related to unvested stock-based awards was $12.0 million, which is expected to be recognized over a weighted average period of 2.8 years. Additionally, as of March 31, 2020 (unaudited), the Company has unrecognized compensation cost related to unvested stock-based awards with performance-based vesting conditions for which performance has not been deemed probable of $2.0 million.

9. Income taxes

For the years ended December 31, 2018 and 2019 and the three months ended March 31, 2020 (unaudited), the Company recorded no income tax benefits for the net operating losses incurred or for the research and development tax credits generated in each year, due to its uncertainty of realizing a benefit from those items. All of the Company's operating losses since inception have been generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2018	**2019**
Federal statutory income tax rate	(21.0)%	(21.0)%
State income taxes, net of federal benefit	(5.6)	(5.9)
Federal and state research and development tax credits	(6.5)	(5.1)
Stock-based compensation expense	1.6	1.0
Other	—	0.2
Change in deferred tax asset valuation allowance	31.5	30.8
Effective income tax rate	0.0%	0.0%

Net deferred tax assets as of December 31, 2018 and 2019 consisted of the following:

	December 31,	
(in thousands)	**2018**	**2019**
Deferred tax assets:		
Net operating loss carryforwards	$ 10,183	$ 25,023
Research and development tax credit carryforwards	2,878	5,998
Deferred rent	—	4,740
Other	1,701	1,469
Total deferred tax assets	14,762	37,230
Deferred tax liabilities:		
Property and equipment	(516)	(4,117)
Total deferred tax liabilities	(516)	(4,117)
Valuation allowance	(14,246)	(33,113)
Net deferred tax assets	$ —	$ —

As of December 31, 2019, the Company had federal net operating loss carryforwards of $91.9 million, which may be available to offset future taxable income, of which $8.2 million of the total net operating loss carryforwards expire at various dates beginning in 2036, while the remaining $83.7 million do not expire but may be limited in their usage to an annual deduction equal to 80% of annual taxable income. As of December 31, 2019, the Company had state net operating loss carryforwards of $90.6 million, which may be available to offset future taxable income and expire at various dates beginning in 2036. In addition, as of December 31, 2019, the Company also had federal and state research and development tax credit carryforwards of $4.0 million and $2.5 million, respectively, which may be available to reduce future tax liabilities and expire at various dates beginning in 2036 and 2032, respectively.

Utilization of the U.S. federal and state net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 and Section 383 of the

Internal Revenue Code of 1986, and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income and tax liabilities. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards may be subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before their utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets, which consist primarily of net operating loss carryforwards and research and development tax credit carryforwards. Management has considered the Company's history of cumulative net losses incurred since inception, estimated future taxable income and prudent and feasible tax planning strategies and has concluded that it is more likely than not that the Company will not realize the benefits of federal and state net deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2018 and 2019. The Company reevaluates the positive and negative evidence at each reporting period.

The changes in the valuation allowance for deferred tax assets during the year ended December 31, 2018 and 2019 related primarily to the increases in net operating loss carryforwards and research and development tax credit carryforwards. The changes in the valuation allowance for 2018 and 2019 were as follows:

	Year ended December 31,	
(in thousands)	**2018**	**2019**
Valuation allowance as of beginning of year	$ 2,976	$14,246
Increases recorded to income tax provision	11,270	18,867
Valuation allowance as of end of year	$14,246	$33,113

The Company assesses the uncertainty in its income tax positions to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more-likely-than-not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than 50% likelihood of being realized upon the ultimate settlement with the relevant taxing authority. No reserve for uncertain tax positions or related interest and penalties has been recorded at December 31, 2018 and 2019.

The Company files income tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company is open to future tax examination under statute from 2016 to the present.

10. License agreements

NIH

The Company has an agreement with the U.S. Department of Health and Human Services, as represented by The National Heart, Lung, and Blood Institute, an Institute of the National Institutes of Health ("NIH"), entered into in 2017, pursuant to which NIH granted the Company a non-exclusive license, with the right to grant sublicenses, under certain NIH intellectual property related to the Company's ceDNA construct. In July 2019, the agreement was amended to include Association Institut de Myologie, Universite Pierre et Marie Curie, Centre National de la Recherche Scientifique, and Inserm Transfert SA, collectively referred to as the French Institutions, as a licensor.

The Company is obligated to make future milestone payments of up to $0.4 million per licensed product upon the achievement of specified milestones as well as royalties on a licensed product-by-licensed product and country-by-country basis of a low single digit percentage of annual net sales of licensed products. The Company is obligated to pay a high single-digit royalty percentage of all sublicensing income. The royalties on net sales may be reduced by up to 25% in certain circumstances as defined in the agreement. The Company's royalty obligation expires on a licensed product-by-licensed product and country-by-country basis upon the expiration of the last-to-expire licensed intellectual property rights in such country. Additionally, the Company is required to reimburse the French Institutions for a portion of certain past and ongoing patent related expenses related to the licensed technology. The agreement requires the Company to use reasonable commercial efforts to meet certain performance milestones and execute a commercial development plan within specified timeframes.

Unless terminated earlier, the agreement remains in effect until the last to expire of the licensed patent rights on a licensed product-by-licensed product and country-by-country basis. NIH and the French Institutions may terminate the agreement if the Company fails to perform its material obligations, including but not limited to its failure to meet the applicable performance milestones despite using commercially reasonable efforts, and has not remediated such deficiency within a specified time period. NIH and the French Institutions can terminate the agreement in the event the Company becomes insolvent, files a petition in bankruptcy, has such a petition filed against it, or determines to file a petition in bankruptcy. In addition, NIH and the French Institutions may terminate the agreement in the event of a material breach by the Company and failure to cure such breach within a certain period of time. The company is currently in compliance with the terms of the agreement. The Company can voluntarily terminate the agreement with prior notice to NIH and the French Institutions.

During each of the years ended December 31, 2018 and 2019 and each of the three months ended March 31, 2019 and 2020 (unaudited), the Company recorded research and development expense of less than $0.1 million under this agreement.

UMass

The Company has an agreement with the University of Massachusetts as represented by and solely on behalf of its Medical School ("UMass"), entered into in 2017, pursuant to which UMass granted the Company an exclusive license, with the right to grant sublicenses, under the UMass intellectual property related to the Company's ceDNA construct.

The Company is obligated to make future milestone payments of up to $0.8 million per licensed product upon the achievement of specified milestones as well as royalties on a licensed product-by-licensed product and country-by-country basis of a low single digit percentage of annual net sales of licensed products, subject to annual minimum royalties as defined in the agreement. Additionally, the Company has agreed to pay a low-to-mid single-digit royalty percentage of all sublicensing income, which will vary depending on when the sublicense agreement to a third party was executed. The milestone payments are non-refundable and

non-creditable against any other payments due to UMass under the agreement. The Company's royalty obligation expires on a licensed product-by-licensed product and country-by-country basis upon the expiration of the last-to-expire licensed intellectual property rights in such country. The agreement requires the Company to use diligent efforts to meet certain performance milestones within specified timeframes.

As part of the arrangement, the Company agreed to issue 125,677 shares of its common stock to UMass. The Company recorded $0.1 million as research and development expense and additional-paid-in capital at the time of the agreement in 2017, representing the fair value of the common stock at that time. The shares were issued in August 2019.

Unless terminated earlier, the agreement will continue until the last-to-expire valid claim of the licensed patents. UMass may terminate the agreement if the Company fails to perform its material obligations, including but not limited to its failure to meet the applicable performance milestones despite using commercially reasonable efforts, and has not remediated such deficiency within a specified time period or negotiated a revised performance timeline. UMass can terminate the agreement if the Company fails to make any payments within a specified period after receiving written notice of such failure, or in the event of a material breach by the Company and failure to cure such breach within a certain period of time. The Company is currently in compliance with the terms of the agreement. The Company can voluntarily terminate the agreement with prior notice to UMass.

During each of the years ended December 31, 2018 and 2019 and the three months ended March 31, 2019 and 2020 (unaudited), the Company recorded research and development expense of less than $0.1 million under this agreement.

Other license agreements

The Company has other license agreements under which it may become subject to future additional fees and milestone payments.

11. Commitments and contingencies

The Company leases its office and laboratory space under a noncancelable operating lease that was entered into in August 2018, as amended in July 2019, and expires in 2029. The Company has an option to extend for one additional term of five years at the greater of the then-current base rent, or the then-current fair market value. The lease agreement includes provisions for a free-rent period and annual rent increases, which are accrued or deferred as appropriate such that rent expense for the lease is recognized on a straight-line basis over the lease term (see Note 2). The Company is responsible for real estate taxes, maintenance, and other operating expenses applicable to the leased premises. The lease provides for a tenant improvement allowance, at the cost of the lessor, not to exceed $14.7 million. Costs incurred by the Company for tenant improvements but not yet reimbursed by the landlord are presented on the accompanying consolidated balance sheets as tenant receivable. As of December 31, 2018 and 2019 and March 31, 2020 (unaudited), the Company had a tenant receivable of $1.3 million, $0.4 million and $0.1 million, respectively. The Company posted a customary letter of credit in the amount of approximately $2.1 million as a security deposit. The letter of credit is subject to increase if the Company were to sublease any portion of the leased premises.

Previously, the Company leased its office and laboratory space under noncancelable operating leases that expired during 2019.

Rent expense for the years ended December 31, 2018 and 2019 was $3.5 million and $7.9 million, respectively. Rent expense for the three months ended March 31, 2019 and 2020 (unaudited) was $2.1 million and $1.9 million, respectively.

Future minimum lease payments as of December 31, 2019 are as follows:

Year ending December 31,	(in thousands)
2020	$ 6,867
2021	7,053
2022	7,251
2023	7,441
2024	7,679
Thereafter	35,451
	$ 71,742

401(k) Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code of 1986 (the “401(k) Plan”). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make, and to date has not made, any contributions to the 401(k) Plan.

Indemnification agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, contract research organizations, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and its executive officers that will 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. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The Company has not incurred any material costs as a result of such indemnifications and is not currently aware of any indemnification claims.

Legal proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the years ended December 31, 2018 and 2019 or during the three months ended March 31, 2020 (unaudited).

12. Net loss and unaudited pro forma net loss per share

Net loss per share

The Company has generated a net loss in all periods presented, therefore the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated:

	Year ended December 31,		Three months ended March 31,	
	2018	2019	2019	2020
			(unaudited)	(unaudited)
Convertible preferred stock (as converted to common stock)	14,961,027	14,961,027	14,961,027	27,094,085
Unvested restricted common stock	2,819,949	1,705,188	2,492,472	1,440,254
Stock options to purchase common stock	2,784,581	3,373,884	3,086,451	5,034,210
	20,565,557	20,040,099	20,539,950	33,568,549

Unaudited pro forma net loss per share

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2019 and for the three months ended March 31, 2020 has been prepared to give effect to adjustments arising upon the completion of a qualified IPO. The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2019 has been prepared to give effect, upon a qualified IPO, to the automatic conversion of all outstanding shares of Series A and Series B into common stock as if the proposed IPO had occurred on the later of January 1, 2019 or the issuance date of the Series A and Series B. The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2019 do not give effect to the issuance of shares of Series C and the resulting adjustment to the Series B conversion ratio that occurred in January 2020 (see Notes 6 and 13).

The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the three months ended March 31, 2020 has been prepared to give effect, upon a qualified IPO, to the automatic conversion of all outstanding shares of Preferred Stock into common stock as if the proposed IPO had occurred on the later of January 1, 2020 or the issuance date of the Preferred Stock. The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of the unaudited pro forma basic and diluted net loss per share attributable to common stockholders give effect to the issuance of shares of Series C and the resulting adjustment to the Series B conversion ratio on the Series C issuance date in January 2020.

Unaudited pro forma basic and diluted net loss per share attributable to common stockholders were calculated as follows:

(in thousands except share and per share amounts)	Year ended December 31, 2019 (unaudited)	Three months ended March 31, 2020 (unaudited)
Numerator:		
Net loss attributable to common stockholders	$ (61,317)	$ (17,717)
Pro forma net loss attributable to common stockholders	$ (61,317)	$ (17,717)
Denominator:		
Weighted average common shares outstanding, basic and diluted	4,731,519	5,495,013
Pro forma adjustment to reflect automatic conversion of convertible preferred stock to common stock upon the completion of the proposed IPO	14,961,027	25,894,112
Pro forma weighted average common shares outstanding, basic and diluted	19,692,546	31,389,125
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (3.11)	$ (0.56)

13. Subsequent events

The Company reviewed for subsequent events through April 9, 2020, the date the consolidated financial statements were issued, and June 8, 2020, the date the revised interim consolidated financial statements were issued, to ensure that these consolidated financial statements include appropriate disclosure of events both recognized in the consolidated financial statements as of December 31, 2019 and events which occurred subsequently but were not recognized in the consolidated financial statements. The Company reviewed for subsequent events through May 12, 2020, the date the interim condensed consolidated financial statements were issued, and June 8, 2020, the date the revised condensed consolidated financial statements were issued, to ensure that these condensed consolidated financial statements included appropriate disclosures of events both recognized in the condensed consolidated financial statements as of March 31, 2020 and events which occurred subsequently but were not recognized in the condensed consolidated financial statements. The Company has concluded that no subsequent events have occurred that require disclosure, except as described below.

(a)

Issuance and sale of Series C

In January 2020, the Company issued and sold 19,936,296 shares of Series C at a price of $5.5914 per share, for gross proceeds of $111.5 million. The terms of the Series C are substantially the same as the terms of the Series A and Series B except for the liquidation preference per share, which is equal to the per share price paid. In connection with the issuance, the Company increased the number of authorized shares of Preferred Stock from 26,425,664 shares to 46,361,960 shares. Because the price per share of the Series C in this transaction was lower than the Conversion Price of the Company's Series B, in accordance with the Company's certificate of incorporation, as amended and restated, the Conversion Price of Series B was adjusted from $16.1540 to $14.2180 per share (when rounded to the nearest ten-thousandth). As a result, the 10,974,644 outstanding shares of Series B as of December 31, 2019 became convertible into 7,059,406 shares of common stock.

(b)

Increase in shares available for issuance under the 2017 Plan

In January 2020, the number of shares of common stock authorized for issuance under the 2017 Plan was increased from 8,407,405 shares to 10,275,717 shares.

(c)

Grant of stock options under the 2017 Plan

On March 5, 2020, the Company granted options with service-based vesting criteria for the purchase of an aggregate of 947,411 shares of common stock, at an exercise price of $5.16 per share. The aggregate grant-date fair value of these options was $3.4 million, which is expected to be recognized over approximately four years.

On March 5, 2020, the Company granted options with performance-based vesting criteria for the purchase of an aggregate of 717,198 shares of common stock, at an exercise price of $5.16 per share. The aggregate grant-date fair value of these options was $2.3 million, which will be recognized once it becomes probable that the milestone will be achieved and the shares will vest.

On March 31, 2020, the Company granted options with service-based vesting criteria for the purchase of an aggregate of 63,834 shares of common stock, at an exercise price of $5.25 per share. The aggregate grant-date fair value of these options was $0.2 million, which is expected to be recognized over approximately four years.

(d)

Reverse stock split

The Company's Board of Directors and stockholders approved a one-for-1.7663 reverse stock split of the Company's common stock that became effective on June 5, 2020. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse split and adjustment of the Preferred Stock conversion ratios.

(e)

License agreement amendment (unaudited)

In June 2020, the Company entered into an amendment to its license agreement with UMass under which UMass, on behalf of Voyager Therapeutics, Inc. ("Voyager"), expanded the license granted to the Company to include an exclusive license to Voyager's rights in the patent application family licensed to the Company under the license agreement, subject to certain non-exclusive rights retained by Voyager. Under the license agreement, as amended, the Company may be obligated to make future milestone payments of up to $1.1 million per licensed product as well as low single digit percentage royalties on net sales of licensed products on a licensed product-by-licensed product and country-by-country basis.

(f)

2020 Equity Plans (unaudited)

In May 2020 the Company's board of directors adopted, and in June 2020 the Company's stockholders approved, the 2020 Stock Incentive Plan (the "2020 Plan"), which will become effective immediately prior to the effectiveness of the registration statement for this offering. The 2020 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. Upon effectiveness of the 2020 Plan, the number of shares

of common stock that will be reserved for issuance under the 2020 Plan will be the sum of (1) 2,547,698 shares; plus (2) the number of shares (up to a maximum of 7,173,014 shares) as is equal to the sum of (x) the number of shares of common stock reserved for issuance under the 2017 Plan that remain available for grant under the 2017 Plan immediately prior to the effectiveness of the registration statement for this offering and (y) the number of shares of our common stock subject to outstanding awards granted under the 2017 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing until, and including, the fiscal year ending December 31, 2030, equal to the lesser of (i) 4% of the number of shares of common stock outstanding on such date, and (ii) an amount determined by the board of directors. Subject to the effectiveness of the 2020 Plan, the Company will cease the grant of additional awards under the 2017 Plan.

In May 2020 the Company's board of directors adopted, and in June 2020 the Company's stockholders approved, the 2020 Employee Stock Purchase Plan (the "2020 ESPP"), which will become effective immediately prior to the effectiveness of the registration statement for this offering. The 2020 ESPP will be administered by the Company's board of directors or by a committee appointed by the board of directors. The 2020 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 481,231 shares of common stock. The number of shares of common stock reserved for issuance under the 2020 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2021 and continuing for each fiscal year until, and including the fiscal year commencing on, January 1, 2030, in an amount equal to the lowest of (1) 1,302,157 shares of common stock, (2) 1% of the number of shares of common stock outstanding on such date, and (3) an amount determined by the board of directors.

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Through and including July 6, 2020, (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 delivery requirement 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.

10,526,316 shares

Common stock

Prospectus

Joint Book-Running Managers

J.P. Morgan **Jefferies** **Cowen**

Lead Manager

Wedbush PacGrow

June 11, 2020