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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019

or

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

For the transition period from to

Commission file number: 001-37553

REGENXBIO Inc.

(Exact name of registrant as specified in its charter)

Delaware	**47-1851754**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
9600 Blackwell Road, Suite 210 Rockville, MD	**20850**
(Address of principal executive offices)	**(Zip Code)**

(240) 552-8181

(Registrant's telephone number, including area code)

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on The Nasdaq Global Select Market on June 30, 2019, the last business day of the registrant's most recently completed second quarter, was $1,355,505,892.

As of February 21, 2020, there were 37,139,199 shares of the registrant's common stock, par value $0.0001 per share, issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's definitive proxy statement with respect to the registrant's 2020 Annual Meeting of Stockholders, which is to be filed pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2019, are incorporated by reference into Part III of this Annual Report on Form 10-K.

REGENXBIO INC.

Form 10-K

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PART I

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). These statements express a belief, expectation or intention and are generally accompanied by words that convey projected future events or outcomes such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “assume,” “design,” “intend,” “expect,” “could,” “plan,” “potential,” “predict,” “seek,” “should,” “would” or by variations of such words or by similar expressions. We have based these forward-looking statements on our current expectations and assumptions and analyses made by us in light of our experience and our perception of historical trends, current conditions and expected future developments, as well as other factors we believe are appropriate under the circumstances. However, whether actual results and developments will conform with our expectations and predictions is subject to a number of risks, uncertainties, assumptions and other important factors, including, but not limited to:

- the ability to obtain and maintain regulatory approval of our product candidates and the labeling for any approved products;
- the timing of enrollment, commencement and completion and the success of our clinical trials;
- the timing of commencement and completion and the success of preclinical studies conducted by us and our development partners;
- the timely development and launch of new products;
- the scope, progress, expansion and costs of developing and commercializing our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates and technology;
- our expectations regarding the development and commercialization of product candidates currently being developed by third parties that utilize our technology;
- our anticipated growth strategies;
- our expectations regarding competition;
- the anticipated trends and challenges in our business and the market in which we operate;
- our ability to attract or retain key personnel;
- the size and growth of the potential markets for our product candidates and the ability to serve those markets;
- the rate and degree of market acceptance of any of our products that are approved;
- our ability to establish and maintain development partnerships;
- our expectations regarding our expenses and revenue;
- our expectations regarding regulatory developments in the United States and foreign countries; and
- the use or sufficiency of our cash and cash equivalents and needs for additional financing.

You should carefully read the factors discussed in the sections titled “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this Annual Report on Form 10-K and in our other filings with the U.S. Securities and Exchange Commission (the SEC) for additional discussion of the risks, uncertainties, assumptions and other important factors that could cause our actual results or developments to differ materially and adversely from those projected in the forward-looking statements. The actual results or developments anticipated may not be realized or, even if substantially realized, they may not have the expected consequences to or effects on us or our businesses or operations. Such statements are not guarantees of future performance and actual results or developments may differ materially and adversely from those projected in the forward-looking statements. These forward-looking statements speak only as of the date of this report. Except as required by law, we disclaim any duty to update any forward-looking statements, whether as a result of new information, future events or otherwise.

As used in this Annual Report on Form 10-K, the terms “REGENXBIO,” “we,” “us,” “our” or the “Company” mean REGENXBIO Inc. and its subsidiaries, on a consolidated basis, unless the context indicates otherwise.

NAV, REGENXBIO and the REGENXBIO logos are our registered trademarks. Any other trademarks appearing in this Annual Report on Form 10-K are the property of their respective holders.

INDUSTRY AND MARKET DATA

We obtained the industry, market and competitive position data used throughout this Annual Report on Form 10-K from our own internal estimates and research, as well as from industry and general publications, in addition to research, surveys and studies conducted by third parties. Internal estimates are derived from publicly-available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. We have not independently verified industry, market and competitive position data from third-party sources, but we believe the sources of such information to be reliable. While we believe the industry, market and competitive position data included in this Annual Report on Form 10-K is reliable and is based on reasonable assumptions, such data involves risks and uncertainties and are subject to change based on various factors, including those discussed in “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

ITEM 1. *BUSINESS*

Overview

We are a leading clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy. Our gene therapy product candidates are designed to deliver functional genes to address genetic defects in cells, enabling the production of therapeutic proteins or antibodies that are intended to impact disease. Through a single administration, gene therapy could potentially alter the course of disease significantly and deliver improved patient outcomes with long-lasting effects.

Our gene therapy product candidates use adeno-associated virus (AAV) vectors from our proprietary gene delivery platform, which we call our NAV® Technology Platform. AAV vectors are non-replicating viral delivery vehicles that are not known to cause disease. Our NAV Technology Platform consists of exclusive rights to a large portfolio of vectors, including AAV7, AAV8, AAV9, AAVrh10 and more than 100 other novel AAV vectors (NAV Vectors). We believe this platform forms a strong foundation for our current programs and with our ongoing research and development, we expect to continue to expand the platform.

We have developed a broad pipeline of gene therapy programs using our NAV Technology Platform to address genetic diseases through two modalities: AAV-mediated antibody delivery and monogenic gene replacement. The AAV-mediated antibody delivery modality is designed to treat serious and chronic diseases by delivering the genes necessary for the sustained production of therapeutic antibodies *in vivo*. Our monogenic gene replacement approach builds upon the well-understood mechanism of replacing a dysfunctional or missing gene with a functional copy of the gene in order to enable sustained production of necessary proteins.

Gene Therapy Using NAV Vectors for AAV-Mediated Antibody Delivery

Our product candidate RGX-314 consists of the NAV AAV8 vector designed to deliver a gene encoding a therapeutic antibody fragment which inhibits vascular endothelial growth factor (VEGF). RGX-314 is being developed as a novel, single- administration gene therapy for the treatment of wet age-related macular degeneration (wet AMD), diabetic retinopathy (DR), and other additional chronic retinal conditions which cause total or partial vision loss for millions of patients in the United States, Europe and Japan. We are advancing two separate routes of administration of RGX-314 to the eye, through a standardized subretinal delivery procedure as well as by delivery to the suprachoroidal space using the SCS Microinjector™ licensed from Clearside Biomedical, Inc.

In May 2019, we completed enrollment in the Phase I/IIa dose escalation trial of RGX-314 delivered subretinally for the treatment of wet AMD, and we announced interim data in October 2019. We plan to initiate a pivotal program for the subretinal delivery of RGX-314 for the treatment of wet AMD in the second half of 2020. We plan to initiate a Phase II trial of the suprachoroidal delivery of RGX-314 using the SCS Microinjector for the treatment of wet AMD in the first half of 2020. In addition, we expect to submit an investigational new drug application (IND) for the suprachoroidal delivery of RGX-314 for the treatment of DR in the first half of 2020 and plan to initiate a Phase II trial in DR in the second half of 2020.

In July 2019, we announced the development of a gene therapy candidate for the treatment of Hereditary Angioedema (HAE), which consists of the NAV AAV8 vector designed to deliver a gene encoding a therapeutic antibody against plasma kallikrein. Plasma kallikrein is a key protein of the plasma contact pathway which is left unregulated in patients with HAE. We expect to select a lead product candidate in the first half of 2020 and provide a program update in the second half of 2020.

We have also established a research program in partnership with Neurimmune AG, a leading clinical-stage Swiss biotechnology company, to discover and develop novel gene therapies using NAV Vectors to deliver antibodies against targets implicated in chronic neurodegenerative diseases, including tauopathies and alpha-synucleinopathies. We expect to provide a program update in the second half of 2020.

Gene therapy using NAV Vectors for Monogenic Gene Replacement

We are developing gene therapy product candidates using a monogenic gene replacement approach, in which we use a NAV Vector designed to deliver a functional copy of a gene in order to enable sustained production of necessary proteins. Our programs using this approach include NAV AAV9-based gene therapies designed to address the unmet neurological symptoms of severe genetic lysosomal storage diseases. These rare diseases include Mucopolysaccharidosis Type II (MPS II), Mucopolysaccharidosis Type I (MPS I) and late infantile neuronal ceroid lipofuscinosis type II (CLN2 disease). MPS II is caused by deficiency of the *IDS* gene, which encodes the iduronate-2-sulfatase (I2S) enzyme; MPS I is caused by deficiency of the *IDUA* gene, which encodes the α-l-iduronidase (IDUA) enzyme; and CLN2 disease is caused by deficiency of the *TPP1* gene, which encodes the tripeptidyl peptidase 1 (TPP1) enzyme. Each of these enzymes are responsible for breakdown of cellular waste products; accumulation of waste products can ultimately result in cell, tissue, and organ dysfunction, and patients with severe forms of these diseases exhibit significant cognitive decline. Our product candidates for these diseases are:

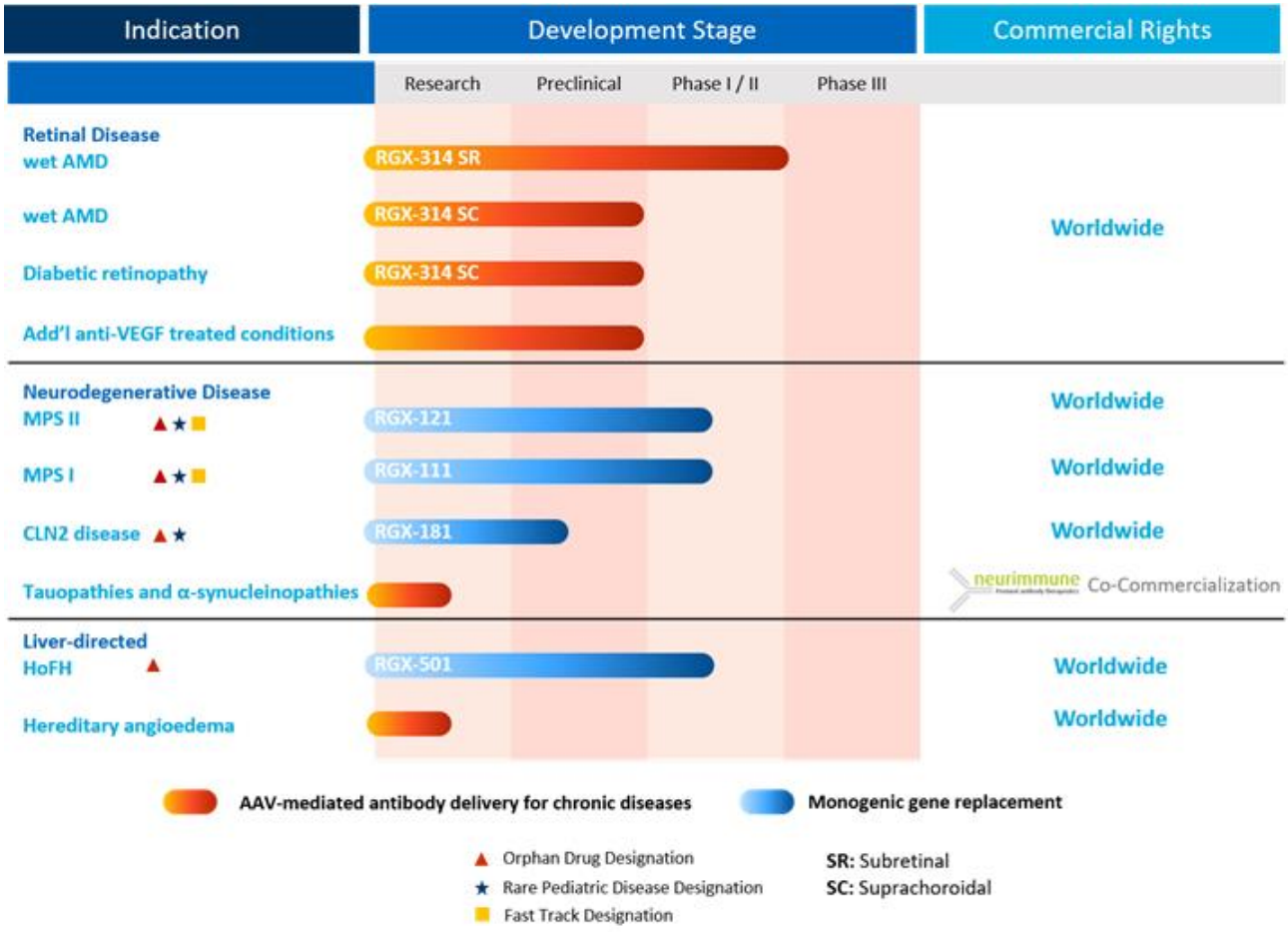
- RGX-121 for the treatment of MPS II. We initiated the ongoing RGX-121 Phase I/II clinical trial in 2018, which includes two dose cohorts. We have completed enrollment in the first dose cohort and initiated dosing in the second cohort. We expect to complete enrollment of Cohort 2 in the first half of 2020 and provide interim data in mid-2020.
- RGX-111 for the treatment of MPS I. We have initiated a Phase I clinical trial of RGX-111, and recruitment, screening and additional site activations are ongoing. We expect to provide a program update in the second half of 2020.
- RGX-181 for the treatment of CLN2 disease. We are conducting ongoing preclinical development of RGX-181. We plan to provide a program update in mid-2020 and submit an IND for a first-in-human trial in the second half of 2020.

Our product candidate RGX-501 is for the treatment of homozygous familial hypercholesterolemia (HoFH), a severe genetic disease characterized by premature and aggressive plaque buildup, life threatening coronary artery disease (CAD) and aortic valve disease predominantly due to abnormalities in the function or expression of the low-density lipoprotein receptor (LDLR) gene. RGX-501 is designed to use the NAV AAV8 to deliver a functional copy of the LDLR gene to the liver through intravenous administration. In 2019, we completed dosing of an expanded Cohort 2 in the Phase I/II trial of RGX-501, which included steroid prophylaxis. We plan to provide interim data related to low-density lipoprotein (LDL-C) levels in the first half of 2020.

We also expect to announce plans for the clinical development of a potential gene therapy treatment for a neuromuscular disorder in the second half of 2020.

In addition to the lead product candidates described above, we have also funded, and plan to continue to fund, preclinical research on potential product candidates that may become part of our internal product development pipeline. We will continue to seek partnerships with innovative academic institutions and biotechnology companies to develop novel NAV gene therapy product candidates.

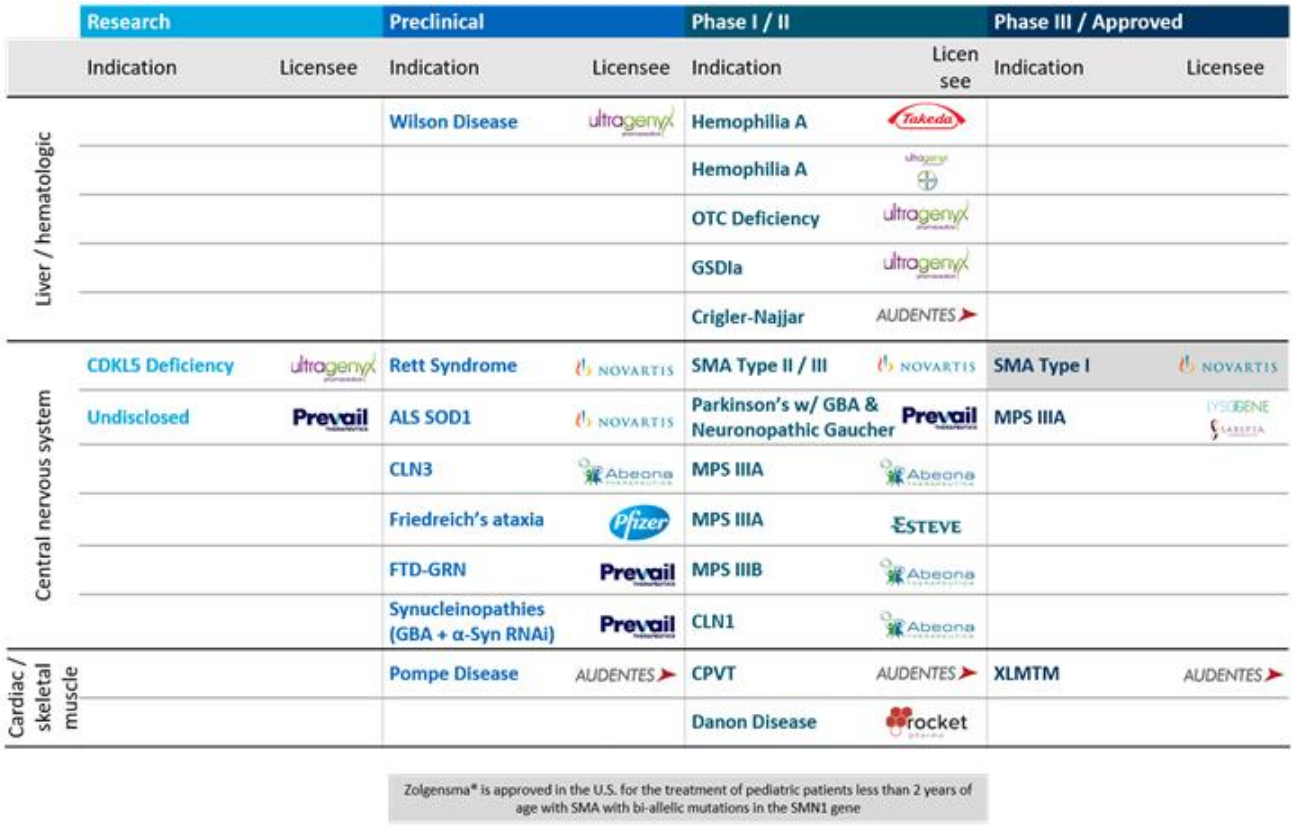
Our internal pipeline is shown below.



We are an industry leader in AAV production and manufacturing, with deep in-house knowledge of vector characterization and strength in technical operations. We have robust suspension cell culture-based production capabilities, with well-integrated process optimization to enable scale and quality of product alongside our network of leading contract manufacturing organizations (CMOs). In May 2019, we announced construction of a new current good manufacturing practice (cGMP) production facility, to be located in our new corporate headquarters in Rockville, Maryland. This facility is expected to support future clinical and commercial production of gene therapies, allowing for production of NAV Technology-based vectors at scales up to 2,000 liters and is designed to meet regulatory requirements for clinical and commercial material supply in the jurisdictions in which we expect to develop and commercialize our product candidates. The cGMP production facility is expected to be operational in 2021, and will complement our current external manufacturing capabilities, enabling a reliable supply of NAV Vectors from both internal and external sources.

In addition to our internal product development efforts, we also selectively sublicense our NAV Vectors to other biotechnology companies with disease-specific expertise, which we refer to as NAV Technology Licensees. As of December 31, 2019, our NAV Technology Platform was being applied in the preclinical and clinical development of more than 20 partnered product candidates by our NAV Technology Licensees. Our partnering strategy provides us the flexibility to sublicense development of treatments designed to address significant unmet medical needs, while remaining focused on our core programs and therapeutic areas internally. We believe that the broad applicability of our NAV Technology Platform and any clinical successes of the treatments utilizing NAV Vectors will create new internal and partnered pipeline opportunities. In May 2019, the U.S. Food and Drug Administration (FDA) approved the first gene therapy that leverages our proprietary NAV Technology Platform, Novartis AG's Zolgensma® (onasemnogene abeparvovec-xioi; AVXS-101). Zolgensma was approved by the FDA as a one-time infusion for pediatric patients with spinal muscular atrophy (SMA) who are less than two years of age.

Our partnered product development program pipeline is shown below.



Our management team includes leaders who are experienced in building and operating innovative healthcare ventures and have expert knowledge in the development of AAV gene therapy, as well as in the disease areas we seek to address. We believe the strength of our team positions us to succeed in developing and bringing to market, independently or with our development partners, unique, best-in-class gene therapy treatments for a range of severe diseases with significant unmet medical needs.

Our Strategy

Our mission is to improve lives through the curative potential of gene therapy. We are seeking to develop, manufacture, commercialize and license product candidates across multiple therapeutic areas and target organs while continuing to expand our NAV Technology Platform. To achieve our mission, we are pursuing the following strategies:

- **Apply our proprietary, next generation AAV vector technology to develop *in vivo* gene therapies for patients.** We believe *in vivo* gene therapy is an ideal treatment paradigm to treat the underlying biological cause of a disease. We believe our NAV Technology Platform is a significant advancement over earlier generations of AAV vectors in delivering genes to cells, with significant differentiating attributes, namely: higher expression and increased durability, broad and novel tissue selectivity, and improved manufacturability. These unique benefits have been demonstrated in our own clinical studies and animal models using our NAV Vectors, as well as third-party clinical trials and animal models using our NAV Vectors. The approval of Novartis' Zolgensma, which uses the NAV AAV9 vector, further validates the potential of the NAV Technology Platform. We believe that our NAV Technology Platform, which underpins our internal development programs and the programs of our NAV Technology Licensees, will continue to enable us and our partners to develop best-in-class gene therapy candidates for a wide range of disease targets.
- **Rapidly advance our broad pipeline gene therapy programs using two modalities: AAV-mediated antibody delivery and monogenic gene replacement.** The AAV-mediated antibody delivery modality is designed to treat serious and chronic diseases which often involve frequent administration of therapeutic antibodies over the course of a patient's lifetime, by delivering the genes necessary to result in the sustained production of therapeutic antibodies *in vivo*. A single-administration gene therapy approach using NAV Vectors may provide improved treatment options for patients by reducing their treatment burden or enabling treatments in tissues where it is difficult to deliver sufficient amounts of therapeutic antibodies via traditional delivery methods, such as in the central nervous system. Our lead program, RGX-314, is based on this approach, delivering the gene encoding an antibody fragment that binds to VEGF. Similarly, we are developing AAV-mediated antibody delivery gene therapies for the treatment of HAE as well as neurodegenerative diseases such as tauopathies and alpha-synucleinopathies.

Many genetic diseases are caused by a mutated or missing gene in specific cells which can affect the ability of the cell to correctly produce a specific protein. Our monogenic gene replacement approach builds upon the well-understood mechanism of using AAV vectors to replace dysfunctional or missing genes with a functional copy of the gene in order to enable sustained production of necessary proteins. We are using this approach to develop potential gene therapies for rare diseases such as MPS II, MPS I, CLN2 disease, and HoFH, each of which requires restoration of particular proteins.

- **Leverage advanced routes of administration to direct gene therapy treatments to specific tissues for efficient transduction and effective protein use at lower titers.** We believe that targeting tissues where diseases manifest is critical to impacting the course of the disease with our NAV gene therapy treatments. For example, we are currently evaluating two routes of administration for RGX-314 to effectively reach the retinal cells to produce the anti-VEGF antibody in the back of the eye without immune response. The subretinal delivery technique is an established route of delivery for gene therapy, with direct and broad transduction of the retina and minimal exposure to the vitreous and anterior segment of the eye. We have also licensed certain exclusive rights to the SCS Microinjector from Clearside Biomedical to deliver gene therapies to the suprachoroidal space, potentially providing a targeted, in-office, non-surgical approach to deliver NAV gene therapy treatments to the retina. Separately, we are seeking to address the central nervous system (CNS)-specific manifestations of MPS II, MPS I and CLN2 disease by using advanced routes of administration for the delivery of our gene therapies.
- **Further establish REGENXBIO as an industry leader in gene therapy manufacturing, with significant advancements in internal capabilities and innovative developments.** We have deep in-house knowledge of AAV production and manufacturing, which provides us with the ability to scale production of our gene therapies while ensuring quality for patients. We maintain a strong network of well-known contract manufacturing organizations, and in 2019, we began construction of our own production facility at our future headquarters in Rockville, Maryland. This facility, which we expect to be operational in 2021, will provide cGMP production space at bioreactor scales up to 2,000 liters. Additionally, we have invested in innovative process development and analytical capabilities, and use an established robust suspension cell culture-based manufacturing process.

- **Strengthen the validation of our NAV Technology Platform through strategic in-licensing and sublicensing of new programs and the progress made by our external NAV Technology Platform Licensees.** Our NAV Technology Platform is currently being applied to more than 20 partnered product candidates in development across a broad range of therapeutic areas, including the FDA-approved Zolgensma. We believe that these programs further validate the versatility of NAV Vectors, and provide additional data that collectively drive the advancement of the AAV gene therapy space. This strategic sublicensing allows us to maintain our internal product development focus in our core disease indications and therapeutic areas while expanding the NAV gene therapy pipeline, developing a greater breadth of treatments for patients, providing additional technological and potential clinical proofs-of-concept for our NAV Technology Platform, and creating potential additional revenue.
- **Maintain and grow our extensive intellectual property portfolio.** We plan to leverage our intellectual property rights and substantial expertise in AAV gene therapy in order to develop and commercialize NAV gene therapy products. We have licensed exclusive rights to a broad portfolio of certain fundamental AAV gene therapy patents and patent applications, including more than 100 patents and patent applications worldwide covering our NAV Vectors, as well as sequences that are at least 95% identical to NAV capsid sequences. We also have composition of matter claims for AAV7, AAV8, AAV9 and AAVrh10, as well as methods for their manufacture and therapeutic uses. In securing these rights, we have focused on obtaining robust rights for the intellectual property that we believe will be most important in providing us with a competitive advantage with respect to AAV gene therapy treatments. We plan to continue to seek to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business.

The Broad Potential and Application of Gene Therapy

The concept of developing human therapies involving the delivery of external genes has existed for decades, driven by the arrival of recombinant technology and the early demonstrations by scientists of the ability to deliver and drive expression of external gene sequences in mammalian cells.

We believe that gene therapy has the potential to become an important class of treatment because it may offer the following benefits:

- **Ability to treat a broad range of diseases.** Given the availability of the sequence of the entire human genome, it could be possible to design gene therapy to express or effect expression of many human proteins whose presence, absence or activity causes disease. We believe gene therapy treatments can also be designed to enable the body to continuously produce therapeutic proteins or antibodies or be efficiently adapted to deliver different genome editing components to address the specific treatment needs of many disease targets.
- **Ability to target mechanisms that cannot be targeted effectively by existing drug classes.** Many proteins that play roles in disease cannot be targeted effectively with small molecules and therapeutic proteins. These limitations on small molecule and protein drugs may not apply to gene therapy, which we believe can be designed to target any gene in the genome.
- **Ability to create convenient treatment profiles.** Because gene therapies are designed to deliver a long-term effect with a single administration, a single gene delivered via gene therapy could potentially do the same work as administering conventional drugs over the course of many years.
- **Simplified discovery of treatment candidates.** Identification of small molecule and protein drug candidates typically requires screening a large number of potential candidates to find prospective leads. Identification of gene therapy candidates has the potential to be simpler and take considerably less time because it can involve relatively standard processes that can be applied in a similar fashion to many successive product candidates.
- **Delivery of new treatment modalities.** In addition to monogenic gene replacement and antibody delivery approaches, viral vectors may be utilized to deliver new and novel approaches to modifying a cell’s DNA, including gene editing constructs and RNA-based therapeutics.

Our Internal Pipeline

Gene Therapy Using NAV Vectors for AAV-Mediated Antibody Delivery

RGX-314 for the Treatment of Wet AMD, DR and Other Anti-VEGF Treated Conditions

We are developing RGX-314 for the treatment of wet AMD, DR and other anti-VEGF treated conditions. These diseases are characterized by loss of vision due to excess fluid accumulation from new blood vessel formation.

Wet AMD is a leading cause of total and partial vision loss, affecting more than 2 million patients in the United States, Europe and Japan. The risk for developing wet AMD increases with age and we anticipate the diagnosis rate will continue to increase with the growth of the aging population. In patients with wet AMD, fluid accumulation can result in physical changes in the structure of the retina and adverse changes in vision. As this process progresses, blindness can result from atrophy and scar formation.

DR is the leading cause of vision loss in the working-age population and affects approximately 8 million people in the United States. DR is a complication of diabetes and is a progressive retinopathy, the severity of which ranges from mild non-proliferative diabetic retinopathy to a more advanced proliferative diabetic retinopathy (PDR). The main causes of vision loss secondary to DR are the vision-threatening complications of PDR, marked by the growth of new abnormal blood vessels onto the surface of the retina and vitreous cavity causing severe vision loss and diabetic macular edema (DME) leading to visual impairment. DME can occur at any stage of DR as the blood vessels in the retina become increasingly fragile and leak fluid.

Anti-VEGF injection therapies are the standard of care in wet AMD and DR due to their ability to reduce fluid accumulation and, on average, improve or stabilize vision in the majority of patients. However, these therapies require repetitive and inconvenient intraocular injections, typically ranging from every four to twelve weeks in frequency, to maintain efficacy. Patients often experience vision loss with reduced frequency of treatment. In addition, patient compliance is a significant concern with anti-VEGF injection therapies due to a variety of factors, including inconvenience and discomfort associated with frequent injections in the eye.

RGX-314 is being developed as a novel, one-time treatment that consists of the NAV AAV8 vector encoding a gene for a monoclonal antibody fragment. The expressed protein is designed to neutralize VEGF activity, modifying the pathway for formation of new leaky blood vessels and retinal fluid accumulation. After delivery of RGX-314, we believe retinal cells will continue to produce the anti-VEGF protein.

We are currently evaluating two routes of administration for RGX-314 to effectively reach the retinal cells to produce the anti-VEGF antibody in the back of the eye. The subretinal delivery technique is an established route of delivery for gene therapy, with direct and broad transduction of the retina and minimal exposure to the vitreous and anterior segment of the eye. We have also licensed rights to the SCS Microinjector from Clearside Biomedical to deliver gene therapies to the suprachoroidal space. This targeted, in-office, non-surgical approach to delivery can potentially allow for widespread transgene expression in the retina without exposing the vitreous and the anterior segment of the eye.

Clinical Development of RGX-314 for the Treatment of Wet AMD and DR

Enrollment in the Phase I/IIa clinical trial of subretinally-administered RGX-314 in the United States in patients with wet AMD began in May 2017. The primary purpose of the clinical trial was to evaluate the safety and tolerability of RGX-314 at 24 weeks after a single dose of RGX-314 administered by subretinal delivery. The trial design allowed for enrollment of up to 42 patients across five dose levels. Patients enrolled in the clinical trial had a documented need and history of response to anti-VEGF therapies. Primary endpoints of the trial included safety and tolerability of RGX-314, including adverse events and certain laboratory measures such as immunological parameters. Secondary endpoints of the trial included evaluation of best corrected visual acuity (BCVA), change in central retinal thickness (CRT) as measured by spectral domain ocular coherence tomography (SD-OCT), presence of RGX-314 protein in aqueous fluid and other outcome measures. The primary study period has completed, and subjects have entered the follow-up period and will continue to be assessed for long-term safety and durability of effect until week 106.

In October 2019, we announced positive interim safety and efficacy data from the RGX-314 subretinal Phase I/IIa clinical trial in wet AMD in all five dose cohorts. These data included that, as of October 9, 2019, RGX-314 continued to be well-tolerated across all cohorts, with no drug-related serious adverse events (SAEs) reported. Up to six months after administration of RGX-314, subjects in Cohort 5 demonstrated a reduction of more than 80% from the mean annualized injection rate during the 12 months prior to administration of RGX-314, and 9 out of 12 (75%) of subjects had not received anti-VEGF injections, with mean improvement in vision and retinal thickness. Durable effects on vision and retinal thickness had been demonstrated over 1.5 years in Cohort 3, and 50% of subjects remained free of anti-VEGF injections 1.5 years after RGX-314 administration.

In the fourth quarter of 2019, we were informed by the FDA that the IND for our Phase I/IIa trial for the treatment of wet AMD was placed on a partial clinical hold while the FDA assessed aspects of certain third-party commercially available devices that are used for the subretinal delivery of RGX-314. The FDA subsequently removed the partial clinical hold after reviewing additional information that we provided. The partial clinical hold was not related to our gene therapy candidate and the hold was removed without requiring modification to the surgical delivery system being used in the trial.

In January 2020, we announced that as of December 31, 2019, RGX-314 continued to be well-tolerated across all cohorts in the Phase I/IIa trial, with no drug-related SAEs reported. Patients in Cohort 5 continued to demonstrate a meaningful reduction in anti-VEGF treatment burden at 6 months following administration of RGX-314, with 8 out of 11 (73%) patients remaining anti-VEGF injection-free, and a reduction across the cohort of more than 80% from the mean annualized injection rate during the 12 months prior to administration of RGX-314. Importantly, the Cohort 5 patients continued to demonstrate a mean improvement in vision of +3 ETDRS letters and mean improvement in retinal thickness of -83 microns, while the 8 patients who were anti-VEGF injection-free after administration of RGX-314 showed a mean improvement in vision of +5 ETDRS letters and mean improvement in retinal thickness of -83 microns.

We expect to initiate a pivotal clinical program for the subretinal delivery of RGX-314 for the treatment of wet AMD in the second half of 2020. The design of this trial will be based on the 12-month assessment of patients in Cohort 5 in the Phase I/IIa trial, which will allow for further characterization of RGX-314-treated patients, enhancements of the trial design and the potential acceleration of the clinical program. We expect to investigate the one-time administration of RGX-314 at a single dose compared to anti-VEGF injection therapy, and for the primary efficacy endpoint to evaluate the mean change in BCVA from baseline assessed at 12 months after treatment with RGX-314. We intend to submit the design of the trial to the FDA in mid-2020 and begin dosing patients in the second half of 2020.

In January 2020, we announced plans to initiate the Phase II trial of the suprachoroidal delivery of RGX-314 using the SCS Microinjector for the treatment of wet AMD in the first half of 2020. Interim data is expected from Cohort 1 by the end of 2020.

We expect to submit an IND for a Phase II trial of the suprachoroidal delivery of RGX-314 using the SCS Microinjector for the treatment of DR in the first half of 2020 and plan to initiate the trial in the second half of 2020. Enrollment of Cohort 1 is expected to be complete by the end of 2020, with interim data expected in 2021.

AAV-Mediated Antibody Delivery Research Program for the Treatment of HAE

In July 2019, we announced expansion of the AAV-mediated antibody gene therapy pipeline to include novel treatments for HAE. HAE is a chronic and severe disease that results from C1-inhibitor deficiency. HAE is characterized by recurring severe swelling (angioedema), most commonly in the face, airway, intestines and limbs. Antibodies to plasma kallikrein, a key protein left unregulated in patients with HAE, have been shown to reduce the swelling and pain associated with HAE. These antibodies, however, require frequent administration to reduce the occurrence of angioedema events.

Our HAE program is focused on developing a novel, one-time treatment utilizing the NAV AAV8 vector to deliver a gene encoding for a therapeutic antibody that targets and binds to plasma kallikrein. Following a single intravenous administration, the HAE product candidate is designed to allow liver cells to produce therapeutic antibodies that are secreted into the blood. In preclinical animal models, we have used NAV Vectors to express therapeutic antibodies that target and bind to plasma kallikrein.

Planned Clinical Development of Treatment of HAE

We expect to select a lead product candidate for the treatment of HAE in the first half of 2020 and provide a program update in the second half of 2020.

AAV-Mediated Antibody Delivery Research Program for the Treatment of Neurodegenerative Diseases

In 2019, we established a research program in partnership with Neurimmune to discover and develop novel AAV gene therapies using NAV Vectors to deliver antibodies against targets implicated in chronic neurodegenerative diseases. Under the exclusive license, development and commercialization agreement, REGENXBIO and Neurimmune will jointly develop and commercialize novel therapies using AAV vectors to deliver human antibodies. We will focus on diseases associated with the accumulation and deposition of the microtubule-associated protein tau (tauopathies) and alpha-synuclein (alpha-synucleinopathies). Delivery of human antibodies using AAV vectors has the potential to provide sustained brain exposure of antibodies for the clearance of abnormal tau or alpha synuclein via a one-time CNS administration.

REGENXBIO and Neurimmune will be jointly responsible for the design and development of vectorized antibody therapies and will share associated development costs equally. Following an initial research phase, on a target-by-target basis, each party will have the option to continue as a co-development and co-commercialization partner in the collaboration or to elect to receive a phase-based worldwide royalty in lieu of continued development investment.

Planned Clinical Development of Treatment of Neurodegenerative Diseases

We expect to provide a program update in the second half of 2020.

Gene Therapy Using NAV Vectors for Monogenic Gene Replacement

RGX-121 for the Treatment of MPS II

RGX-121 is our product candidate for the treatment of MPS II. MPS II, also known as Hunter syndrome, is a rare, X-linked recessive, or sex-linked, disease caused by a deficiency of the *IDS* gene which encodes the I2S enzyme. I2S is responsible for the breakdown of polysaccharides heparan sulfate (HS) and dermatan sulfate (DS) in lysosomes, which are intracellular structures that dispose of waste products inside cells. These polysaccharides, called glycosaminoglycans (GAGs), accumulate in tissues of MPS II patients, resulting in diverse clinical signs and symptoms. HS is a key biomarker of I2S enzyme activity and high amounts of HS accumulate in the CNS of MPS II patients, which closely correlates with neurocognitive decline. In severe forms of the disease, early developmental milestones may be met during the first year after birth, but developmental delay is readily apparent by 18 to 24 months. Developmental progression begins to plateau between three and five years of age, with regression reported to begin around six and a half years. By the time of death, most patients with CNS involvement are severely mentally handicapped and require constant care.

MPS II is estimated to occur in approximately 1 in 100,000 to 1 in 170,000 births worldwide. Based on global population, this equates to approximately 500 to 1,000 MPS II patients born each year worldwide.

In 2006, the recombinant form of human I2S (Elaprase), an enzyme replacement therapy (ERT), was approved by the FDA for the treatment of MPS II and has subsequently been approved for use internationally. However, ERT does not treat CNS manifestations of MPS II since the enzyme cannot cross the blood-brain barrier. Specific treatment to address the neurological manifestations of MPS II and prevent or stabilize cognitive decline remains a significant unmet medical need. Overall, the limitations of ERT leave a significant unmet need for a method to safely achieve long-term enzyme reconstitution in the CNS for MPS II patients experiencing neurological complications.

RGX-121 is designed to use the AAV9 vector to deliver the human *IDS* gene to cells in the CNS. Delivery of the gene therapy and expression of the enzyme that is deficient within cells in the CNS could provide a permanent source of secreted I2S on the CNS side of the blood-brain barrier, allowing for long-term cross-correction of cells throughout the CNS. We believe this strategy could provide rapid I2S delivery to the brain, potentially preventing the progression of cognitive deficits that otherwise occur in MPS II patients.

We have received orphan drug product designation, rare pediatric disease designation and fast track designation from the FDA for RGX-121.

Clinical Development of RGX-121 for the Treatment of MPS II

Enrollment in the Phase I/II clinical trial of RGX-121 in subjects with MPS II began in the second half of 2018. The trial design calls for enrollment of up to six subjects in two dose cohorts with MPS II. Subjects in the study must be greater than or equal to four months of age and less than five years of age. All subjects must have documented evidence of neurocognitive deficits due to MPS II or have a relative diagnosed with severe MPS II who has the same IDS mutation as the subject. The primary endpoint will be a safety assessment. The secondary and exploratory endpoints include the effect of RGX-121 on biomarkers of IDS activity in the cerebrospinal fluid (CSF), serum and urine, and effect of RGX-121 on neurocognitive deficits, as well as other outcome measures.

As reported in February 2020, RGX-121 was well-tolerated in Cohort 1 of the Phase I/II trial of RGX-121, and no drug-related SAEs were reported. Patients in Cohort 1 demonstrated consistent and sustained reduction in HS in the cerebral spinal fluid (CSF) and early signs of neurocognitive stability. We have initiated dosing in the second cohort at an increased dose and expect to complete enrollment of Cohort 2 in the first half of 2020 and provide interim data in second half of 2020. We expect to provide additional details for a potentially accelerated program pathway following evaluation of interim data from Cohort 2 in the second half of 2020 and subsequent interactions with the FDA, in accordance with the fast track designation.

RGX-111 for the Treatment of MPS I

We are developing RGX-111 for the treatment of MPS I. MPS I is a rare autosomal recessive, or non-sex-linked, genetic disease caused by deficiency of IDUA, an enzyme required for the breakdown of polysaccharides in lysosomes. Similar to MPS II, many MPS I patients develop symptoms related to GAG storage in the CNS, which can include excessive accumulation of fluid in the brain, spinal cord compression and cognitive impairment. MPS I patients span a broad spectrum of disease severity and extent of CNS involvement. The severe form of MPS I is also referred to as Hurler syndrome. Hurler patients have two mutations in the *IDUA* gene, resulting in no active enzyme. These patients typically present with symptoms before two years of age and universally exhibit severe cognitive decline after an initial period of normal development.

MPS I is estimated to occur in approximately 1 in 100,000 births worldwide. Based on global population, this equates to more than 1,000 MPS I patients born each year worldwide. Studies suggest that severe forms of MPS I represent between one-half and two-thirds of all MPS I patients.

The current standard of care for patients with an attenuated form of MPS I is a recombinant form of human IDUA (Aldurazyme). Given as a weekly intravenous infusion, this ERT has demonstrated improvement in hepatosplenomegaly, growth, mobility and respiratory function. However, as the enzyme cannot cross the blood-brain barrier, ERT does not treat the CNS manifestations of MPS I.

The first disease modifying therapy developed for severe MPS I was bone marrow transplant (BMT). Though BMT has demonstrated improvements in survival, growth, cardiac and respiratory function, mobility and intellect, it is also associated with clinically relevant morbidity and an estimated 10% to 20% mortality. Accordingly, the procedure is reserved for patients with severe disease before two years of age because the risk-benefit ratio is thought to be more favorable in younger patients who have not yet experienced advanced cognitive decline. Another critical limitation of BMT is that cognitive decline continues for up to a year after transplant before stabilizing, leaving permanent cognitive deficits. Overall, the limitations of BMT and ERT leave a significant unmet need for a method to safely achieve long-term IDUA reconstitution in the CNS for MPS I patients experiencing neurological complications.

RGX-111 is designed to use the AAV9 vector to deliver the human IDUA gene to the CNS. Delivery of the enzyme that is deficient within cells in the CNS could provide a permanent source of secreted IDUA beyond the blood-brain barrier, allowing for long-term cross-correction of cells throughout the CNS. We believe this strategy could also provide rapid IDUA delivery to the brain, potentially preventing the progression of cognitive deficits that otherwise occurs in MPS I patients.

We have received orphan drug product designation, rare pediatric disease designation and fast track designation from the FDA for RGX-111.

Clinical Development of RGX-111 for the Treatment of MPS I

Recruitment, screening and additional site activations are ongoing in a Phase I clinical trial of RGX-111. The primary endpoint of this trial is safety and the secondary endpoints include the effect of RGX-111 on biomarkers of IDUA activity in the CSF, serum and urine, neurocognitive development and other outcome measures. We expect to provide a program update in the second half of 2020.

In November 2019, we announced that RGX-111 was administered to a patient with MPS I through an investigator-initiated study at CHOC Children's Hospital, following review and agreement by the FDA.

RGX-181 for the Treatment of CLN2 Disease

RGX-181 is our product candidate for the treatment of CLN2 disease, a form of Batten disease. CLN2 disease is a rare, pediatric-onset, autosomal recessive, neurodegenerative lysosomal storage disorder caused by mutations in the *TPP1* gene. Mutations in the *TPP1* gene, and subsequent deficiency in TPP1 enzyme activity, result in lysosomal accumulation of storage material and degeneration of tissues including the brain and retina. CLN2 disease is characterized by seizures, rapid deterioration of language and motor functions, cognitive decline, loss of vision and blindness, and premature death by mid-childhood. Onset of symptoms is generally between two to four years of age with initial features of recurrent seizures (epilepsy), language delay, and difficulty coordinating movements (ataxia).

CLN2 disease is estimated to occur in approximately 1 in 250,000 births worldwide. Based on global population, this equates to as many as 500 patients born each year worldwide.

There is currently no cure for CLN2 disease. Current treatment options include palliative care or ERT. In 2017, recombinant TPP1 (Brineura), an ERT, was approved by the FDA for the treatment of CLN2 disease. Brineura is administered into the lateral ventricles via an implanted device on a biweekly basis. While an improvement over palliative care in slowing disease progression, we believe frequent administration of ERT into the CNS, reliance on limited and specialized infusion centers, the need for and complications associated with a permanently implanted device, and lack of a treatment for the underlying genetic cause of CLN2 disease represent an area of significant unmet medical need.

RGX-181 is designed to use the AAV9 vector to deliver the human *TPP1* gene to the CNS. Delivery of the gene that is deficient within cells in the CNS could provide a permanent source of secreted TPP1 enzyme, allowing for long-term cross-correction of cells throughout the CNS.

We have received orphan drug product designation and rare pediatric disease designation from the FDA for RGX-181.

Planned Clinical Development of RGX-181 for the Treatment of CLN2 Disease

We are conducting ongoing preclinical development of RGX-181, including assessment of unmet clinical needs such as neurologic and ophthalmologic manifestations of the disease. We expect to provide a program update in mid-2020 and submit an IND for a first-in-human trial in the second half of 2020.

RGX-501 for the Treatment of HoFH

We are developing RGX-501 for the treatment of HoFH. HoFH is a monogenic disorder caused predominantly by abnormalities in the function or expression of the LDLR gene. LDLR plays an important role in the regulation of cholesterol by facilitating uptake and degradation of low-density lipoprotein (LDL) in the liver. HoFH patients have very low levels or are completely deficient of LDLR, resulting in very high blood cholesterol levels which are typically greater than 500 milligrams per deciliter (mg/dl). Patients with HoFH develop progressive atherosclerosis, or narrowing and blockage of the arteries beginning at an early age, which leads to a high incidence of heart attacks in children and teenagers, among other severe symptoms. If untreated, HoFH patients usually die of causes related to CAD or aortic valve disease before the age of 30.

Published medical literature suggests that the worldwide prevalence of HoFH is estimated to be as high as 1 in 200,000. Based on disease severity and molecular characteristics, we estimate there are approximately 11,000 individuals globally who are primary candidates for gene therapy treatment of HoFH. Multiple studies have compared HoFH patients based on LDLR activity and have shown that small differences in residual activity can lead to significant reductions in cholesterol levels and better long-term outcomes.

Available treatment options for HoFH are limited. Lipoprotein apheresis, a physical method of filtering the plasma of LDL-C, is laborious and requires frequent intravenous access that can be challenging, expensive and not readily available. Other available treatments include statins, a class of pharmaceuticals commonly used to lower cholesterol levels, cholesterol absorption inhibitors and other cholesterol lowering medications. The FDA has approved two drugs as add-on therapy specifically for HoFH: lomitapide and mipomersen. Both result in a reduction of LDL-C, but their use is associated with an array of adverse events that may affect tolerance and long-term adherence. Other available treatments include PCSK9 inhibitors, which are designed to increase LDLR on the surface of the liver by reducing LDLR clearance by the PCSK9 protein. Effectiveness of PCSK9 inhibitors relies on patients having functional LDLR, so we believe a substantial unmet medical need remains for the population of HoFH patients who are LDLR negative or severely deficient in LDLR function. With all current HoFH therapies, even in combination, providing sub-optimal treatment for patients, a better solution is needed.

RGX-501 is designed to use the AAV8 vector to deliver the human LDLR gene to liver cells. We believe that the liver is the preferred target organ for gene therapy of HoFH since LDLRs produced in the liver contribute to greater than 90% of the capture and breakdown of LDL, making the liver by far the most important LDLR producing organ. Additionally, the liver is also the only organ capable of excreting cholesterol from the body, a function that is critical to the maintenance of cholesterol balance. Finally, studies have shown that liver transplantation in HoFH patients corrects the disease, providing strong support that correction of hepatic LDL receptor activity by gene therapy is sufficient for metabolic correction of the disease.

We have received orphan drug product designation from the FDA for RGX-501.

Clinical Development of RGX-501 for the Treatment of HoFH

Enrollment in the Phase I/II clinical trial of intravenously administered RGX-501 in the United States in subjects with HoFH began in March 2017. The primary endpoint is a safety assessment and the secondary endpoints are reduction in LDL-C and other outcome measures. Based on previous clinical trials and recent approvals in HoFH, we believe reduction in LDL-C is an endpoint that is an acceptable measure on which regulatory approval could be based. In early 2019, following previously reported elevations of transaminases in three patients of Cohort 2, three to six weeks post-dosing with $7.5x10^{12}$ GC/kg of RGX-501, we submitted an amendment to the Phase I/II clinical trial protocol to allow for an expansion of Cohort 2 to include three additional patients to be dosed at the same level along with corticosteroid prophylaxis. Per protocol, patients received at least a 13-week steroid treatment.

As of December 31, 2019, the three patients in the expanded Cohort 2 have been followed for an average of 17 weeks after administration of RGX-501, all beyond the 3-6 week window during which previous transaminase elevations occurred at this dose level. No SAEs or significant elevations in liver enzyme levels were reported in the expanded Cohort 2 and all patients have completed their steroid treatment or initiated the taper from steroid treatment.

We plan to assess low-density lipoprotein (LDL-C) levels in the expanded Cohort 2 after all patients have completed their steroid treatment, and expect to provide interim data in the first half of 2020.

Gene Therapy Using NAV Vectors for the Treatment of Neuromuscular Disorders

We expect to announce plans for the clinical development of a potential gene therapy treatment for a neuromuscular disorder in the second half of 2020.

Our Preclinical Programs

In addition to our lead product candidates, we have also funded, and plan to continue to fund, preclinical research on potential product candidates that may become part of our internal product development pipeline in and beyond our current retina, neurodegenerative and metabolic franchise areas.

AAV Vector Production

We believe that we have the internal capabilities and access to the resources necessary to enable us to successfully commercialize NAV gene therapy products following regulatory approval, if any, by developing scalable processes to manufacture such products efficiently and in commercial quantities.

We have invested significantly in our internal capabilities and infrastructure, including the establishment of our advanced manufacturing and analytics lab, which currently accommodates operations at 500-liter scale across multiple platforms to support our emerging research activities. Our internal team possesses deep knowledge of AAV characterization and production, as well as significant experience and expertise in biologics process development (upstream, purification and formulation), scale-up and production at large scale. We believe our capabilities and infrastructure will enable us to continue to be leaders in development of scalable, proprietary production methods for NAV gene therapy products.

In May 2019, we announced construction of a new cGMP production facility, to be located in our new corporate headquarters in Rockville, Maryland. This facility is expected to support future clinical and commercial production of gene therapies starting in 2021, allowing for production of NAV Technology-based vectors at scales up to 2,000 liters, and is designed to meet regulatory requirements for clinical and commercial material supply in the jurisdictions in which we expect to develop and commercialize our product candidates. The cGMP production facility will complement our current external manufacturing capabilities, enabling a reliable supply of NAV Vectors from both internal and external sources.

We have agreements with multiple biologics CMOs for production of material under cGMP requirements to support our current and future clinical trials, as well as potential future commercialization of our product development programs. We select our CMOs based on capability, capacity and expertise, and we believe partnering with multiple CMOs provides us with flexibility and diversity in suppliers, as well as access to potential future capacity to accommodate the scale that may be required for future clinical trials and commercialization.

In 2018, we entered into a strategic partnership with FUJIFILM Diosynth Biotechnologies (FUJIFILM) for the manufacture of our lead product candidates, which will support late-stage clinical development and early commercialization. Under the terms of the agreement with FUJIFILM, we gain guaranteed capacity for the supply of NAV AAV drug substance manufactured under cGMP at large scale—up to 2,000 liters—for three years, with the option to extend the agreement for an additional three years. We believe FUJIFILM facilities are compliant with regulatory standards in support of the initiation of worldwide clinical trials for our lead product candidates.

In addition, we believe we have established a robust supply chain for our key raw materials to ensure both high quality standards and assurance of raw material supply as we advance our programs. We have established dual supply sources for critical raw materials to minimize the potential for disruption of ongoing manufacturing activities. We believe our management team retains significant expertise in managing a diverse network of CMOs and suppliers and that this expertise will enable us to execute on our manufacturing strategy in connection with our external partners.

Proprietary Methods

We have obtained rights to all of the proprietary technology underlying our NAV Technology Platform through our Platform Licenses (described below) and our sponsored research agreements (SRAs), under which we have exclusively licensed rights to certain manufacturing-related patents and non-exclusively licensed rights to certain know-how owned or developed by The University of Pennsylvania (Penn). This intellectual property encompasses areas including scalable AAV production methods, methods of increasing the packaging yield of AAV and methods of purification of AAV vectors.

We have examined several methods of larger-scale manufacturing of AAV, which have been optimized to yield high titer and quality vectors. Further improvements to the efficiency and simplicity of the process may remain important to address future needs for commercial applications. Our production methods utilize linearly scalable unit operations, which produce robust yield and purity of the target vector.

Scientists at Penn discovered that in contrast to earlier generation AAV2, most NAV Vectors were released primarily into the medium of production cultures and not retained in the cell. Because these vectors are secreted directly into the media, we are able to efficiently deliver a product of high purity and with relatively high yield with less need for complicated purification steps. This method, for which we have licensed from Penn the exclusive patent rights, is high-yielding and versatile for the production of different NAV Vectors and has been demonstrated to scale into a cGMP setting with comparable yields and product quality. Our future process development activities will build upon this platform to target higher yield of vector without impacting the product purity profile.

Other Capabilities

We have prepared and characterized several proprietary HEK293 master cell banks and other components (plasmid DNA banks) required for clinical vector production. Our master cell banks and other components are being used by us and a subset of our NAV Technology Licensees for the production of NAV Vectors under cGMP for use in clinical trials.

Commercial Licenses to NAV Technology Licensees

We sublicense our NAV Technology Platform to select third parties in order to develop and bring to market NAV gene therapy for a range of severe diseases with significant unmet medical needs. Sublicensing allows us to maintain our internal product development focus on our core disease indications and therapeutic areas while still expanding the NAV gene therapy pipeline, developing a greater breadth of treatments for patients, providing additional technological and potential clinical proofs-of-concept for our NAV Technology Platform, and creating potential additional revenue.

Each sublicense specifies the vector or vectors and disease indication or indications as well as whether the sublicense is exclusive or non-exclusive. In determining whether to sublicense, we first evaluate whether the disease indication is of interest to us, in which case we may develop a therapeutic for the disease indication internally using our NAV Technology Platform. If it is not, we consider such factors as the size of the potential market and unmet need; competition; licensee development history; and capabilities and licensee's ability to pay in evaluating whether to enter into a license agreement. As of December 31, 2019, our NAV Technology Platform was being applied in the development of more than 20 partnered product candidates, most under a license to specific NAV Vectors for specific indications.

Our license agreements include upfront and annual fees, milestone fees based on licensee candidate progression, and low-single to low-double digit royalties on sales. Such royalties are subject to customary reductions, such as if the licensee must obtain a license from a third party to avoid infringement of such third party's rights in order to exercise its rights under the license granted by us. We are obligated to make payments to our licensors with respect to the revenues we receive from our licensees for these sublicenses in accordance with the terms of our agreements with our licensors.

Gene Therapy Overview and History of Earlier Generation AAV

Historically, the primary challenge for gene therapy has been the safe and effective delivery of genes into cells. Genes are made of DNA, which is a large, highly charged molecule that is difficult to transport across a cell membrane and deliver to the nucleus, where it can be transcribed and translated into protein. The genetic material needs to be delivered efficiently and to the desired target tissues and cell types, which will vary depending on the disease to be treated. Based on this need, scientists have designed and developed a variety of gene vectors in order to facilitate gene delivery in cells.

To date, the study of gene vectors as treatments in humans has involved approaches with *in vivo* and *ex vivo* techniques using a variety of different gene vectors. Each approach presents different features and benefits for the treatment of a particular disease. *Ex vivo* gene therapy approaches generally are employed to target correction in blood and bone marrow. These methods typically involve harvesting and isolating a patient's own cells. Both the patient and cells undergo several preparatory steps to allow for modification of the cells by gene vectors. Ultimately, the modified cells are re-administered to the patient. *In vivo* gene therapy approaches involve directly administering (e.g., by infusion or injection) gene vectors into patients in order to reach desired cells in target tissues (e.g., liver, brain, eye, muscle, heart). These methods rely on a combination of the route of administration and the gene vectors themselves to facilitate the correction in the target tissues.

We focus on *in vivo* gene therapy. Among vectors available for *in vivo* gene therapy, viral vectors have been adopted with the greatest frequency because they have demonstrated the greatest efficiency in gene delivery to date. This efficiency exists because viral vectors are derived from naturally occurring viruses with normal life-cycles that rely on gene delivery of their own genomes. In other words, they are naturally optimized to deliver genes to cells. Many viral vectors have presented sub-optimal safety profiles for *in vivo* treatment in humans because the viruses from which they are derived are pathogenic (causing disease), immunogenic (causing immune response) or create genomic toxicity (delivering a gene to a place where it interrupts normal function). Vectors derived from adenovirus, herpes virus and retroviruses have been tested as *in vivo* viral vectors, and other technologies are evolving.

Vectors derived from AAV have among the best safety profiles for gene therapy given that AAVs are not known to be associated with disease in humans. The earlier generation AAV vectors were designed by scientists in the mid-1980s and the first clinical trials using AAV began in the mid-1990s. There were only a handful of AAV vectors available to scientists at the time of the first clinical trials because AAV vectors were designed based on the capsid (the protein shell of a virus that encloses the genetic material of the virus) of AAV viruses known to be in existence, and only six distinct serotypes (groups within a single species of microorganisms, such as bacteria or viruses, which share distinctive surface structures) had been discovered at that time. These earlier generation AAV vectors were shown to be limited in their application due to a variety of limitations and challenges, including:

- low or unmeasurable gene expression, meaning the delivered gene was enabling production of low or unmeasurable amounts of the therapeutic protein;
- short-term gene expression, meaning if gene expression was measurable, it was transient;
- limited tissue selectivity, meaning concentrated gene expression was not observed in the target organ; and
- high levels of immune response, meaning the body may neutralize the gene delivery vector with pre-existing antibodies or generate T-cells that inhibit the therapeutic effect.

Discovery of Next Generation AAV

In recognition of the limitations and challenges of earlier generation AAV vectors, an effort was undertaken in the early 2000s at Penn to discover other naturally occurring AAV sequences. The identification of such sequences was based on the observation that wild-type AAV (in contrast to recombinant AAV) can undergo a latent cycle in which the AAV genome stays within the cell, meaning the virus, including its capsid gene sequence, remains intact within the cell but does not reproduce. This allowed for identification of new sequences not by purifying viruses from tissues, but by searching for capsid gene sequences in a variety of tissues isolated from non-human primates and from humans, based on regions of the AAV capsid gene that did not vary between the known AAV vectors. By searching for capsid gene sequences in this manner, many more capsid protein sequences were discovered than would have been found by purifying viruses from tissues.

More than 100 new capsid sequences were identified by the process. The first few were initially designated AAV7, AAV8 and AAV9, after which, other sequences were identified by species from which it was isolated (e.g., “rh” indicating rhesus macaque) followed by a number (e.g., 10, for rh10). Early characterization of the initial discoveries of AAV7, AAV8, AAV9 and AAVrh10 suggested that these vectors may be significantly more efficient in various applications important for clinical translation than other previously known AAVs.

After patenting the next generation AAV vectors, Penn initiated a distribution program through a material-transfer process that enabled researchers to access the next generation AAV vectors for research use only, under specific restrictions. Thousands of custom reagents were sent to independent researchers, who began to characterize and validate the beneficial features of AAV vectors in animal models of disease. In 2010, the first clinical trials were conducted using the next generation AAV vectors and initial proof-of-concept and safety in humans was established from these trials. These clinical trials also produced longer-term efficacy results which reinforced our belief that these next generation vectors have beneficial properties not seen in the earlier generation AAV vectors.

We believe the next generation AAV vectors, which form the basis of our NAV Technology Platform, have many improved properties relative to earlier generation AAV vectors for development and commercialization of AAV treatments, including:

- higher gene transfer;
- longer-term gene expression;
- broad and novel tissue selectivity;
- lower immune response; and
- improved manufacturability.

Our Proprietary NAV Technology Platform for Gene Delivery

In 2009, we licensed rights to the next generation AAV vectors discovered at Penn. Our NAV Vectors form the foundation of our NAV Technology Platform. Our NAV Technology Platform has been used in a number of clinical trials conducted by us, our partners and third-party investigators.

We are developing therapeutics using NAV Vectors that contain genes which are synthesized to code for the expression of therapeutic proteins in target cells to correct the underlying causes of the diseases we seek to treat. Each product candidate is designed with a NAV Vector for a specific cell target and to express a specific protein. We incorporate proprietary modifications to both the AAV and the gene, which enhance properties such as potency, stability and tissue distribution. Our proprietary technology, including the use of vectors derived from novel sequences of AAV such as AAV7, AAV8, AAV9 and AAVrh10, are protected by more than 100 licensed patents and patent applications. The rights to our NAV Technology Platform provide our product candidates with what we believe to be a competitive advantage over product candidates developed with earlier generation AAV vectors due to the novel and beneficial properties of our NAV Vectors.

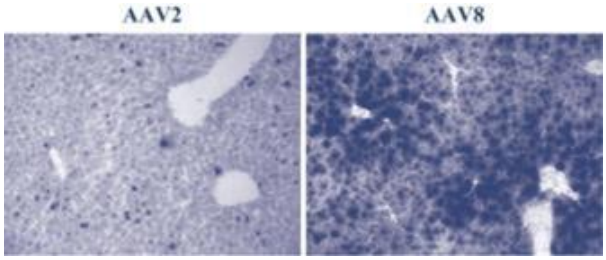
Key Potential Benefits of NAV Technology

The properties that make NAV Vectors unique from and potentially an improvement to earlier generation AAV vectors, as well as provide support that they are potentially best-in-class for development and commercialization of AAV treatments, are set forth below.

Higher Gene Transfer

NAV Vectors have been shown to generate higher levels of gene transfer in animals than earlier generation AAV vectors such as AAV2. In mouse livers, AAV8 produced levels of gene expression that were 10- to 100-fold higher than was achieved with AAV2. The figure below shows the contrast in the amount of gene expressed using the two vectors at the same dose.

AAV Transduction in Mouse Liver



In this experiment, the reporter gene LacZ, a gene which encodes a protein that turns a clear substrate blue in a specific medium, was included in the transgene sequence delivered by the vector so that cells expressing the transgene are stained blue, visually denoting expression level. It was possible to transduce the entire mouse liver and achieve long-term expression with AAV8. Higher gene expression creates the possibility of achieving therapeutic benefit in more diseases than was possible using earlier AAV vectors, as more therapeutic protein is generated with vectors that enable higher expression.

Longer-Term Gene Expression

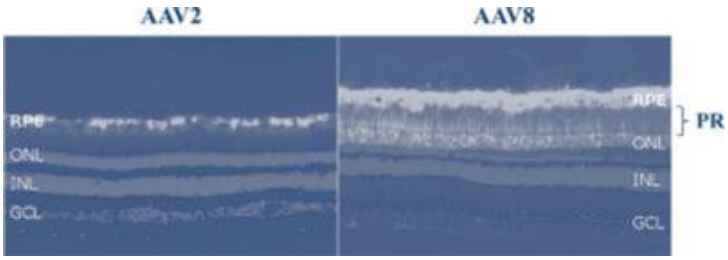
We believe the longer-term gene expression seen using NAV Vectors is due to more stable genomic persistence and reduced cellular immunity, which are a function of novel capsid structure and lower dosing required using NAV Vectors due to the greater gene expression discussed earlier herein. NAV Vectors have demonstrated stable expression in animals for over eight years. Moreover, AAV8 vectors have demonstrated stable expression for over eight years in clinical trials for hemophilia B patients.

Broad and Novel Tissue Selectivity

NAV Vectors also display high levels of tissue specificity. This property is important because it allows for development of therapeutics to target cells that earlier generation AAV vectors do not target or do not target well. AAV9 has emerged as a vector that enables efficient gene delivery when directly injected into the CNS. AAV9 has also demonstrated novel tissue selectivity for the CNS when delivered intravenously, resulting in efficient gene expression in the brain and spinal cord, and AAV9 can also be transported throughout the CNS, enabling broader delivery with a single injection. This was the first time a gene therapy vector was demonstrated to cross the blood-brain barrier, producing results in both small and large animals, including non-human primates. This route of administration has recently been used clinically by one of our NAV Technology Licensees to treat SMA Type I, which was approved by the FDA in 2019.

NAV Vectors have also shown novel properties in the eye when investigated for the treatment of acquired disease and inherited retinal degenerations. AAV8 expressing a fluorescent protein was administered by subretinal injection in the non-human primate eye in order to show gene expression in the retina itself, which contains the cell types to be treated. As is depicted in the graphic below, a cross-section of the non-human primate retina below showed more efficient gene delivery (as demonstrated by the much greater amount of the fluorescent protein expressed) with AAV8 as compared to AAV2 in the retinal pigment epithelium (RPE) and to the photoreceptor (PR) layer. The majority of genes associated with retinal degeneration are located in the RPE and PR layer. These genes influence the cell's development or function and are therefore critical to most inherited retinal degenerations.

AAV Transduction of Layers in the Non-Human Primate Eye(1)



(1) Science Translational Medicine: *Dosage Thresholds for AAV2 and AAV8 Photoreceptor Gene Therapy in Monkey*, Luk H. Vandenberghe, et al. (2011). Reprinted with permission from the American Association for the Advancement of Science.

Lower Immune Response

Lower immune response to the gene therapy vector used to deliver the transgene is important for longer-term gene expression, higher expression and higher potency. Data indicate that more than two thirds of certain human populations have a high level of neutralizing antibodies (NAbs) against the capsids of AAV1 and AAV2. This represents a major obstacle to the effective use of these earlier generation vectors due to the inhibition of gene delivery via particle neutralization in the circulation, as pre-existing antibodies neutralize the vector carrying the transgene before it can reach the target cells. Several studies have investigated the seroprevalence of neutralizing antibodies directed against AAV in humans. Although data can vary geographically, neutralizing antibodies against AAV1 and AAV2 are usually detected in 70% of individuals, while seroprevalence is reported to be 45% for AAV6 and AAV9 and less than 40% for AAV8. Shared amino acid sequences and common overall structure allow for antibody cross-reactivity between AAV serotypes and neutralizing antibodies recognizing virtually all serotypes can be found in most subjects.

T-cell responses to AAV vectors have also been studied in mice and nonhuman primates, in which high levels of T-cells specific to capsids of AAV2 were detected. AAV8, however, did not lead to activation of capsid-specific T-cells. In a recent clinical trial of an AAV8-based gene therapy for the treatment of hemophilia B, there was low liver toxicity from T-cells generated and reactive with AAV8. We believe this is likely due to differences in immunogenic capsid epitopes as well as the lower doses of AAV8 needed to be efficacious.

Improved Manufacturability

The manufacturing process for NAV Vectors can be designed to reduce the number of difficult processing steps required for the earlier AAV vectors, improving overall yield at larger scale. NAV Vectors are derived from naturally "fit" viruses, which are stable structures that efficiently assemble, in contrast to the earlier generation AAV vectors. During production, NAV Vectors are secreted by AAV producer cells, eliminating the need for lysing (breaking down of the membrane of a cell, often by viral, enzymic or osmotic mechanisms that compromise the cells integrity) of cells, which can complicate purification and impact yield. This is a novel aspect of NAV Vectors that increases yield and efficiency in production.

Platform License Agreements and Other Licenses

Platform Licenses

We have exclusively licensed many of our rights in our NAV Technology Platform from Penn and GlaxoSmithKline LLC (GSK), which together we refer to as our Platform Licenses. We currently use our NAV Technology Platform to develop treatments for retinal neurodegenerative and metabolic diseases. We also sublicense our NAV Technology Platform to third parties in order to develop and bring to market NAV Gene Therapy for a range of severe diseases with significant unmet medical needs outside of our core disease indications and therapeutic areas. For further information regarding our commercial sublicenses, please see "Commercial Licenses to NAV Technology Licensees" located elsewhere in this Annual Report on Form 10-K.

The Trustees of the University of Pennsylvania. In February 2009, we entered into an exclusive, worldwide license agreement with Penn for patent and other intellectual property rights relating to a gene therapy technology platform based on AAVs discovered at Penn in the laboratory of James M. Wilson, M.D., Ph.D. This license was amended in September 2014, April 2016 and April 2019. In February 2009, we also entered into an SRA with Penn (the 2009 SRA) under which we funded the nonclinical research of Dr. Wilson relating to AAV gene therapy and obtained an option to acquire an exclusive worldwide license in certain intellectual property created pursuant to such 2009 SRA. We entered into an additional SRA (the 2013 SRA) with Penn in November 2013 which was funded entirely by our NAV Technology Licensee, Dimension Therapeutics, Inc. (since acquired by Ultragenyx Pharmaceutical Inc.) (Dimension). In December 2014, we entered into another SRA with Penn funding related nonclinical research of Dr. Wilson (the 2014 SRA).

Our license agreement with Penn, as amended, provides us with an exclusive, worldwide license under certain patents and patent applications in order to make, have made, use, import, offer for sale and sell products covered by the claims of the licensed patents and patent applications as well as all patentable inventions (to the extent they are or become available for license) that:

- were discovered by Dr. Wilson or other Penn researchers working under his direct supervision at Penn; and
- are related to the AAV technology platform discovered by Dr. Wilson at Penn prior to February 2009, pursuant to a sponsored research agreement or subsequent amendment to a sponsored research agreement; or
- are necessary or useful for the practice of Penn's patent rights in the treatment of CLN2 disease, a form of Batten disease, and conceived and reduced to practice since October 2015; and
- are owned and controlled by Penn.

Prior to entering into the license agreement with us, Penn had previously entered into two license agreements with third parties with respect to certain of the licensed patents and patent applications. Our license from Penn is subject to those preexisting license grants. With respect to the first third party license granted by Penn, our license is non-exclusive with respect to the patents and patent applications licensed to the third party for so long as that preexisting license grant remains in effect and will become exclusive upon the expiration or termination of that existing license agreement. The pre-existing licenses also include a license agreement Penn entered into with GSK in May 2002 granting a license to certain patents and patent applications, of which we subsequently sublicensed certain rights to from GSK in March 2009. For further information regarding our GSK sublicense, please see "Platform License Agreements and Other Licenses—Platform Licenses—GlaxoSmithKline LLC" located elsewhere in this Annual Report on Form 10-K. Our license agreement with Penn provides that should the rights Penn licensed to GSK ever revert to Penn, such rights shall automatically be included in our license agreement with Penn.

The Penn license agreement, as amended, also provides us with a non-exclusive, worldwide license to use (i) all data and information generated in the performance of clinical research relating to the RGX-501 clinical trial, (ii) all data and information that was developed since October 2015 by Dr. Wilson, or other Penn researchers working under his direct supervision at Penn, that is related to Batten disease, owned by Penn, and necessary or useful for the practice of the licensed patent rights in the treatment of CLN2 disease; and (iii) all know-how that:

- was developed by Dr. Wilson, or other Penn researchers working under his direct supervision at Penn; and
- is related to the AAV technology platform discovered by Dr. Wilson prior to September 2014; or
- is related to the AAV technology platform discovered by Dr. Wilson at Penn after September 2014 during the performance of a research program we sponsored; and
- is owned by Penn; and
- is necessary or useful for the practice of the licensed patent rights.

Under the terms of the Penn license agreement, we issued equity to Penn and are also obligated to pay Penn:

- Up to $20.5 million upon the achievement of various development and sales-based milestones;
- low- to mid-single digit royalties on net sales of licensed pharmaceutical products sold by us or our affiliates;
- low-single digit to low-double digit royalty percentages of net sales on licensed products intended for research purposes only;
- low- to mid-double digit royalty percentage on royalties received from third parties on net sales of licensed pharmaceutical products by such third parties;
- low-double digit to mid-teen digit percentages of sublicense fees we receive for the licensed intellectual property rights from sublicensees; and
- reimbursements for ongoing patent prosecution and maintenance expenses.

Our Penn license agreement, as amended, will terminate with respect to licensed products in a field of use other than the treatment of familial hypercholesterolemia (FH) on a product-by-product and country-by-country basis on the date each particular licensed product ceases to be covered by at least one valid claim, issued or pending, under the licensed patent rights. With respect to licensed products for treating FH, our Penn license agreement, as amended, will terminate on a product-by-product and country-by-country basis on the later of (i) the date the licensed product for treating FH ceases to be infringed or covered by a valid claim, issued or pending, under the licensed patent rights, and (ii) seven years following the first sale of such licensed product for treating FH. We can terminate this license agreement by giving Penn prior written notice. Penn has the right to terminate:

- with notice if we are late in paying money due under the license agreement;
- with notice if we fail to achieve a diligence event on or before the applicable completion date or otherwise breach the license agreement;
- if we or our affiliates experience insolvency; or
- if we commence any action against Penn to declare or render any claim of the licensed patent rights invalid or unenforceable.

Under the current 2014 SRA, as amended, we fund research at Penn and pay certain intellectual property legal and filing expenses and receive the rights to the research results, if any. The Penn license agreement, as amended, and the 2014 SRA, as amended, provide that all patentable inventions conceived, created, or conceived and reduced to practice pursuant to the 2014 SRA, together with patent rights represented by or issuing from the U.S. patents and patent applications, including provisional patent applications, automatically become exclusively licensed to us and all research results become automatically licensed to us as know-how. Under the 2009 SRA, as amended, in consideration for our funding of research at Penn, we received an option to acquire a worldwide license on commercially reasonable terms to practice all patentable inventions conceived, created, or reduced to practice pursuant to the 2009 SRA, together with patent rights represented by or issuing from the U.S. patents and patent applications, including provisional patent applications. Under our 2014 SRA with Penn, as amended, we have agreed to fund research at Penn through 2020.

GlaxoSmithKline LLC. In March 2009, we entered into a license agreement with GSK, which was amended in April 2009, in order to secure the exclusive rights to patents and patent applications covering NAV Technology that GSK had previously licensed from Penn (subject to certain rights retained by GSK and Penn). Under this GSK license agreement, we receive an exclusive, worldwide sublicense under the licensed patent rights to make, have made, use, import, sell and offer for sale products covered by the licensed patent rights anywhere in the world. Our rights under this GSK license agreement are subject to certain rights retained by GSK for the benefit of itself and other third parties, including rights relating to: domain antibodies; RNA interference and antisense drugs; internal research purposes and GSK's discovery research efforts with non-profit organizations and GSK collaborators; AAV8 for the treatment of hemophilia B; AAV9 for the treatment of Muscular Dystrophy, congestive heart failure suffered by Muscular Dystrophy patients and cardiovascular diseases by delivery of certain genes; and non-commercial research in the areas of Muscular Dystrophy, hemophilia B, congestive heart failure suffered by Muscular Dystrophy patients, and other cardiovascular disease. Under the terms of the license agreement, we issued equity to GSK and are obligated to pay GSK:

- up to $1.5 million in aggregate milestone payments, all of which have been paid as of December 31, 2019;
- low- to mid-single digit royalty percentages on net sales of licensed products;
- low- to mid-double digit percentages of any sublicense fees we receive from sublicensees for the licensed intellectual property rights; and
- reimbursements for certain patent prosecution and maintenance expenses.

Under our GSK license agreement, we are required to use commercially reasonable efforts to develop and commercialize licensed products. Our GSK license agreement will terminate upon the expiration, lapse, abandonment or invalidation of the last licensed claim to expire, lapse, become abandoned or unenforceable in all the countries of the world where the licensed patent rights existed. However, if no patent ever issues from patent rights licensed from GSK, this license agreement will terminate a specified number of years after the first commercial sale of the first licensed product in any country. We may terminate this license agreement for any reason upon a specified number of days' written notice. GSK can terminate this license agreement if:

- we are late in paying GSK any money due under the agreement and do not pay in full within a specified number of days of GSK's written demand;
- we materially breach the agreement and fail to cure within a specified number of days; or
- we file for bankruptcy.

Other Licenses

Regents of the University of Minnesota. In November 2014, we entered into a license agreement with Regents of the University of Minnesota (Minnesota) for the exclusive rights to Minnesota's undivided interest in intellectual property jointly owned by Minnesota and us relating to the delivery of AAV vectors to the CNS. This license was amended in November 2016. Under this Minnesota license agreement, as amended, we receive an exclusive license under the licensed patent rights to make, have made, use, offer to sell or sell, offer to lease or lease, import or otherwise offer to dispose or dispose of products covered by the licensed patent rights in all fields of use in any country or territory in which a licensed patent has been issued and is unexpired or a licensed patent application is pending until November 2019, after which time the field of use would be limited to all fields of use using our NAV Vectors in addition to certain additional indications and areas. Under the terms of the agreement, we are obligated to pay Minnesota upfront fees, annual maintenance fees, royalties on net sales, if any, sublicense fees and fees upon the achievement of various milestones.

Emory University. In August 2018, we entered into a license agreement with Emory University (Emory) for the exclusive rights to Emory's undivided interest in intellectual property jointly owned by Emory and us relating to the delivery of AAV vectors to the CNS. Under this Emory license agreement, we receive an exclusive license under the licensed patent rights to make, have made, use, import, offer to sell or sell licensed products in all fields of use in any country. Under the terms of the agreement, we are obligated to pay Emory an upfront fee, annual maintenance fees under certain circumstances, royalties on net sales, sublicense fees, and fees upon the achievement of various milestones for the first licensed product.

Intellectual Property

Our success depends in part on our ability to obtain and maintain intellectual property protection for our product candidates, core technologies and other know-how, to operate without infringing on the rights of others and to prevent others from infringing our rights. We strive to protect and enhance the proprietary technology, inventions, and improvements that are important to our business, including by seeking, maintaining and defending patent rights. We also rely on trade secrets relating to our technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our position in the field of gene therapy. Additionally, we intend to rely on regulatory protection afforded through orphan drug designations, data exclusivity and market exclusivity as well as patent term extensions, where available.

We anticipate that our patent portfolio will continue to expand as a result of our SRAs with academic institutions, including the 2014 SRA with Penn, and our commercial licenses to NAV Technology Licensees. For further information regarding our commercial sublicenses, please see “Commercial Licenses to NAV Technology Licensees” located elsewhere in this Annual Report on Form 10-K.

Product Candidates

As of December 31, 2019, in addition to the patents related to our NAV Technology described below, our patent portfolio included a total of three issued U.S. patents, one pending U.S. non-provisional patent application, six pending International Patent applications filed pursuant to the Patent Cooperation Treaty (PCTs) and 14 PCTs that have entered national stage relating to our product candidates, which are summarized below:

- *RGX-314*: Two PCTs that have entered national stage for which any issued U.S. or European patent would expire in 2037 and two pending PCTs for which any issued U.S. or European patent would expire in 2038 or 2039, in each case without taking into account any possible patent term adjustment or extension;
- *RGX-111/RGX-121*: Nine PCTs that have entered national stage and two pending PCTs for which any issued U.S. or European patents would expire in 2034, 2036, 2037, 2038 or 2039, in each case without taking into account any possible patent term adjustment or extension;
- *RGX-111*: Two issued U.S. patents that will expire in 2034, in each case without taking into account any possible patent term extension;
- *RGX-181*: One pending U.S. non-provisional patent application for which any issued U.S. patent would expire in 2034, one PCT that has entered national stage for which any issued U.S. or European patent would expire in 2038 and one pending PCT for which any issued U.S. or European patent would expire in 2039, in each case without taking into account any possible patent term adjustment or extension; and
- *RGX-501*: One issued U.S. patent that will expire in 2026, without taking into account any possible patent term extension, two PCTs that have entered national stage for which any issued U.S. or European patent would expire in 2036 or 2038 and one pending PCT for which any issued U.S. or European patent would expire in 2039, without taking into account any possible patent term adjustment or extension with respect to the pending national stage applications and PCT.

NAV Technology

We have exclusively licensed rights relevant to our NAV Technology which includes novel recombinant AAV vectors AAV7, AAV8, AAV9, and AAVrh10, among others. Our licensed patent portfolio includes exclusive rights to more than 100 patents and patent applications worldwide relating to composition of matter patents and/or patent applications for our novel AAV vectors, as well as methods for their manufacture and therapeutic uses. We also possess substantial know-how and trade secrets relating to our NAV Technology. As of December 31, 2019, our licensed patent portfolio included 13 issued U.S. patents and five European patents relating to the AAV7, AAV8, AAV9 and AAVrh10 vectors and uses thereof. These patents have terms that will expire as late as 2026, not including patent term extensions.

Our licensed patent portfolio also includes composition of matter claims for novel AAV vectors having certain other capsids as well as AAV capsids that have an amino acid sequence at least 95% or at least 97% identical to the capsids of certain of the NAV Vectors.

Our patent portfolio also includes exclusive rights to patents and patent applications relating to:

- therapeutic compositions and methods involving the foregoing AAV vectors further comprising certain transgenes that encode therapeutic products, and their use in treating specified diseases;
- specific formulations or methods of delivery of the recombinant AAV vectors of interest for our in-house development programs;
- technology related to engineering AAV therapeutics including recombinant AAV vectors engineered to target conducting airway cells, methods of altering the targeting and cellular uptake efficiency of an AAV viral vector having a capsid containing an AAV9 cell surface binding domain, the design of recombinant AAV viral vectors that confer passive immunization to airborne pathogens (the aforementioned gene therapy systems can include the use of certain gene expression regulation technology; we have exclusively licensed the patents and patent applications relating to this technology);
- methods of detecting an AAV nucleotide sequence useful in diagnostics; and
- methods of manufacture of recombinant AAV, including patents and applications directed to scalable AAV production methods; methods of increasing the packaging yield, transduction efficiency, and gene transfer efficiency of an AAV, and methods of purification of viral vectors, such as AAV vectors.

Customers

Our revenues for the years ended December 31, 2019, 2018 and 2017 consisted primarily of license and royalty revenue. Three customers (AveXis, Inc. (AveXis) and two other customers) accounted for approximately 92% of our total revenue for the year ended December 31, 2019. Two customers (AveXis and Abeona Therapeutics Inc. (Abeona)) accounted for approximately 97% of our total revenue for the year ended December 31, 2018. One customer (AveXis) accounted for approximately 68% of our total revenue for the year ended December 31, 2017. No other customer accounted for more than 10% of revenue in 2017. We expect future license and royalty revenue to continue to be derived from a limited number of licensees. Future license and royalty revenue is uncertain due to the contingent nature of our licenses granted to third-parties and may fluctuate significantly from period to period.

Research and Development

We are building a research and development organization that includes extensive expertise in AAV gene therapy and related scientific disciplines. We operate cross-functionally and are led by an experienced research and development management team. We use rigorous project management techniques to assist us in making disciplined strategic research and development program decisions and to help limit the risk profile of our product pipeline. We also access relevant market information and key opinion leaders in creating target product profiles when appropriate, as we advance our programs towards commercialization. We engage third parties to conduct portions of our preclinical research. In addition, we are utilizing multiple clinical sites to conduct our clinical trials.

Competition

We are aware of a number of companies focused on developing gene therapies in various disease indications, including Adverum Biotechnologies, Inc., Amicus Therapeutics, Inc., Applied Genetic Technologies Corporation, BioMarin Pharmaceutical, Inc., bluebird bio, Inc., MeiraGTx Limited, Novartis AG, PTC Therapeutics, Inc., Roche, Sangamo Therapeutics, Inc., Sanofi Genzyme, Sarepta Therapeutics, Inc., Solid Biosciences, Inc., Voyager Therapeutics, Inc., and uniQure N.V., as well as a number of companies addressing other methods for modifying genes and regulating gene expression. Additionally, we have sublicensed our NAV Technology Platform for developing gene therapies in various disease indications to our NAV Technology Licensees. Not only must we compete with other companies that are focused on gene therapy products using earlier generation AAV technology and other gene therapy platforms, but any products that we may commercialize will have to compete with existing therapies and new therapies that may become available in the future.

There are other organizations working to improve existing therapies or to develop new therapies for our initially selected disease indications. Depending on how successful these efforts are, it is possible they may increase the barriers to adoption and success for our product candidates, if approved. These efforts include the following:

- **Wet AMD and DR.** Marketed competition for wet AMD and DR largely consists of anti-VEGF therapies developed by Novartis (Beovu), Regeneron Pharmaceuticals, Inc. (Eylea), and Roche/Genentech, Inc. (Lucentis, Avastin). Companies with products in development for the treatment of wAMD and DR include, but may not be limited to, Adverum, Allergan Inc., Graybug Vision, Inc., Kodiak Sciences, Inc. and Roche.
- **MPS I.** There is one principal competitor with a marketed product for the treatment of MPS I, Sanofi Genzyme (Aldurazyme). Companies with products in development for the treatment of MPS I include, but may not be limited to, ArmaGen, Inc., Orchard Therapeutics plc and Sangamo.
- **MPS II.** The principal marketed competition for MPS II is a systemic enzyme replacement therapy, which is marketed by Takeda Pharmaceutical Company, Ltd. (Elaprase). Companies with products in development for the treatment of MPS II include, but may not be limited to, Denali Therapeutics Inc., JCR Pharmaceuticals Co., Ltd. and Sangamo.
- **CLN2 Disease.** There is one principal competitor with a marketed product for the treatment of CLN2 disease, BioMarin (Brineura). Companies with products in development for the treatment of CLN2 disease include, but may not be limited to, Roche.
- **HoFH.** There are several companies with marketed products for the treatment of HoFH, including Aegerion Pharmaceuticals, Inc. (Juxtapid), Amgen, Inc. (Repatha) and Kastle Therapeutics (Kynamro). Companies with products in development for the treatment of HoFH include, but may not be limited to, Novartis, Regeneron and Sanofi Genzyme.
- **HAE.** There are two principal marketed competitors for the prophylactic treatment of HAE, including Takeda (Tahkzyro, Cinryze) and CLS Behring (Haegarda). There is one principal competitor currently under regulatory review for marketing authorization in the United States and Japan, BioCryst Pharmaceuticals, Inc. (berotralstat).

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do. Our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. Our competitors' treatments may be more effective, or more effectively marketed and sold, than any treatment we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our treatments.

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

We anticipate that we will face intense and increasing competition as new drugs and treatments enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Government Regulation

In the United States, biological products, including gene therapy products, are subject to regulation under the Federal Food, Drug, and Cosmetic Act (FD&C Act), and the Public Health Service Act (PHS Act) and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products. Applications to the FDA are required before conducting clinical testing of biological products, and each clinical study protocol for a gene therapy product is reviewed by the FDA.

Within the FDA, the Center for Biologics Evaluation and Research (CBER) regulates gene therapy products. The FDA has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy studies for delayed adverse events, potency testing, and chemistry, manufacturing and control information in gene therapy INDs.

Ethical, scientific, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products 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 our product candidates 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.

U.S. Biological Products Development Process

The process required by the FDA before a biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, including evaluations of product chemistry, formulations, toxicity in animal studies in accordance with good laboratory practice (GLP) and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical studies may begin;
- performance of adequate and well-controlled human clinical studies according to the FDA's requirements for good clinical practice (GCP) and additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- submission to the FDA of a Biologics License Application (BLA) for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical studies, as well as information on the chemistry, manufacturing and controls to ensure product identity and quality, and proposed labeling;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practice (GTP), for the use of human cellular and tissue products;
- potential FDA inspection of the nonclinical and clinical study sites and the clinical study sponsor that generated the data in support of the BLA; and
- FDA review and approval, or licensure, of the BLA.

The clinical study sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical studies due to safety concerns or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

Clinical studies involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical studies are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical study will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical studies must be conducted and monitored in accordance with the FDA's regulations imposing the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical study must be reviewed and approved by an independent institutional review board (IRB) at or servicing each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical study subject or his or her legal representative and must monitor the clinical study until completed. Clinical studies generally also must be reviewed by an institutional biosafety committee (IBC), a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. Some

studies also employ a Data and Safety Monitoring Board (DSMB), which operates with independence from the study sponsor and has access to unblinded study data during the course of the study and may halt a study for ethical reasons such as undue safety risks.

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

- Phase I. The biological product is initially introduced into healthy human subjects and tested for safety. However, in the case of some products for rare, severe or life-threatening diseases, the initial human testing is often conducted in patients.
- Phase II. The biological product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase III. Clinical studies are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product approval and labeling. Post-approval clinical studies, sometimes referred to as Phase IV clinical studies, may be conducted after initial marketing approval. These clinical studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. In some cases, Phase IV studies may be required by the FDA as a condition of approval. The FDA recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for as long as 15 years.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Annual progress reports detailing the results of the clinical studies must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for expedited reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase I, Phase II and Phase III clinical studies may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its DSMB may suspend a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Human gene therapy products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period, the number of patients the FDA will require to be enrolled in the studies in order to establish the safety, efficacy, purity and potency of human gene therapy products, our ability to recruit sufficient numbers of study subjects for any trial, or that the data generated in these studies will be acceptable to the FDA to support marketing approval.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

After the completion of clinical studies of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. Under the Prescription Drug User Fee Act (PDUFA), the BLA must be accompanied by a substantial user fee payment unless an exception or waiver applies. In addition, under the Pediatric Research Equity Act (PREA), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological 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. The FDA may grant deferrals for submission of pediatric data or full or partial waivers of pediatric requirements. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted. The testing and

approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, including whether it is effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality, potency and purity as those factors relate to the safety or effectiveness of the product. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy (REMS) is necessary to assure the safe use of the biological product upon marketing. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with GTP. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue based products (HCT/Ps) which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical studies were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP, GTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical studies designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under PDUFA is to review 90% of standard BLAs in 10 months of the 60-day filing date and 90% of priority BLAs in six months of the 60-day filing date, whereupon a review decision is to be made. Two months are added to these time periods for new molecular entities. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information, or clarification regarding information already provided in the submission, constituting a major amendment to the BLA.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is defined under the FD&C Act as a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be

recovered from sales of the product. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for that product for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union (EU) has similar, but not identical, benefits.

Orphan drug products are also eligible for Rare Pediatric Disease Designation if greater than 50% of patients living with the disease are under age 18. A priority review voucher will be given to the sponsor of a product with a Rare Pediatric Disease Designation at the time of product approval that is transferable to another company.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products, including precision drugs or biological products, that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast Track product at any time during the clinical development of the product. Also under the Fast Track program, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as Breakthrough Therapy designation, priority review, and accelerated approval. Under the Breakthrough Therapy program, products intended to treat a serious or life-threatening disease or condition may be eligible for additional benefits when preliminary clinical evidence demonstrates that such product may have substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product receives timely advice and interactive communications to help the sponsor design and conduct a development program as efficiently as possible. In addition, gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues, may be eligible for regenerative medicine advanced therapy (RMAT) designation. Products with an RMAT designation are eligible for the benefits of Breakthrough Therapy in addition to allowing the sponsor the ability to participate in meetings with the FDA to discuss whether accelerated approval would be appropriate based on surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a serious or life-threatening disease or condition compared to marketed products. Specific priority review programs exist for material threat medical countermeasures, rare pediatric diseases and tropical diseases. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review, in accordance with FDA guidance. Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA will require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical studies to confirm the clinical benefit of the medicine. In addition, the FDA currently requires as a condition for accelerated approval pre-submission of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, Breakthrough Therapy or RMAT

designation, priority review and accelerated approval do not change the standards for approval. Rather, these programs are intended to expedite the development and approval process, but do not necessarily accomplish that intent.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, strength, quality, potency, or purity of a distributed product in a manner that may impact the safety or effectiveness of the product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, 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 release by the FDA, the manufacturer submits samples of each lot of product to the FDA 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. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

We also must comply with the FDA's advertising and promotion and related medical communication requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), the requirement to balance promotion information on efficacy with important safety information and limitations on use, industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product or conditions of approval, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant BLA.

A biological product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted in the case of a biologic approved under a BLA, adds six months to existing exclusivity periods. This six-month exclusivity, which runs from the end of other exclusivity protection, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The Patient Protection and Affordable Care Act (PPACA) signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHS Act attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, 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. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations. Equivalent laws have been adopted in other countries that impose similar obligations.

Other U.S. Healthcare Laws and Regulations

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and use of pharmaceutical products that are granted marketing approval. Arrangements with third-party payors, existing or potential customers and referral sources are subject to broadly applicable fraud and abuse and other healthcare laws and regulations, and these laws and regulations may constrain the business or financial arrangements and relationships through which manufacturers market, sell and distribute the products for which they obtain marketing approval. Such restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or kind, in exchange for, or to induce, 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 healthcare programs such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, patients, purchasers and formulary managers on the other. PPACA amends the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;
- the federal False Claims Act (FCA), which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other federal healthcare programs that are false or fraudulent. Federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, also may implicate the FCA:
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services (CMS) information related to payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members;
- the Health Insurance Portability and Accountability Act of 1996 (HIPAA) imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to: items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances. Many of these state and foreign laws differ from federal law and from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Violation of any of the laws described above or any other governmental laws and regulations may result in penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs and imprisonment. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly for manufacturers of branded prescription products.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and markets in other countries, sales of any product candidates for which regulatory approval for commercial sale is obtained will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all FDA-approved drugs for a particular indication. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. New metrics frequently are used as the basis for reimbursement rates, such as average sales price, average manufacturer price and actual acquisition cost. In order to obtain coverage and reimbursement for any product that might be approved for sale, it may be necessary to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the products, in addition to the costs required to obtain regulatory approvals. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. Health Technology Assessment which is intended to take account of medical, social, economic and ethical issues when determining the suitability of a medicinal product for reimbursement has increasingly become an element of the pricing and reimbursement decisions of the competent authorities in EU Member States.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, PPACA contains provisions that may reduce the profitability of drug products, including, for example, increasing the minimum rebates owed by manufacturers under the Medicaid Drug Rebate Program, extending the rebate program to individuals enrolled in Medicaid managed care plans, addressing a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected and establishing annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act (FCPA), to which we are subject, prohibits corporations and individuals from engaging in bribery and corruption when dealing with foreign government officials. It is illegal to pay, offer to pay, promise or authorize the payment of money or anything of value, directly or indirectly, to any foreign government official, political party or political candidate in an attempt to secure an improper advantage in order to obtain or retain business or to otherwise improperly influence a foreign official in his or her official capacity. Comparable laws have been adopted in other countries that impose similar obligations. We are also subject to the FCPA's accounting provisions, which require us to keep accurate books and records and to maintain a system of internal accounting controls sufficient to assure management's control, authority, and responsibility over our assets. The failure to comply with the FCPA and similar laws could result in civil or criminal sanctions or other adverse consequences.

Government Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Many countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. In the EU, for example, an application for authorization of a clinical trial must be submitted to the competent regulatory authorities and a request for a related positive opinion must be submitted to the competent Ethics Committees in the EU Member States in which the clinical trial takes place, much like the FDA and the IRB, respectively. Once the clinical trial has been approved by the competent regulatory authorities and a positive opinion has been provided by the competent Ethics Committees in accordance with the EU and the EU Member State requirements, the corresponding clinical trial may proceed. The approval procedures and ethics committee involvement requirements vary to some extent among the EU Member States. Until the new EU Regulation on Clinical Trials (Reg. EU No. 536/2014) becomes applicable, trial sponsors must obtain individual approvals in every EU Member State where a trial site is located.

To obtain regulatory approval of a biological medicinal product under EU regulatory systems, we must submit a marketing authorization application. The grant of marketing authorization in the EU 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 and Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing the European Medicines Agency (the EMA), commonly referred to as the EMA Regulation. 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. The EMA's Committee for Advanced Therapies (CAT) is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products (ATMP). ATMP include gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for an ATMP candidate that is submitted to the EMA. The EMA then provides a final opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization after the EMA has delivered its opinion.

Innovative medicinal products are authorized in the EU on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies, in whole or in part, on data in the marketing authorization dossier for another, previously approved medicinal product). Applications for marketing authorization for innovative medicinal products must contain the results of pharmaceutical tests, preclinical tests and clinical trials conducted with the medicinal product for which marketing authorization is sought. Innovative medicinal products for which marketing authorization is granted are entitled to eight years of data exclusivity. During this period, applicants for approval of generics or biosimilars of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product to support their application. Innovative medicinal products for which marketing authorization is granted are also entitled to ten years of market exclusivity. During these ten years of market exclusivity, no generic or biosimilar medicinal product may be placed on the EU market even if a marketing authorization application for approval of a generic or biosimilar of the innovative product has been submitted to the EMA or to the competent regulatory authorities in the EU Member States and marketing authorization has been granted. The ten years of market exclusivity 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 their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be an innovative medicinal product which is eligible for the relevant periods of data and market exclusivity.

Products authorized as “orphan medicinal products” in the EU are entitled to benefits additional to those granted in relation to innovative medicinal products. In accordance with Article 3 of Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, a medicinal product may be designated as an orphan medicinal product if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the incentives derived from orphan medicinal product status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Further guidance on such criteria is provided in European Commission Regulation (EC) No. 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts “similar medicinal product” and “clinical superiority”. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and following grant of a marketing authorization, the EMA and the EU Member States’ competent authorities are not permitted to accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication of a similar medicinal product for ten years following grant or authorization. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant may receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity that an orphan drug enjoys may 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 designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product during the 10-year period of market exclusivity for the same therapeutic indication at any time if:

- The second applicant can establish in its application that its product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- The holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- The holder of the marketing authorization for the original orphan medicinal product cannot supply enough orphan medicinal product.

Similar to obligations imposed in the United States, medicinal products authorized in the EU may be subject to post-authorization obligations, including the obligation to conduct Post Marketing Safety Studies (PASS) or Post Marketing Efficacy Studies (PAES).

Moreover, in the EU, the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC (the Price Transparency Directive). The aim of the Price Transparency Directive is to ensure that pricing and reimbursement mechanisms established in EU Member States are transparent and objective, do not hinder the free movement and trade of medicinal products in the EU and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not, however, provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual EU Member States. Neither does it have any direct consequence for pricing or levels of reimbursement in individual EU Member States. The national authorities of the individual EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices and/or reimbursement of medicinal products for human use. Individual EU Member States adopt policies according to which a specific price or level of reimbursement is approved for the medicinal product. Other EU Member States adopt a system of reference pricing, basing the price or reimbursement level in their territory either, on the pricing and reimbursement levels in other countries, or on the pricing and reimbursement levels of medicinal products intended for the same therapeutic indication. Furthermore, some EU Member States impose direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Health Technology Assessment (HTA) of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States. These countries include France, Germany, Ireland, Italy, and Sweden. The HTA process in the EU Member States is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of the use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the national healthcare system. Those elements of medicinal products are compared with other treatment options available on the market.

The outcome of HTA may influence the pricing and reimbursement status for specific medicinal products within individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of a specific medicinal product vary between the EU Member States.

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive concerns the application of patients' rights in cross-border healthcare. The Directive is intended to establish rules for facilitating access to safe and high-quality cross-border healthcare in the EU. It also provides for the establishment of a voluntary network of national authorities or bodies responsible for HTA in the individual EU Member States. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This could lead to harmonization of the criteria taken into account in the conduct of HTA between EU Member States and in pricing and reimbursement decisions and negatively impact price in at least some EU Member States. On January 31, 2018, the European Commission adopted a new legislative proposal to amend Directive 2011/24/EU. The proposal aims at boosting the cooperation regarding HTA among the EU Member States. It covers new medicinal products and certain new medical devices. The proposal provides the possibility for EU Member States to use common HTA tools, methodologies and procedures across the EU and to perform joint clinical assessments. The proposal has not yet been adopted as new legislation.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

The United Kingdom (UK) formally left the EU on January 31, 2020. During the subsequent transition period, EU pharmaceutical law as laid out in the “Acquis Communautaire” is expected to continue to be applicable to the UK. When the withdrawal from the EU becomes fully effective by December 31, 2020, the UK will have the status of a third country with regard to the EU, and it is uncertain if and to what extent its legislation and regulatory procedures will continue to be aligned with the EU.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees

As of February 21, 2020, we employed 257 full-time employees, of which 198 were engaged in research and development activities, including preclinical, manufacturing and clinical study related functions, and 59 were engaged in general administrative activities, including commercial, corporate development, finance, legal, human resources, information technology, facilities and other general and administrative functions. We have never had a work stoppage, and none of our employees are represented by a labor organization or under any collective bargaining arrangements. We consider our relationship with our employees to be good.

Corporate Information

We were originally formed on July 16, 2008 as ReGenX, LLC, a Delaware limited liability company, and we were subsequently renamed ReGenX Biosciences, LLC on December 22, 2009. On September 16, 2014, we underwent a corporate reorganization pursuant to which we were converted into a Delaware corporation under the name REGENXBIO Inc. Our principal offices are located at 9600 Blackwell Road, Suite 210, Rockville, MD 20850, and our telephone number is (240) 552-8181.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the SEC under the Exchange Act. You may obtain any reports, proxy and information statements, and other information that we file electronically with the SEC at www.sec.gov.

You also may view and download copies of our SEC filings free of charge at our website, www.regenxbio.com, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The information contained on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and is not considered part of, this Annual Report on Form 10-K. Investors should also note that we use our website, as well as SEC filings, press releases, public conference calls and webcasts, to announce financial information and other material developments regarding our business. We use these channels, as well as any social media channels listed on our website, to communicate with investors and members of the public about our business. It is possible that the information that we post on our social media channels could be deemed material information. Therefore, we encourage investors, the media and others interested in our company to review the information that we post on our social media channels.

ITEM 1A. *RISK FACTORS*

You should carefully consider the risk factors set forth below as well as the other information contained in this Annual Report on Form 10-K and in our other public filings in evaluating our business. Any of the following risks could materially and adversely affect our business, financial condition or results of operations. In addition, these risks could cause actual results and developments to differ materially and adversely from those projected in the forward-looking statements contained in this Annual Report on Form 10-K (please read the Information Regarding Forward-Looking Statements appearing at the beginning of this Form 10-K).

We have organized the risks described below into (i) risks related to our NAV Technology Platform and the development of our product candidates, (ii) risks related to our financial position, (iii) risks related to third parties, (iv) risks related to manufacturing, (v) risks related to the commercialization of our product candidates, (vi) risks related to our business operations, (vii) risks related to our intellectual property and (viii) risks related to ownership of our common stock. However, these categories of risks and the specific risk factors described below are not the only risks we face. Additional risks and uncertainties not currently known to us or that we currently view to be immaterial may also materially adversely affect our business, financial condition or results of operations. In these circumstances, the market price of our common stock would likely decline and you could lose all or part of your investment.

Risks Related to our NAV Technology Platform and the Development of Our Product Candidates

Our gene therapy product candidates are based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. Only a few gene therapy products have been approved in the United States, the European Union or elsewhere.

We have concentrated our research and development efforts on our proprietary adeno-associated virus (AAV) gene delivery platform (our NAV Technology Platform), and our future success depends on our and our licensees' successful development and commercialization of viable gene therapy product candidates. There can be no assurance that we or our licensees will not experience problems or delays in developing current or future product candidates or that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. We also may experience unanticipated problems or delays in expanding our manufacturing capacity, and this may prevent us from completing our clinical trials, meeting the obligations of our collaborations or commercializing our products on a timely or profitable basis, if at all. For example, we, a partner or another group may uncover one or more previously unknown risks associated with AAV or our NAV Technology Platform, and this may prolong the period of observation required for obtaining regulatory approval, necessitate additional clinical testing or invalidate our NAV Technology.

In addition, the clinical trial requirements of the U.S. Food and Drug Administration (the FDA), the European Medicines Agency (the EMA) and other regulatory authorities and the criteria these regulators use to determine the quality, safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be significantly more expensive and take longer than for other, better known or more extensively studied product candidates. Only a few gene therapy products have been approved in the United States, the European Union or elsewhere. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union or elsewhere, or how long it will take to commercialize our product candidates. Furthermore, approvals by one regulatory authority may not be indicative of what other regulatory authorities may require for approval, and approvals of *ex vivo* gene therapy products may not be indicative of what may be required for approval of *in vivo* gene therapy products.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. Additionally, we may seek regulatory approval in territories outside the United States and the European Union, which may have their own regulatory authorities along with frequently changing requirements or guidelines. The regulatory review committees and advisory groups in the United States, the European Union and elsewhere, 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 our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. 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 product revenue, and our business, financial condition, results of operations and prospects would be materially harmed.

Our business depends substantially on the success of our lead product candidates. If we are unable to obtain regulatory approval for, or successfully commercialize, our lead product candidates, our business will be materially harmed.

Our lead product candidates are in the early stages of development and will require substantial clinical development and testing, manufacturing bridging studies and process validation and regulatory approval prior to commercialization. Successful continued development and ultimate regulatory approval of our lead product candidates is critical for our future business success and our ability to generate product revenue. We have invested, and will continue to invest, a significant portion of our financial resources in the development of our lead product candidates. We will need to raise sufficient funds for, and successfully complete, our clinical trials of our lead product candidates in appropriate subjects. The future regulatory and commercial success of these product candidates is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources or patient availability to complete the necessary clinical trials for our lead product candidates;
- we may not be able to provide evidence of quality, efficacy and safety for our lead product candidates;
- we do not know the degree to which our lead product candidates will be accepted by patients, the medical community and third-party payors as a therapy for the respective diseases to which they relate, even if approved;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA, EMA or comparable foreign regulatory bodies for marketing approval, and modifications to the design of our clinical trials could delay their enrollment, commencement or completion;
- subjects in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to our lead product candidates;
- subjects in clinical trials undertaken by licensees under a license we grant of certain intellectual property related to our NAV Technology Platform (our NAV Technology Licensees), or undertaken by others using AAV, may die or suffer other adverse effects for reasons that may or may not be related to our NAV Technology Platform or AAV;
- certain patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes;
- we may not successfully establish commercial manufacturing capabilities;
- if approved for treatment of the expected conditions, our lead product candidates will likely compete with other treatments then available, including the off-label use of products already approved for marketing and other therapies currently available or which may be developed;
- our products and products developed by our NAV Technology Licensees may not maintain a continued acceptable safety profile following regulatory approval;
- we may not maintain compliance with post-approval regulation and other requirements; and
- we may not be able to obtain, maintain or enforce our rights under our licensed patents and other intellectual property rights.

Of the large number of biologics and drugs in development in the biopharmaceutical industry, only a small percentage result in the submission of a Biologics License Application (BLA) to the FDA or marketing authorization application (MAA) to the EMA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market our lead product candidates, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that our lead product candidates will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, our lead product candidates, we may not be able to generate sufficient revenue to continue our business.

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

The success of our business depends in large part upon our ability to identify, develop and commercialize products based on our NAV Technology Platform. We have a limited number of clinical programs and our research programs may fail to identify other potential product candidates for clinical development for various reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or for multiple programs, which would materially harm our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

We have limited clinical results for our product candidates and success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.

Gene therapy development has inherent risks. Our lead product candidates have limited clinical and preclinical results and we may experience unexpected results in the future. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates containing our proprietary vectors are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including our lead product candidates, may not have favorable results in later clinical trials, if any, or receive regulatory approval. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations that may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could materially harm our business, financial condition, results of operations and prospects.

Because we are developing product candidates for the treatment of certain diseases in which there is little clinical experience and we are using new endpoints or methodologies, there is increased risk that the FDA, the EMA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

During the FDA review process, we will need to identify success criteria and endpoints such that the FDA will be able to determine the clinical efficacy and safety profile of our product candidates. As we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results (reflecting a tangible benefit to patients). In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance. Further, even if we do achieve the pre-specified criteria, we may produce results that are unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. The EMA and other regulatory authorities in the European Union and other countries may make similar comments with respect to these endpoints and data.

The results from our preclinical studies or clinical trials for our product candidates may not support as broad a marketing approval as we seek, and the FDA, the EMA or other regulatory authorities may require us to conduct additional clinical trials or evaluate subjects for an additional follow-up period.

While we believe our product candidates should be applicable for the treatment of patients with certain conditions, the results from our preclinical and planned clinical trials may not support as broad of a marketing approval as we seek. Even if we obtain regulatory approval for our product candidates, we may be required by the FDA, the EMA or other regulatory bodies to conduct additional clinical trials to support approval of our product candidates for patients diagnosed with different mutations of the respective diseases to which our product candidates relate. This could result in our experiencing significant increases in costs and substantial delays in obtaining, or never obtaining, marketing approval for our product candidates to treat patients. The inability to market our product candidates to treat patients for the intended indications would materially harm our business, financial condition, results of operations and prospects.

We may find it difficult to enroll patients in clinical trials, and this could delay or prevent us from proceeding with clinical trials of our product candidates.

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 planned clinical trials in a timely manner. Patient enrollment and trial completion is affected by factors including:

- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of gene therapy-based approaches to treatment of diseases;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- need and length of time required to discontinue other potential treatment options;
- availability of genetic testing for potential patients;
- proximity and availability of clinical trial sites for prospective subjects;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

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

We may encounter substantial delays in our planned clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive, time-consuming and uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely commencement and completion of preclinical and clinical development include:

- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board or independent Ethics Committee approval at each clinical trial site;
- delays in recruiting suitable subjects to participate in our clinical trials;
- imposition of a clinical hold by regulatory authorities, including as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA good clinical practice (GCP), or applicable regulatory guidelines in the European Union and other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;

- clinical trial sites or subjects 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 in trials of the same class of agents conducted by other sponsors; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

In the fourth quarter of 2019, we were informed by the FDA that the IND for our Phase I/IIa trial for the treatment of wet AMD was placed on a partial clinical hold while the FDA assessed aspects of certain third-party commercially available devices that are used for the subretinal delivery of RGX-314. The FDA subsequently removed the partial clinical hold after reviewing additional information that we provided. The partial clinical hold was not related to our gene therapy candidate and the hold was removed without requiring modification to the surgical delivery system being used in the trial. The imposition of a clinical hold by regulatory authorities may hinder us from achieving our projected development goals for our product candidates in the time frames we have announced, or at all. Any failure or significant delay in completing clinical trials for our product candidates would adversely affect our ability to obtain regulatory approval and our commercial prospects and ability to generate product revenue will be diminished.

Any inability to successfully complete research studies, preclinical and clinical development 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 our product candidates, we may need to conduct additional studies 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 our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

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

- be delayed in obtaining marketing approval for our 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 or other requirements;
- have regulatory authorities withdraw, vary or suspend their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our NAV Technology Platform, our product candidates or NAV Technology Licensees' product candidates, and the process for administering such product candidates may cause undesirable side effects or have other properties that could delay or prevent regulatory approval of product candidates, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia in trials using lentivirus vectors and death seen in other trials using adenovirus vectors. While new recombinant vectors have been designed to reduce these side effects, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the 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 the genetic material. Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration which could substantially limit the effectiveness of the treatment. In previous clinical trials involving AAV vectors for

gene therapy, some subjects experienced the development of a T-cell response, whereby after the vector is within the target cell, the cellular immune response system triggers the removal of transduced cells by activated T-cells. Similarly, a T-cell response may be the cause of the transaminase elevations that have been observed in the RGX-501 trial. In addition to side effects caused by product candidates, the administration process or related procedures also can cause adverse side effects. If any such adverse events occur in our or third party trials, our clinical trials could be suspended or terminated.

As a result of these concerns, we may decide, or the FDA, the European Commission, the EMA or other regulatory authorities could order us, to halt, delay or amend preclinical development or clinical development of our product candidates or we may be unable to receive regulatory approval of our product candidates for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, 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 of our product candidates, 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.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy (REMS) and other regulatory authorities could impose other specific obligations as a condition of approval to ensure that the benefits of our product candidates outweigh their risks, which could delay approval of our product candidates. A REMS may include, among other things, a medication guide outlining the risks of the product for distribution to patients; a communication plan to health care practitioners or patients; and elements to assure safe use, which can severely restrict the distribution of a product by, for example, requiring that health care providers receive particular training and obtain special certification prior to prescribing and dispensing the product, limiting the healthcare settings in which the product may be dispensed, and subjecting patients to monitoring and enrollment in a registry. If the FDA requires us to adopt a REMS for our products and we are unable to comply with its requirements, the FDA may deem our products to be misbranded and we may be subject to civil money penalties. The European Commission, the EMA and other regulatory authorities may, following grant of marketing authorization in their territory, impose similar obligations.

Any of these events could prevent us from achieving or maintaining market acceptance of our NAV Technology Platform and our product candidates and could materially harm our business, prospects, financial condition and results of operations.

We may be unable to obtain orphan drug designation or exclusivity for some product candidates. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Food, Drug and Cosmetic Act as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, following the opinion of the EMA's Committee for Orphan Medicinal Products, the European Commission grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

Generally, if a product candidate with an orphan drug designation 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 European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the United States can be extended by six months if the BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. 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 or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency 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 patients with the rare disease or condition.

If we request orphan drug designation for any of our product candidates, there can be no assurances that the FDA or the European Commission will grant any of our product candidates such designation. Additionally, the designation of any of our product candidates as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

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 and the approval may be for a narrower indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities 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 on additional government regulation from future legislation or administrative action or based on changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially harm our business, financial condition, results of operations and prospects.

Further, the regulatory authorities may require concurrent approval or the CE mark (a mandatory conformity assessment marking for certain products sold within the European Economic Area (the EEA)) of a companion diagnostic device, since it may be necessary to use FDA-cleared or FDA-approved, or CE-marked, diagnostic tests or diagnostic tests approved by other comparable foreign regulatory authorities to diagnose patients or to assure the safe and effective use of our product candidates in trial subjects. FDA refers to such tests as *in vitro* companion diagnostic devices. The FDA has articulated a policy position that, when safe and effective use of a therapeutic product depends on a diagnostic device, the FDA generally will require approval or clearance of the companion diagnostic device at the same time that FDA approves the therapeutic product. The FDA's guidance allows for two exceptions to the general rule of concurrent drug/device approval, namely, when the therapeutic product is intended to treat serious and life-threatening conditions for which no alternative exists, and when a serious safety issue arises for an approved therapeutic agent, and no FDA-cleared or FDA-approved companion diagnostic test is yet available. It is unclear how the FDA will apply this policy to our current or future gene therapy product candidates. Should the FDA deem genetic tests used for diagnosing patients for our therapies to be *in vitro* companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval of a BLA for our product candidates.

In the European Union, companion diagnostics are subject to the European Union Directive on *in vitro* diagnostic medical devices and its implementation in the European Union Member States. Recently revised European Union laws on *in vitro* diagnostics will apply beginning in 2022 and provide stricter requirements for *in vitro* diagnostic medical devices and impose additional obligations on manufacturers of *in vitro* diagnostic medical devices that may impact the development and authorization of our product candidates in the European Union. For example, the new regulation extends the requirement for performance assessment procedures and requires greater involvement of notified bodies in the development of *in vitro* diagnostic medical devices. This may result in additional regulatory and premarket requirements to market new *in vitro* diagnostic medical devices. Companies producing *in vitro*

diagnostic medical devices will be required to have a responsible person to oversee regulatory compliance. In addition, the new regulation introduces risk classification of *in vitro* diagnostic medical devices and significantly increases the number of products that will be subject to stricter regulation. It also introduces the requirement to involve a notified body in the conformity assessment procedure.

We face significant competition in an environment of rapid technological change and there is a possibility that our competitors may achieve regulatory approval before us or develop products that are safer, less expensive or more convenient or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

We are aware of a number of companies focused on developing gene therapies in various indications, as well as a number of companies addressing other methods for modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly or earlier 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 our product candidates against those of competitors. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and harm our business.

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. We intend to submit a marketing authorization application to EMA for approval of our product candidates by the European Commission in the European Union. However, obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. Additionally, the approval procedures in the United Kingdom (UK) for our product candidates may be uncertain following the UK's exit from the European Union.

Even if a product candidate is approved, the FDA or the European Commission, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the European Union also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects will be harmed.

Risks Related to Our Financial Position

We have incurred cumulative net losses and have had few profitable quarters since inception. We expect to normally incur losses for the foreseeable future and may never again achieve or maintain profitability.

Since inception, we have incurred cumulative net losses. We have historically financed our operations primarily through private and public offerings of our equity securities and licensing rights to our NAV Technology Platform. We have devoted substantially all of our efforts to licensing our NAV Technology Platform and to research and development, including preclinical and clinical development of our product candidates, as well as to building out our team. We expect that it could be several years, if ever, before we commercialize a product candidate. We license certain intellectual property related to our NAV Technology Platform to our NAV Technology Licensees. Our NAV Technology Licensees have multiple preclinical studies and clinical trials in progress. However, only one gene therapy product based on such licensing program, Novartis AG's Zolgensma, has been approved or commercialized. Other than revenue in connection with sales of Zolgensma, we expect to generate only limited revenue, if any, in the near term from our current NAV Technology Licensees and any future NAV Technology Licensees. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:

- further develop our licensing activities and NAV Technology Platform;
- continue our research studies and preclinical and clinical development of our product candidates, including our lead product candidates;
- initiate additional preclinical studies and clinical trials for our lead product candidates and future product candidates, if any;
- initiate additional activities relating to manufacturing, including building out additional laboratory and manufacturing capacity;
- seek to identify additional product candidates;
- prepare our BLA and MAA for our lead product candidates and seek marketing approvals for any of our other product candidates that successfully complete clinical trials, if any;
- expand our medical affairs efforts;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval, if any;
- maintain, expand and protect our intellectual property portfolio; and
- acquire or in-license other product candidates and technologies.

For us to become profitable, we and our NAV Technology Licensees must develop and commercialize product candidates with significant market potential. This will require us and our NAV Technology Licensees to be successful in a range of business challenges, including expansion of the licensing of our NAV Technology Platform, completing preclinical studies of product candidates, commencing and completing clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are sufficient to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

We may need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our licensing activities, product development efforts or other operations.

We expect to require substantial future capital in order to complete research studies, preclinical and clinical development for our current product candidates and any future product candidates, and potentially commercialize these product candidates. We expect our spending levels to increase in connection with our preclinical and clinical trials of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our licensing activities, our research and development programs or other operations.

Our operations have consumed significant amounts of cash since inception. Our future capital requirements will depend on many factors, including:

- the timing of enrollment, commencement and completion of our clinical trials;
- the results of our clinical trials;
- the results of our preclinical studies for our product candidates and any subsequent clinical trials;
- our planned expansion of the licensing of our NAV Technology Platform;
- the scope, progress, results and costs of drug discovery, laboratory testing, preclinical development and clinical trials for our product candidates;
- the costs associated with building out additional laboratory and manufacturing capacity;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future product sales, medical affairs, marketing, manufacturing and distribution activities for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- revenue received from commercial sales of Zolgensma and other revenue, if any, received in connection with commercial sales of our NAV Technology Licensees' products, should any of their product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- our current licensing agreements or collaborations remaining in effect;
- our ability to establish and maintain additional licensing agreements or collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Many of these factors are outside of our control. 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 regulatory and marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, and any commercial milestones or royalty payments under our licensing agreements, will be derived from or based on sales of products that may not be commercially available for many years, if at all. In addition, revenue from our NAV Technology Platform licensing is dependent in part on the clinical and commercial success of our licensing partners. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

The issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline. Adequate additional financing may not be available to us on acceptable terms, or at all. We also could be required to seek funds through arrangements with partners or otherwise that may require us to relinquish rights to our intellectual property, our product candidates or otherwise agree to terms unfavorable to us.

We may not successfully expand our licensing activities.

Our ability to generate revenue from our NAV Technology Platform licensing depends on the acceptance by third parties of our NAV Technology Platform as their primary gene therapy technology and our ability to market and license our technology platform. Our ability to generate future revenues from our NAV Technology Platform licensing depends on many factors, including:

- our NAV Technology Licensees successfully developing and commercializing gene therapy products using our NAV Technology Platform, including the commercialization of Zolgensma;
- obtaining and maintaining market acceptance of our NAV Technology Platform as a primary gene therapy technology;
- maintaining our licensing agreements with our licensor partners, including GlaxoSmithKline LLC (GSK) and the University of Pennsylvania (Penn);
- addressing any competing technological and market developments;

- implementing additional internal systems and infrastructure, as needed;
- negotiating favorable terms in any licensing or other arrangements into which we may enter and performing our obligations in such agreements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- avoiding and defending against third-party interference, infringement and other intellectual property related claims.

Although we have generated significant revenues from licensing our NAV Technology Platform, we have never generated revenue from sales of our product candidates.

We have generated significant revenues from licensing our NAV Technology Platform, including sublicense fees, milestone payments and royalties on net sales of a licensed product, Zolgensma. However, our ability to generate revenue from sales of our internal product candidates will depend on our ability, alone or with partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates.

Our ability to generate future revenues from sales of our product candidates and in connection with sales of our NAV Technology Licensees' products depends heavily on our, and our NAV Technology Licensees', success in:

- completing research studies and preclinical and clinical development of product candidates and identifying new gene therapy product candidates;
- obtaining regulatory and marketing approvals for product candidates for which clinical trials are completed;
- commercializing product candidates for which regulatory and marketing approval is obtained by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we or our NAV Technology Licensees may enter and performing our obligations in such collaborations;
- qualifying for adequate coverage and reimbursement by government and third-party payors for product candidates;
- maintaining and enhancing a sustainable, scalable, reproducible and transferable manufacturing process for our vectors and product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for product candidates, if approved;
- obtaining market acceptance of product candidates as a viable treatment option;
- competing effectively when other companies may develop products that are priced lower, reimbursed more favorably by government or other third-party payors, safer, more effective or more convenient to use than our products, if any, or our NAV Technology Licensees' products;
- implementing additional internal systems and infrastructure, as needed;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding and defending against third-party interference, infringement and other intellectual property related claims; and
- attracting, hiring and retaining qualified personnel.

Many of these factors as they relate to our NAV Technology Licensees' products, including Zolgensma, will be outside our control, and future revenues in connection with sales of such products may be precluded or limited by any of these factors.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from sales of any of our product candidates or in connection with sales of any of our NAV Technology Licensees' products, we may not become profitable and may need to obtain additional funding to continue operations.

We currently hold, and in the future may acquire, material equity interests in collaborators, partners or NAV Technology Licensees, and we are exposed to the volatility, liquidity and other risks inherent in holding such equity interests.

We own common stock of Prevail Therapeutics Inc. (Prevail), a publicly listed company (the Prevail Shares). We originally acquired the securities as consideration for a commercial license to the NAV Technology Platform granted to Prevail in August 2017. Following Prevail's initial public offering in June 2019, the securities were reclassified from non-marketable equity securities without a readily determinable fair value to marketable securities and are measured at fair value. The fair value of the Prevail Shares is subject to fluctuation in the future due to the volatility of the stock market, changes in general economic conditions, and the performance of Prevail. We will recognize all changes in the fair value of the Prevail Shares (whether realized or unrealized) as gains or losses in our financial statements, which introduces volatility into our financial performance that is not associated with the results of our business operations. Significant declines in the fair value of the Prevail Shares would cause significant declines in our reported income for the corresponding period.

While there is an established trading market for Prevail's common stock, there are limitations on our ability to dispose of the Prevail Shares, should we wish to sell all or a portion of the Prevail Shares. We may be subject to restrictions on our ability to transfer the Prevail Shares under applicable securities laws. Furthermore, if we sell some or all of the Prevail Shares, there can be no assurance that we will be able to sell them at prices equivalent to the value of the Prevail Shares that we have reported in our financial statements, and we may be forced to sell them at significantly lower prices.

We may acquire equity interests in other collaborators, partners or NAV Technology Licensees in the future, including as consideration for commercial licenses to the NAV Technology Platform. In these instances, we would be exposed to volatility, liquidity and other risks associated with acquiring equity interest in other companies. We evaluate prospective collaborators, partners and NAV Technology Licensees and the potential value of their equity based on a variety of factors. The process by which we obtain equity interests in our collaborators, partners and NAV Technology Licensees and the factors we consider in deciding whether to acquire, hold or dispose of these equity positions may differ significantly from those that an independent investor would consider when purchasing equity interests in the relevant entity. One significant factor we may consider would be our expectation as to the success of our efforts to assist the entity in developing products enabled by our technologies.

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.

Our company was formed in July 2008. Our operations to date have predominantly focused on organizing and staffing our company, business planning, raising capital, acquiring our technology, administering and expanding our NAV Technology Platform sublicensing, identifying potential product candidates, undertaking research, preclinical studies and clinical trials of our product candidates and establishing licensing arrangements and collaborations. We have not yet fully demonstrated the ability to continue expansion of our NAV Technology Platform sublicensing efforts, complete and report clinical trials of our product candidates, obtain marketing approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a rapidly developing business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We have been transitioning from a company with a licensing and research focus to a company that is also capable of supporting clinical development activities and we may need to transition to supporting commercial activities in the future. We may not be successful in these transitions.

Changes in U.S. federal, state and local or foreign tax laws, interpretations of existing tax laws, or adverse determinations by tax authorities, could increase our tax burden or otherwise adversely affect our financial condition or results of operations.

We have incurred substantial net losses since inception and expect to normally incur losses for the foreseeable future. Under the Internal Revenue Code of 1986, as amended (the Code), we can carry forward our net operating losses (NOLs) and other unused tax attributes, such as tax credits, to offset our future taxable income, if any, until such NOLs or other tax attributes are used or expire. If we undergo an "ownership change," generally defined as a greater than 50% change by value in our equity ownership over a three-year period, the Code would limit our ability to use carryovers of our pre-ownership change NOLs, tax credits and certain other tax attributes to reduce our tax liability for periods after the ownership change. Therefore, an ownership change could result in increased U.S. tax liability for us if we generate taxable income in a future period.

The Tax Cuts and Jobs Act of 2017 (the TCJA) significantly reformed the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for NOLs to 80% of current year taxable income, elimination of NOL carrybacks, one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain significant exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modification or repeal of many business deductions and credits, including the orphan drug tax credit. Our business and financial condition could be adversely affected by the TCJA. In particular, if we have taxable income in any year going forward, we may be required to pay significantly higher taxes due to the TCJA's limitation of the deduction for NOLs and elimination of NOL carrybacks, as described above. Additionally, the impact of the TCJA on our securityholders could be adverse. Prospective investors should consult with their legal and tax advisors with respect to the TCJA and the potential tax consequences of investing in or holding our securities.

Risks Related to Third Parties

We rely on third parties to conduct certain preclinical research and development activities and aspects of our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the preclinical research and development activities and trials as required, our preclinical and clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.

We do not have the ability to conduct all aspects of our preclinical research and development activities or clinical trials ourselves. We are dependent on third parties to conduct certain aspects of our clinical trials and, therefore, the timing of the initiation and completion of these trials may be controlled by such third parties and may occur on substantially different timing from our estimates. Specifically, we rely on third parties to conduct a portion of our preclinical research and development activities and we may also rely on CROs, medical institutions, clinical investigators, consultants or other third parties to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. A loss or deterioration of our relationships with such third parties or the principal investigators for our preclinical and clinical programs could materially harm our business.

There is no guarantee that any third party on which we rely for our preclinical research and development activities and the administration and conduct of our clinical trials will devote adequate time and resources to such activities or trials or perform as contractually required. If any such third party fails to meet expected deadlines, fails to adhere to our preclinical or clinical protocols or otherwise performs in a substandard manner, our preclinical programs and clinical trials may be extended, delayed, or terminated, which could materially harm our business. Additionally, if any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. Furthermore, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the integrity of the data generated at the applicable clinical trial site may be jeopardized, which could result in substantial delays in our clinical trials and materially harm our business.

We have in the past, and in the future may, enter into licensing agreements or collaborations with third parties licensing parts of our NAV Technology Platform for the development of product candidates. If these licensing arrangements or collaborations are not successful, our business could be harmed.

We have entered into agreements involving the licensing of parts of our NAV Technology Platform and relating to the development and commercialization of certain product candidates and plan to enter into additional licensing agreements or collaborations in the future. We have limited control over the amount and timing of resources that our current and future licensees and collaborators, including our NAV Technology Licensees, dedicate to the development or commercialization of product candidates or of products utilizing licensed components of our NAV Technology Platform. Our ability to generate revenues from these arrangements will depend on our and our licensees' and collaborators' abilities to successfully perform the functions assigned to each of us in these arrangements. In addition, our licensees and collaborators have the ability to abandon research or development projects and terminate applicable agreements. Moreover, an unsuccessful outcome in any clinical trial for which our licensee or collaborator is responsible could be harmful to the public perception and prospects of our NAV Technology Platform or product candidates.

Any current or future licensing agreements or future collaborations we enter into may pose additional risks, including the following:

- subjects in clinical trials undertaken by licensees or future collaborators, including our NAV Technology Licensees, may suffer adverse effects, including death;
- licensees or collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the licensees' or collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- licensees or collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the licensees or 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;
- product candidates developed in collaboration with us may be viewed by our licensees or collaborators as competitive with their own product candidates or products, which may cause licensees or collaborators to cease to devote resources to the commercialization of our product candidates;
- a licensee or collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;
- licensees or collaborators may breach their reporting, payment, intellectual property or other obligations to us, which could prevent us from complying with our contractual obligations to GSK and Penn;
- disagreements with licensees or collaborators, including disagreements over intellectual property and other proprietary rights, payment obligations, contract interpretation or the preferred course of development of any product candidates, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may result in litigation or arbitration, any of which would be time-consuming and expensive and could potentially lessen the value of such agreements and collaborations;
- licensees or collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of our other rights to intellectual property developed pursuant to our licensing agreements or collaborations;
- licensees or collaborators may infringe or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- licensing agreements or collaborations may be terminated for the convenience of the licensee or collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our licensing agreements or collaborations do not result in the successful development and commercialization of products, or if one of our licensees or collaborators terminates its agreement with us, we may not receive any future milestone or royalty payments, as applicable, under the license agreement or collaboration. If we do not receive the payments we expect under these agreements, our development of product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our licensees or collaborators terminates its agreement with us, we may find it more difficult to attract new licensees or collaborators and the perception of us in the business and financial communities could be harmed. Each of our licensees and collaborators is subject to similar risks with respect to product development, regulatory approval and commercialization, and any such risk could result in its business being harmed, which could adversely affect our collaboration.

We may in the future decide to partner or collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates. 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 licensing agreement or 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 a variety of factors. If we license rights to product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate the licensed product candidates with our existing operations.

We may not be successful in finding strategic collaborators for continuing development of certain of our product candidates or successfully commercializing our product candidates.

We may seek to establish strategic partnerships for developing and/or commercializing certain of our product candidates, due to capital costs required to develop the product candidates or manufacturing constraints. We may not be successful in our efforts to establish such a strategic partnership or other alternative arrangements for our product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy or market opportunity. In addition, we may be restricted under existing collaboration agreements from entering into future agreements with potential collaborators. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

If we are unable to reach agreements with suitable licensees or collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program, delay its potential commercialization, reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates and our business, financial condition, results of operations and prospects may be materially harmed.

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

Because we rely on third parties, including contractors, to research, develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, these provisions may be breached, and the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may materially harm our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we collaborate with, or may collaborate with in the future, will sometimes be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and harm our business.

Risks Related to Manufacturing

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

We currently have development, manufacturing and testing agreements with third parties to manufacture supplies of our product candidates, in addition to our internal manufacturing laboratory. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, a decline in stability of a product that reduces its shelf life, natural disasters, disruption in utility services, human error or disruptions in the operations of suppliers.

Our product candidates require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of biologics such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that may not be detected in standard release testing, which could result in lot failures, product recalls, declines in stability, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable foreign standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot or batch until the competent authority 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/batch failures or product recalls. Lot/batch failures or product recalls could cause us to delay clinical trials or product launches which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

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

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

Delays in obtaining regulatory approval of our manufacturing process or disruptions in our manufacturing process, including the development of our current good manufacturing practice (cGMP) production facility, may delay or disrupt our commercialization efforts.

Before we can begin to commercially manufacture our product candidates in third-party or our own facilities, we must obtain regulatory approval from the FDA, which includes a review of the manufacturing process and facility. A manufacturing authorization must also be obtained from the appropriate European Union Member State regulatory authorities and may be required by other foreign regulatory authorities. The timeframe required to obtain such approval or authorization is uncertain. In order to obtain approval, we will need to ensure that all of our processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors, contract laboratories or suppliers. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

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

We currently plan to have some of the material manufactured for our planned preclinical and clinical programs by third parties. We currently rely, and expect to continue to rely, on third parties for the production of our preclinical study and planned clinical trial materials and, therefore, we can control only certain aspects of their activities.

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

- reduced control for certain aspects of manufacturing activities;
- termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us;
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of, or legal or regulatory actions against, the manufacturer or service provider;
- reduced capacity of our third-party manufacturers and service providers caused by increased demand by their other customers;
- discovery of data integrity issues with our third-party manufacturers and service providers which directly or indirectly impact our ability to use our product candidates; and
- legal or regulatory actions against our third-party manufacturers and service providers which adversely affect our ability to use our product candidates.

FDA, EMA or other regulatory authority action could include injunction, recall, seizure or total or partial suspension of product manufacture or manufacturing authorization. Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future product candidates, and therefore may cause our business, financial condition, results of operations and prospects to be materially harmed.

Failure to comply with ongoing manufacturing regulatory requirements could cause us to suspend production or put in place costly or time-consuming remedial measures.

Regulatory authorities may, at any time following approval of a product for sale, audit the manufacturing facilities for such product. If any such inspection or audit identifies a failure to comply with applicable regulations, or if a violation of product specifications or applicable regulations occurs independent of such an inspection or audit, the relevant regulatory authority may require remedial measures that may be costly or time-consuming to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a manufacturing facility. Any such remedial measures imposed upon us or any of our third-party manufacturers could materially harm our business, financial condition, results of operations and prospects.

If we or any of our third party-manufacturers fail to comply with applicable cGMP regulations, regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be materially harmed.

Additionally, if supply from a manufacturing facility is interrupted, there could be a significant disruption in commercial supply of our products. An alternative manufacturer would need to be qualified, through a supplement to its regulatory filing, which could result in further delay. Regulatory authorities also may require additional trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and could result in a delay in our desired clinical and commercial timelines.

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

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

Some of the resources, raw materials and components required in our manufacturing or research and development processes are derived from biologic sources, and we normally rely on suppliers to provide such resources, raw materials and components. These may be difficult to procure and subject to contamination or recall. Certain resources, raw materials and components, especially those that are specifically catered to the gene therapy industry, may become unavailable to us in sufficient quantities from time to time due to increased demand.

In December 2019, a novel strain of coronavirus was reported to have surfaced in Wuhan, China. The extent to which the coronavirus impacts our ability to procure resources, raw materials or components necessary for our research studies or preclinical or clinical development will depend on unpredictable future developments, including new information that may emerge about the severity of the coronavirus and the actions to contain the coronavirus or treat its effects, among others.

A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates may be beyond our control and 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.

Risks Related to the Commercialization of Our Product Candidates

If we are unable to establish sales, medical affairs and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may be unable to generate any product revenue.

We currently have no products to sell and therefore no product sales and marketing organization. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any products we may develop will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may enter into collaborations regarding one or more of our product candidates with other entities to utilize their marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current licensees or future licensees or collaborators do not commit sufficient resources to commercialize our products, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded medical affairs, marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our potential products. If any of our product candidates is approved but fails to achieve market acceptance among physicians, patients or third-party payors, we will not be able to generate significant revenues from such product, which could materially harm our business, financial condition, results of operations and prospects.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include, but are not limited to, the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings, the announcement of results from scientific studies or clinical trials and the announcement of additional product candidates. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

Our gene therapy approach utilizes vectors derived from viruses which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product candidates and harm our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with only a few gene therapy products approved to date in the United States, the European Union or elsewhere. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product candidates, prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would harm our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases

of leukemia and death seen in other trials using other vectors. Serious adverse events related to clinical trials we conduct, clinical trials involving our NAV Technology Platform conducted by others or any gene therapy products, even if such adverse events are not ultimately attributable to the relevant product candidates or products, may result in increased government 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.

Even if we receive regulatory approval, we still may not be able to successfully commercialize our lead product candidates or any future product candidate, and the revenue that we generate from any approved product's sales, if any, could be limited.

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. From time to time, public sentiment may be more adverse to commercialization of gene therapy as a therapeutic technique. Even with the requisite approvals from the FDA, the EMA and other regulatory authorities, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA, European Commission, or other comparable foreign regulatory authority-approved labeling;
- acceptance of a new formulation by health care providers and their patients;
- the prevalence and severity of any adverse effects;
- new procedures or methods of treatment that may be more effective in treating or may reduce the conditions which our products are intended to treat;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain and maintain sufficient third-party coverage and reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- unfavorable publicity relating to product candidates or gene therapy generally; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or reimbursement.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payors on the benefits of our lead product candidates or any future product candidates may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidates will depend on our ability to manufacture our products, differentiate our products from competing products and defend and enforce our intellectual property rights relating to our products. Additionally, if the market opportunities for our lead product candidates or any future product candidates are smaller than we believe they are, our product revenues may be harmed and our business may suffer.

We focus our research and product development on treatments for severe genetic and orphan diseases. Our understanding 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 our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would harm our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive any products we develop less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions such as the conditions our lead product candidates are intended to treat, will likely diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell death. Lastly, certain patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.

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

We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the prices 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 payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products, including potential one-time gene therapies. In the United States, third-party payors, including government payors such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors and government payors develop their coverage and reimbursement policies. It is difficult to predict what the Centers for Medicare & Medicaid Services (CMS), the agency responsible for administering the Medicare program, will decide with respect to coverage and reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these types of products. We cannot be assured that Medicare or Medicaid will cover any of our products, if approved, or provide reimbursement at adequate levels to realize a sufficient return on our investment. In addition, government regulators and legislative bodies in the United States are considering numerous proposals that may result in limitations on the prices at which we could charge customers for our products if we have products that are approved for sale. At this time, we are unable to predict how these potential legislative changes might affect our business. Moreover, reimbursement agencies in the European Union may be more conservative than CMS. It is difficult to predict what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

- Outside the United States, international operations generally are subject to extensive government price controls and other market regulations, and increasing emphasis on cost-containment initiatives in the European Union and other countries may put pricing pressure on us. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. It also can take a significant amount of time after approval of a product to secure pricing and reimbursement for such product in many countries outside the United States. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medical 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 our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the reimbursement in the United States and may be insufficient to generate commercially reasonable product revenues.

Moreover, increasing efforts by government and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. Payors increasingly are considering new metrics as the basis for reimbursement rates, and the existing data for reimbursement based on some of these metrics is limited. Therefore, it may be difficult to project the impact of these evolving reimbursement metrics on the willingness of payors to cover candidate products that we or our partners are able to commercialize. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes.

Additionally, our lead product candidates are designed to provide therapeutic benefit after a single administration and, therefore, the pricing and reimbursement of a single administration of our lead product candidates, if approved, must be adequate to support our commercial infrastructure. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be harmed. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and limit our ability to market or sell our products.

If we obtain approval to commercialize our product candidates outside of the United States, in particular in the European Union or United Kingdom, a variety of risks associated with international operations could materially harm our business.

We expect that we will be subject to additional risks in commercializing our product candidates outside the United States, any of which could materially harm our business, which could include:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, natural disasters, including earthquakes, floods and fires, or disease pandemics.

Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for any of our product candidates, if approved, which would adversely affect our revenue and results of operations.

We expect that coverage and reimbursement of drugs and biologics may be increasingly restricted in the United States and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. In particular, pricing by biopharmaceutical companies recently has come under increased scrutiny and continues to be subject to intense political and public debate in the United States and abroad. Government and private third-party payors have proposed health care reforms and cost reductions of drugs and biologics. A number of federal and state proposals to control the cost of health care have been made in the United States. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state bills designed to, among other things, bring more transparency to pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies. In some international markets, the government controls drug and biologic pricing, which can affect profitability.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation or negative publicity related to the pricing of drugs and biologics generally could restrict the amount that we are able to charge for our future products, if any, which could adversely affect our revenue and results of operations.

Risks Related to Our Business Operations

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity or for which there is a greater likelihood of success.

The success of our business depends upon our ability to identify, develop and commercialize product candidates based on our NAV Technology Platform. Research programs to identify new product candidates require substantial technical, financial and human resources. Although certain of our product candidates are currently in research studies or preclinical development, we may fail to identify potential product candidates for clinical development for several reasons. For example, our research may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects, may be commercially impracticable to manufacture or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate, which could materially harm our business, financial condition, results of operations and prospects.

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

We are highly dependent on members of our executive team, the loss of any of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. We currently do not have "key person" insurance on any of our employees. The loss of the services of one or more of our current employees, consultants and advisors might impede the achievement of our research, development, licensing and commercialization objectives.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel is, and will continue to be, critical to our success. There currently is a shortage of skilled individuals with substantial gene therapy experience, which we believe is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies and academic institutions for individuals with similar skill sets. In addition, failure to succeed in preclinical studies or clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of any of our key executives, employees, consultants or advisors may impede the progress of our research, development, licensing and commercialization objectives and materially harm our business, financial condition, results of operations and prospects.

If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development and licensing activities and, in the longer term, build a sales and marketing infrastructure to support commercialization of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and product candidates requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

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

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with 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 business 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.

Healthcare legislative reform measures may materially harm our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory initiatives regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities or affect our ability to profitably sell any product candidates for which we obtain marketing approval. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (PPACA), was passed. PPACA made major changes in how healthcare is delivered and reimbursed, and increased access to health insurance benefits to the uninsured and underinsured population of the United States.

PPACA, among other things, increased the number of individuals with Medicaid and private insurance coverage, implemented reimbursement policies that tie payment to quality, facilitated the creation of accountable care organizations that may use capitation and other alternative payment methodologies, strengthened enforcement of fraud and abuse laws and encouraged the use of information technology.

Such changes in the regulatory environment may also result in changes to our payor mix that may affect our operations. While PPACA is expected to increase the number of persons with covered health benefits, we cannot accurately estimate the payment rates for any additional persons that are expected to be covered by health benefits. For example, PPACA's expansion of Medicaid coverage could cause patients who otherwise would have selected private healthcare to participate in government sponsored healthcare programs, and Medicaid and other government programs typically reimburse providers at substantially lower rates than private payors. Our revenue may be adversely impacted if states pursue lower rates or cost-containment strategies as a result of any expansion of their existing Medicaid programs to include additional persons, particularly in states experiencing budget deficits. Exchanges created to facilitate coverage for new persons to be covered by health benefits may also place additional pricing pressure on all providers, regardless of payor. The full impact of many of the provisions under PPACA, or the rules adopted under PPACA, is unknown at this time. Furthermore, PPACA may be modified, repealed or replaced with new regulations, and the full impact of any such modification, repeal or replacement is unknown at this time. PPACA and individual provisions thereunder have been challenged in numerous lawsuits. For example, in December 2018, a federal district court in Texas ruled that PPACA is unconstitutional as a result of the passage of the TCJA, which eliminated the individual mandate portion of PPACA. The Fifth Circuit Court of Appeals subsequently upheld the lower court decision. The Supreme Court of the United States (the Supreme Court) declined to hear an appeal on an expedited basis and, therefore, any decision by the Supreme Court on the case would not be expected to occur until 2021 at the earliest. We cannot predict the effect of any potential court decision relating to PPACA or modification, repeal or replacement of PPACA or any other healthcare reform legislation on our business.

Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges, rules regarding fraud and abuse, and enforcement. Continued implementation of PPACA, or the repeal or replacement of PPACA, and the passage of additional laws and regulations may result in the expansion of new programs such as Medicare payment for performance initiatives, and may impact existing government healthcare programs, such as by improving the physician quality reporting system and feedback program.

Other legislative changes have been proposed and adopted in the United States since PPACA was enacted. For example, the Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction, or the Joint Committee, to recommend proposals in spending reductions to Congress. The Joint Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs, including Medicare payments to healthcare providers of up to 2.0% per fiscal year, starting in 2013. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. 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 and other third-party payors will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures and thereby adversely affect our business, financial condition and results of operations.

Various states, such as California, have also taken steps to consider and enact laws or regulations that are intended to increase the visibility of the pricing of biopharmaceutical products with the goal of reducing the prices at which such products can be sold. Because these various actual and proposed legislative changes are intended to operate on a state-by-state level rather than a national one, we cannot predict what the full effect of these legislative activities may be on our business in the future.

Additionally, in the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biologic products that are demonstrated to be "highly similar" or "biosimilar or interchangeable" with an FDA-approved biologic product. This new pathway could allow competitors to reference data from biologic products already approved after 12 years from the time of approval. This could expose us to potential competition by lower-cost biosimilars even if we commercialize a product candidate faster than our competitors.

The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union Member States have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval. Furthermore, healthcare legislative reform measures in countries outside the United States and the European Union may materially delay or restrict our business activities or otherwise materially harm our business.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain the approval of the FDA, the European Commission or other regulatory authorities for any of our product candidates and begin commercializing those products in the United States or outside the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal, state and foreign fraud and abuse laws and regulations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations, and similar laws in foreign jurisdictions. These laws will impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Health Care Program Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. Liability may be established under the federal Anti-Kickback Statute without proving actual knowledge of the statute or specific intent to violate it;
- federal civil and criminal false claims laws and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent. PPACA provides and recent government cases against pharmaceutical and medical device manufacturers support the view that federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes that prohibit a person from knowingly and willfully executing a scheme or from making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and its implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act;

- Other Modifications to HIPAA, published in January 2013, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and health care providers;
- federal transparency laws, including the federal Physician Payment Sunshine Act, that require disclosure of payments and other transfers of value provided 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;
- national laws, industry codes and professional codes of conduct applicable to certain European Union Member States which require payments made to physicians to be publicly disclosed and agreements with physicians to often be the subject of prior notification and approval by the physicians' employer, his or her competent professional organization and/or the regulatory authorities of the individual Member States;
- federal, state and foreign laws relating to the processing, storage and transfer of personal data, including, but not limited to, the California Consumer Privacy Act and the European Union's General Data Protection regulation, which may require us to incur substantial costs or change our business practices with respect to the treatment of personal data; and
- state and foreign law equivalents of each of the above federal laws, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts in certain circumstances, such as specific disease states.

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 health care programs, such as Medicare and Medicaid, imprisonment, reputational harm, public reprimands, third party actions, such as cease and desist letters or injunctions, and the curtailment or restructuring of our operations, any of which could harm our ability to operate our business and our results of operations.

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. Infringement of these laws could result in substantial fines and imprisonment.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit licensing of our NAV Technology Platform or commercialization of any product candidates that we may develop.

We face an inherent risk of product liability exposure related to our licensed NAV Technology Platform and the testing of our product candidates in clinical trials and may face an even greater risk if products utilizing our NAV Technology Platform are commercialized. If we cannot successfully defend ourselves against claims that our technology or product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our technology, including any product candidates that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;
- the inability to license our NAV Technology Platform or commercialize any product candidates that we may develop; and
- injury to our reputation and significant negative media attention.

Although we maintain product liability insurance coverage, this insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will evaluate the need to increase our insurance coverage each time we commence a clinical trial and may from time to time purchase additional coverage for clinical trials. We may need to increase our product liability insurance coverage if we successfully commercialize any product candidates. Insurance coverage is increasingly expensive and 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 we, our development partners, including our NAV Technology Licensees, or our third-party manufacturers or suppliers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could materially harm the success of our business.

We, our development partners, including our NAV Technology Licensees, and our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biologic and radioactive materials. Our operations and the operations of our development partners and third-party manufacturers and suppliers also produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by us, our development partners or our third-party manufacturers or suppliers, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to work-related injuries to our employees, this insurance may not provide adequate coverage against potential liabilities. Although we maintain insurance for claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials, this insurance may not be adequate to cover all liabilities that we may incur in connection with such claims.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair us or our development partners', including our NAV Technology Licensees', research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially harm our business, financial condition, results of operations and prospects.

We and third parties on which we rely may be harmed by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations or the operations of our third parties' manufacturing or supply facilities and materially harm our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. Our third party manufacturing and supply facilities, as well as substantially all of our current supply of product candidates, are located in a small number of geographic locations, and should a natural disaster, power outage or other event occur that affects one of our third party manufacturing or supply facilities, manufacturing or supply delays may result should we need to transfer manufacturing or supply operations to another facility. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could materially harm our business, financial condition, results of operations and prospects.

We are increasingly dependent on information technology systems, infrastructure and data.

We are increasingly dependent upon information technology systems, infrastructure and data. Our computer systems or our business partners' computer systems may be vulnerable to service interruption or destruction, malicious intrusion and random attack. Security breaches pose a risk that sensitive data, including intellectual property, trade secrets or personal information, may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, denial-of service, social engineering and other means to affect service reliability, threaten data confidentiality, integrity and availability and fraudulently obtain funds. Our business partners face similar risks, and a security breach of their systems could adversely affect our security posture. While we continue to invest in data protection and information technology, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our business or financial operations, including our licensing and product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we believe we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business or financial operations, including our licensing and development programs. Unauthorized disclosure of sensitive or confidential patient or employee data, including personally identifiable information, whether through breach of computer systems, systems failure, employee negligence, fraud or misappropriation, or otherwise, or unauthorized access to or through our information systems and networks, whether by our employees or third parties, could result in negative publicity, legal liability and damage to our reputation. Unauthorized disclosure of personally identifiable information could also expose us to sanctions for violations of data privacy laws and regulations around the world, especially since the regulatory environment surrounding data privacy laws are increasingly demanding, with frequent imposition of new and changing requirements. To the extent that any disruption or security breach results in a loss of, or damage to, our trade secrets, data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further licensing of our NAV Technology Platform and development and commercialization of our product candidates could be delayed. For example, the loss of, or damage to, clinical trial data for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Although we have general liability and cybersecurity insurance coverage, our insurance may not cover all claims, continue to be available on reasonable terms or be sufficient in amount to cover one or more large claims; additionally, the insurer may disclaim coverage as to any claim. The successful assertion of one or more large claims against us that exceed or are not covered by our insurance coverage or changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could materially harm our business, financial condition, results of operations and prospects.

Our customers are concentrated and therefore the loss of a significant customer may harm our business.

Our current revenues are derived from a concentrated customer base. Our revenues for the years ended December 31, 2019 and 2018 consisted primarily of license and royalty revenue. Three customers accounted for approximately 92% of our total revenue for the year ended December 31, 2019. Two customers accounted for approximately 97% of our total revenue for the year ended December 31, 2018. We expect future license and royalty revenue to be derived from a limited number of licensees. Future license and royalty revenue is uncertain due to the contingent nature of our licenses granted to third-parties.

Risks Related to Our Intellectual Property

Our rights to license our NAV Technology Platform and to develop and commercialize our product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to license our platform or develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories not included in all of our licenses. For example, under our license agreement with GSK, GSK retained certain exclusive and non-exclusive rights under the patent rights that it licensed from Penn.

Licenses to additional third-party technology that may be required for our licensing or development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could materially harm our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from third parties. For example, under our license agreement with Penn, Penn is entitled to control the preparation, prosecution and maintenance of the patent rights licensed to us. However, if we determine that we desire a greater degree of control over such patent rights, the Penn license agreement provides that Penn will work in good faith with us to enter into an arrangement for such additional control with reimbursement by us of certain expenses. If our licensors fail to maintain such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be impacted. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future.

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

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 license our NAV Technology Platform and commercialize our products and technology may be harmed.

Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary NAV Technology Platform, our product candidates and our manufacturing technology. Our licensors have sought and we intend to seek to protect our proprietary position by filing patent applications in the United States and abroad related to many of our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, certain patents in the field of gene therapy that may have otherwise potentially provided patent protection for certain of our product candidates have expired or will soon expire. In some cases, the work of certain academic researchers in the gene therapy field has entered the public domain, which we believe precludes our ability to obtain patent protection for certain inventions relating to such 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.

We are a party to intellectual property license agreements with GSK and Penn, each of which is important to our business, and other entities and we expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, development and commercialization timelines, milestone payments, royalties and other obligations on us. If we or our licensees fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

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 our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We may not be aware of all third-party intellectual property rights potentially relating to our technology and product candidates. 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 be certain that we were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Even if the patent applications we license or may own in the future do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may avail themselves of safe harbor under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments) to conduct research and clinical trials and may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology, increase our financial or other obligations to our licensors or decrease financial or other obligations of our licensees.

The agreements under which we currently license intellectual property or technology from or to third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, increase what we believe to be our financial or other obligations under the relevant agreement, or decrease what we believe to be the financial or other obligations of our licensee under the relevant agreement, any of which could materially harm our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research, to expand our licensing program or to allow commercialization of our product candidates. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology or product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to redesign our platform technology or to develop or commercialize the affected product candidates, which could materially harm our business. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current platform technology, manufacturing methods, product candidates or future methods or products, resulting in either an injunction prohibiting our licensing, manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In many of our existing license agreements, patent prosecution of our licensed technology is controlled primarily by the licensor, and we are required to reimburse the licensor for certain costs of patent prosecution and maintenance. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. Further, in our license agreements, we could be responsible for bringing actions against any third party for infringing on the patents we have licensed. Certain of our license agreements in which we are the licensee also require us to meet development milestones to maintain the license, including establishing a set timeline for developing and commercializing products and minimum diligence obligations in developing and commercializing the product. 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;
- the extent to which our technology and processes infringe on or otherwise violate intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing and corresponding payment obligations of patent and other intellectual property rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship or ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

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

We currently have rights to intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of intellectual property or other proprietary rights held by third parties, the growth of our business may depend, in part, on our ability to acquire, in-license or use such intellectual property and proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes (and patents for such technology) or other intellectual property rights from third parties that we identify as necessary for our technology platform and product candidates. 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. 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 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. Some of these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration, and our sponsored research agreement entered into with Penn in December 2014 provides that any patentable inventions developed automatically accrue to our existing license with Penn. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate and our business, financial condition, results of operations and prospects could suffer.

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 applications will be due to be paid to the U.S. Patent and Trademark Office (the USPTO) and various patent agencies outside of the United States over the lifetime of our licensed patents and/or applications and any patent rights we may own or license in the future. We may rely on our licensing partners to pay these fees due to non-U.S. patent agencies with respect to our licensed patent rights. The USPTO and various non-U.S. patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms 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 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 materially harm our business.

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

Filing, prosecuting and defending patents on our platform technology or product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. Although our license agreements with Penn and GSK grant us worldwide rights, certain of our in-licensed U.S. patent rights lack corresponding foreign patents or patent applications. For example, under our license agreement with Minnesota, our rights are limited to those countries and territories, including the United States, in which a licensed patent has been issued and is unexpired or a licensed patent application is pending. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, 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 of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Issued patents covering our NAV Technology Platform or our product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court.

If one of our licensing partners or we initiate legal proceedings against a third party to enforce a patent covering our NAV Technology Platform or one of our product candidates, the defendant could counterclaim that the patent covering our product candidate 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 subject-matter eligibility, novelty, non-obviousness, written description or 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, post grant review, *inter partes* review and equivalent 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 our NAV Technology Platform or our product candidates. 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 defendant 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. Such a loss of patent protection could materially harm our business.

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 technology, 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 and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have 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. While we have confidence in these individuals, organizations and systems, agreements or 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.

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

Our commercial success depends, in part, upon our ability to license our NAV Technology Platform, and upon our ability and our NAV Technology Licensees' ability to develop, manufacture, market and sell products and use our proprietary technologies without infringing or otherwise violating the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference proceedings, post grant review and *inter partes* review before the USPTO. 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 materially harm our ability to license our technology platform or commercialize our lead product candidates or any future 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 licensing, developing, manufacturing and marketing our product candidates and 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 licensing, 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 licensing our technology platform or manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could similarly harm our business, financial condition, results of operations and prospects.

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

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement or that our intellectual property is invalid or unenforceable. To counter infringement or unauthorized use claims or to defend against claims of infringement or other intellectual property related claims can be expensive and time consuming. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could materially harm 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 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 and other intellectual property litigation or proceedings could materially harm our ability to compete in the marketplace.

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 personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

The patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and "gene patents" have recently been decided by the Supreme Court. On March 20, 2012, the Supreme Court issued a decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc. (Prometheus), a case involving patent claims directed to a process of measuring a metabolic product in a patient to optimize a drug dosage for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as "administering" or "determining" steps was not enough to transform an otherwise patent-ineligible natural phenomenon into patent-eligible subject matter. On July 3, 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 not patent-eligible subject matter. On June 13, 2013, the Supreme Court issued its decision in Association for Molecular Pathology v. Myriad Genetics, Inc. (Myriad), a case involving patent claims held by Myriad relating to the breast cancer susceptibility genes BRCA1 and BRCA2. Myriad held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent eligible.

The USPTO has issued a number of guidance memoranda to instruct USPTO examiners on the ramifications of the Prometheus and Myriad rulings and the application of the Myriad ruling to natural products and principles including all naturally occurring nucleic acids. The USPTO's guidance may be further updated in view of developments in the case law and in response to public feedback. Patents for certain of our product candidates contain claims related to specific DNA sequences that are naturally occurring and, therefore, could be the subject of future challenges made by third parties. In addition, the recent USPTO guidance could make it impossible for us to pursue similar patent claims in patent applications we may prosecute in the future.

We cannot assure you that our efforts to seek patent protection for our technology and products will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court's decisions in Prometheus and Myriad may have on the ability of life science companies to obtain or enforce patents relating to their products and technologies in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could materially harm our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Moreover, although the Supreme Court has held in Myriad that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or paying to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business, financial condition, results of operations or prospects.

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

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the 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 drug, a method for using it or a method for manufacturing it may be extended. 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. 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, possibly materially.

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

We have registered trademarks with the USPTO, including for the marks "NAV" and "REGENXBIO," as well as for the REGENXBIO logos. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other 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 harmed. 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 and could harm our financial condition or results of operations.

Risks Related to Ownership of Our Common Stock

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

Our stock price is likely to be volatile. In recent years, the stock market in general, and the market for biotechnology or pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares of our common stock at or above the price they paid for their shares. The market price of our common stock could be subject to wide fluctuations in response to various factors, many of which are beyond our control. These factors include those discussed elsewhere in this "Risk Factors" section.

In the past, following periods of volatility in the overall market and the market price of a particular company's securities, securities class action litigation has often been instituted against these companies. This litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert our management's attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

Our operating results may fluctuate substantially, which makes our future operating results difficult to predict and could cause the price of our common stock to fluctuate substantially.

We expect our operating results to be subject to fluctuations. Our net income or loss and other operating results may be affected by numerous factors, including:

- any variations in the level of expenses related to our NAV Technology Platform, lead product candidates or future product candidates and technologies;
- the addition or termination of any clinical trials and the timing and outcomes of clinical trials;
- any regulatory or clinical developments affecting our lead product candidates, any future product candidates or our NAV Technology Licensees' product candidates;
- our execution of any collaborative, licensing or similar arrangements, including with our NAV Technology Licensees, and the timing of any payments we may make or receive under these arrangements;
- changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- the nature and terms of any stock-based compensation grants;
- any intellectual property infringement lawsuits in which we may become involved;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, we believe that comparing our operating results on a period-to-period basis is not necessarily meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of securities or industry analysts or investors for any period. If our operating results fall below the expectations of investors or analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we have provided.

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

We may seek to raise additional capital through public or private equity offerings, debt financings, strategic partnerships, licensing arrangements or other means. We have an effective shelf registration statement on file with the SEC, which could allow us to access capital in a timely manner. To the extent that we raise additional capital by issuing equity securities, the share ownership of existing stockholders will be diluted. Any future debt financing may involve covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments or engage in certain merger, consolidation, or asset sale transactions. In addition, if we seek funds through arrangements with collaborative partners, these arrangements may require us to relinquish rights to some of our technologies or products or otherwise agree to terms unfavorable to us.

Our executive officers, directors and principal stockholders own a significant percentage of our stock and maintain the ability to exert substantial influence over matters subject to stockholder approval.

Our executive officers, directors, holders of more than five percent of our capital stock and their respective affiliates beneficially own a significant percentage of our outstanding capital stock. As a result, these stockholders may be able to exert substantial influence over all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets or other major corporate transaction. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire or result in management of our company with which our public stockholders disagree.

Substantial future sales of shares by existing stockholders, including pursuant to our equity incentive plans, or the perception that such sales may occur, could cause our stock price to decline, even if our business is performing well.

If our existing stockholders, particularly our directors and executive officers and the entities affiliated with our current and former directors, sell substantial amounts of our common stock in the public market, or are perceived by the public market as intending to sell substantial amounts of our common stock, the trading price of our common stock could decline.

Shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended. Additionally, some of our existing stockholders have demand and piggyback rights to require us to register with the SEC up to a certain number of shares of our common stock. If we register these shares of common stock, the stockholders would be able to sell those shares freely in the public market, subject to Rule 144 transfer restrictions applicable to affiliates. We registered 5,057,458 shares of common stock held by certain of our stockholders in an automatic shelf registration statement on Form S-3 filed with the SEC on August 8, 2018. Such stockholders are able to freely trade such shares of common stock.

Furthermore, certain of our employees, directors, officers or affiliates have entered into Rule 10b5-1 plans providing for transactions of our securities from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the securityholder when entering into the plan, without further direction from the securityholder. Accordingly, sales under these plans may occur at any time, including possibly before, simultaneously with, or immediately after significant events involving us. A Rule 10b5-1 plan may be amended or terminated in some circumstances. If any additional shares of our common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. We do not undertake to report the entry into, or the amendment or termination of, any Rule 10b5-1 plans adopted by our employees, directors, officers or affiliates in the future, except to the extent required by law.

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

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

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

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

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

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit the board of directors to establish the number of directors;
- provide that directors may only be removed “for cause”;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and amended and restated bylaws;
- authorize the issuance of “blank check” preferred stock that our board of directors could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- provide that the board of directors is expressly authorized to make, alter or repeal our bylaws; and
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on merger, business combinations and other transactions between us and holders of 15% or more of our common stock.

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Pursuant to our restated certificate of incorporation, 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 does not have jurisdiction, the federal district court for the District of Delaware), will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our restated certificate of incorporation or our amended and restated bylaws or (4) any action asserting a claim governed by the internal affairs doctrine. Additionally, if the subject matter of any action within the scope of the preceding sentence is filed in a court other than a court located with the State of Delaware (a Foreign Action) in the name of any stockholder, such stockholder shall be deemed to have consented to (i) the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to enforce the preceding sentence and (ii) having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the Foreign Action as agent for such stockholder.

The forum selection clause in our restated certificate of incorporation may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us, our directors, officers or other employees. Alternatively, if a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against many companies in the biopharmaceutical industry over the last several years, and proxy advisory firms may recommend changes to our business operations, provisions in our restated certificate of incorporation or amended and restated bylaws, or the composition of our board of directors or its committees. If faced with a proxy contest or other type of stockholder activism, or a proxy advisory firm recommendation that is adverse to a management proposal, we may not be able to respond successfully to the contest or dispute, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by such a contest or dispute involving us or our partners because:

- responding to proxy contests or other actions by activist stockholders, or adverse proxy advisory firm recommendations, can be costly and time-consuming, disrupting operations and diverting the attention of management and employees;
- perceived uncertainties as to future direction may result in the loss of potential acquisitions, collaborations or licensing opportunities, and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals are elected to our board of directors with a specific agenda, it may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

These actions could cause our stock price to decrease and experience periods of increased volatility.

ITEM 1B. *UNRESOLVED STAFF COMMENTS*

None.

ITEM 2. ***PROPERTIES***

Our corporate headquarters are currently located in Rockville, Maryland. We occupy approximately 19,000 square feet of office space at this location under a lease that expires in September 2023, renewable for an additional five-year term. We also occupy approximately 73,000 square feet of office and laboratory space at other locations in Rockville, Maryland, and 15,000 square feet of office space in New York, New York, under leases that expire at various dates through 2027, some of which are renewable for additional years.

In November 2018, we entered into a lease agreement, as amended, for approximately 177,0000 square feet of office, laboratory and manufacturing space in a new facility to be constructed in Rockville, Maryland. The new facility will serve as our future corporate, manufacturing and research headquarters. The initial construction of the new facility is being performed by the landlord and is expected to be completed in 2020, and we expect to make significant additional improvements to the leased premises once construction is completed. The lease expires approximately 16 years from the date the landlord delivers the leased premises to us, subject to certain extension and termination options that we hold under the lease agreement.

We believe that our facilities, including the construction-in-progress for our future corporate, manufacturing and research headquarters, will be adequate to meet our operating needs for the foreseeable future.

ITEM 3. ***LEGAL PROCEEDINGS***

From time to time, we are party to various lawsuits, claims or other legal proceedings that arise in the normal course of our business. We do not believe that we are currently party to any pending legal actions that could reasonably be expected to have a material adverse effect on our business, financial condition, results of operations or cash flows.

ITEM 4. ***MINE SAFETY DISCLOSURES***

Not applicable.

PART II

ITEM 5. *MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES*

Market Information

Our common stock is traded on The Nasdaq Global Select Market under the symbol "RGNX." On February 21, 2020, the last reported sale price for our common stock on The Nasdaq Global Select Market was $52.69 per share.

Stock Performance Graph

The graph set forth below compares the cumulative total stockholder return on our common stock between September 17, 2015 (the date of our initial public offering) and December 31, 2019, with the cumulative total return of (a) the Nasdaq Composite Index (^IXIC) and (b) the Nasdaq Biotechnology Index (^NBI), over the same period. This graph assumes the investment of $100 on September 17, 2015 in our common stock, the Nasdaq Biotechnology Index and the Nasdaq Composite Index and assumes the reinvestment of dividends, if any. The graph assumes our closing sales price on September 17, 2015 of $30.45 per share as the initial value of our common stock and not the initial offering price to the public of $22.00 per share.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock. Information used in the graph was obtained from the Nasdaq Stock Market LLC, a financial data provider and a source believed to be reliable. The Nasdaq Stock Market LLC is not responsible for any errors or omissions in such information.

The following performance graph and related information shall not be deemed "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or the Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

Holders

As of February 21, 2020, there were six holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have not declared or paid any cash dividends on our common stock since our inception. We do not plan to pay dividends in the foreseeable future.

ITEM 6. ***SELECTED FINANCIAL DATA***

The following selected consolidated financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations," the consolidated financial statements and related notes and other financial information included in this Annual Report on Form 10-K.

We derived the consolidated statements of operations data for the years ended December 31, 2019, 2018 and 2017 and the consolidated balance sheet data as of December 31, 2019 and 2018 from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. We derived the consolidated statements of operations data for the years ended December 31, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017, 2016 and 2015 from our historical audited consolidated financial statements that are not included in this Annual Report on Form 10-K. Historical results are not necessarily indicative of the results to be expected in future periods.

	Years Ended December 31,				
	2019 (a)	2018 (a)	2017	2016	2015
	(in thousands, except per share data)				
Consolidated Statements of Operations Data:					
Total revenues	$ 35,233	$ 218,505	$ 10,393	$ 4,589	$ 7,588
Total operating expenses	184,231	130,405	86,278	69,929	30,725
Income (loss) from operations	(148,998)	88,100	(75,885)	(65,340)	(23,137)
Net income (loss)	(94,733)	99,937	(73,169)	(62,967)	(22,811)
Net income (loss) per share:					
Basic	$ (2.58)	$ 2.99	$ (2.45)	$ (2.38)	$ (2.59)
Diluted	$ (2.58)	$ 2.73	$ (2.45)	$ (2.38)	$ (2.59)
Weighted-average common shares outstanding:					
Basic	36,690	33,427	29,878	$ 26,409	$ 9,173
Diluted	36,690	36,648	29,878	$ 26,409	$ 9,173

(a) Effective January 1, 2018, we adopted Accounting Standards Update (ASU) 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in Accounting Standards Codification (ASC) 605, *Revenue Recognition* (Topic 605). The consolidated statements of operations data for the years ended December 31, 2019 and 2018 is presented in accordance with the requirements of Topic 606, while prior period amounts have not been adjusted and, accordingly, may not be comparable. Please refer to Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further information regarding the adoption on Topic 606.

	December 31,				
	2019 (a)	2018	2017	2016	2015
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 69,514	$ 75,561	$ 46,656	$ 24,840	$ 54,116
Marketable securities	330,481	395,019	129,738	134,126	162,251
Working capital	311,356	315,737	153,560	83,702	113,809
Total assets	497,908	543,814	198,677	172,732	221,380
Non-current liabilities	14,035	12,790	1,211	1,326	233
Total liabilities	47,711	34,966	15,648	10,995	4,572
Common stock and additional paid-in capital	627,814	592,584	371,500	276,357	269,147
Total stockholders' equity	450,197	508,848	183,029	161,737	216,808

(a) Effective January 1, 2019, we adopted ASU 2016-02, *Leases* (Topic 842) which supersedes the lease accounting requirements in ASC 840, *Leases* (Topic 840). The consolidated balance sheet data as of December 31, 2019 is presented in accordance with the requirements of Topic 842, while prior period amounts have not been adjusted and, accordingly, may not be comparable. Please refer to Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further information regarding the adoption on Topic 842.

ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the audited financial statements and the notes thereto included elsewhere in this Annual Report on Form 10-K. In addition, you should read the "Risk Factors" and "Information Regarding Forward-Looking Statements" sections of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a leading clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy. Our gene therapy product candidates are designed to deliver genes to cells to address genetic defects or to enable cells in the body to produce therapeutic proteins that are intended to impact disease. Through a single administration, our gene therapy product candidates are designed to provide long-lasting effects, potentially significantly altering the course of disease and delivering improved patient outcomes.

Overview of Product Candidates

We have developed a broad pipeline of gene therapy programs using our proprietary adeno-associated virus (AAV) gene therapy delivery platform (NAV Technology Platform) to address genetic diseases through two modalities: AAV-mediated antibody delivery and monogenic gene replacement. The AAV-mediated antibody delivery modality is designed to treat serious and chronic diseases by delivering the genes necessary for the sustained production of therapeutic antibodies *in vivo*. Our monogenic gene replacement approach builds upon the well-understood mechanism of replacing a dysfunctional or missing gene with a functional copy of the gene in order to enable sustained production of necessary proteins.

Gene therapy using NAV Vectors for AAV-mediated antibody delivery

- **RGX-314:** We are developing RGX-314 as a novel, single-administration gene therapy for the treatment of wet age-related macular degeneration (wet AMD), diabetic retinopathy (DR), and other additional chronic retinal conditions which cause total or partial vision loss. We are advancing two separate routes of administration of RGX-314 to the eye, through a standardized subretinal delivery procedure as well as by delivery to the suprachoroidal space using the SCS Microinjector™ licensed from Clearside Biomedical, Inc.

  We have enrolled 42 patients in the Phase I/IIa clinical trial of RGX-314 for the treatment of wet AMD and have reported positive interim data for all five dose level cohorts. We expect to initiate a pivotal program for the subretinal delivery of RGX-314 for the treatment of wet AMD in the second half of 2020.

  We plan to initiate a Phase II trial for the suprachoroidal delivery of RGX-314 using the SCS Microinjector for the treatment of wet AMD in the first half of 2020 and expect to report interim data from Cohort 1 of the trial by the end of 2020. Additionally, we expect to submit an IND for a Phase II trial of the suprachoroidal delivery of RGX-314 using the SCS Microinjector for the treatment of DR by the end of 2020, and expect to report interim data in 2021.

- **AAV-Mediated Antibody Expression for the Treatment of Neurodegenerative Diseases:** We have established a research program in partnership with Neurimmune AG (Neurimmune) to jointly develop and commercialize novel gene therapies using NAV Vectors to deliver human antibodies for chronic neurodegenerative diseases, with an initial focus on diseases associated with the accumulation and deposition of the microtubule-associated protein tau (tauopathies) and alpha-synuclein (alpha-synucleinopathies). We expect to provide a program update in the second half of 2020.

- **AAV-Mediated Antibody Expression for the Treatment of Hereditary Angioedema (HAE):** We are developing a novel, one-time treatment utilizing a NAV Vector to deliver a gene encoding for a therapeutic antibody that targets and binds to plasma kallikrein, a key protein left unregulated in patients with HAE. HAE is a chronic and severe disease characterized by recurring severe swelling (angioedema), most commonly in the face, airway, intestines and limbs. We expect to select a lead product candidate in the first half of 2020 and provide a program update in the second half of 2020.

Gene therapy programs for the potential treatment of rare monogenic diseases

- **RGX-501:** We are developing RGX-501 for the treatment of homozygous familial hypercholesterolemia (HoFH), a severe genetic disease characterized by premature and aggressive plaque buildup, life threatening coronary artery disease and aortic valve disease predominantly due to abnormalities in the function or expression of the receptor for low-density lipoprotein (LDL-C). We have completed dosing of patients in the expanded second cohort of the Phase I/II clinical trial

for RGX-501 with corticosteroid prophylaxis, and we plan to assess LDL-C after all patients have completed steroid prophylaxis treatment. We expect to provide interim data in the first half of 2020.

- **RGX-121:** We are developing RGX-121 for the treatment of the neurological symptoms of Mucopolysaccharidosis Type II (MPS II), a severe genetic lysosomal storage disease caused by deficiency of iduronate-2-sulfatase (IDS), an enzyme that is responsible for breakdown of cellular waste products. Initial data from the first cohort demonstrated consistent and sustained reduction in heparan sulfate (HS) in the cerebral spinal fluid (CSF) and available data support early signs of neurocognitive stability. We expect to provide additional data from the first cohort in mid-2020, and we plan to complete enrollment in the second cohort in the first half of 2020, with interim data available in the second half of 2020.
- **RGX-111:** We are developing RGX-111 for the treatment of the neurological symptoms of Mucopolysaccharidosis Type I (MPS I), a severe genetic lysosomal storage disease caused by deficiency of α-l-iduronidase (IDUA), an enzyme required for breakdown of cellular waste products. Recruitment, screening and additional site activations are ongoing in the Phase I clinical trial for RGX-111. In October 2019, RGX-111 was administered to a subject with MPS I through an investigator-initiated study.
- **RGX-181:** We are developing RGX-181 for the treatment of late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease, one of the most common forms of Batten disease, caused by mutations in the tripeptidyl peptidase 1 (TPP1) gene. We are conducting preclinical development of RGX-181, including asessement of unmet clinical needs such as neurologic and ophthalmologic manifestations of the disease. We expect to provide a program update in mid-2020 and submit an IND for a first-in-human trial in the second half of 2020.
- **Gene Therapy Research Program for the Treatment of Neuromuscular Disorders:** We expect to announce plans for the clinical development of a potential treatment for a neuromuscular disorder in the second half of 2020.

In addition to our lead product candidates described above, we have also funded, and plan to continue to fund, preclinical research on potential product candidate programs that may become part of our internal product development pipeline. We have partnered with a number of leading academic institutions and will continue to seek partnerships with innovative institutions to develop novel NAV gene therapy product candidates.

Overview of Our NAV Technology Platform

In addition to our internal product development efforts, we also selectively license the NAV Technology Platform to other leading biotechnology and pharmaceutical companies, which we refer to as NAV Technology Licensees. As of December 31, 2019, our NAV Technology Platform was being applied in one FDA approved product (Zolgensma®), and the clinical development of 15 partnered product candidates, with over 20 partnered programs in total. Licensing the NAV Technology Platform allows us to maintain our internal product development focus on our core disease indications and therapeutic areas while still expanding the NAV gene therapy pipeline, developing a greater breadth of treatments for patients, providing additional technological and potential clinical proof-of-concept for our NAV Technology Platform, and creating potential additional revenue.

Financial Overview

Revenues

Our revenues to date primarily consist of license and royalty revenue resulting from the licensing of our NAV Technology Platform. We have not generated any revenues from commercial sales of our own products. If we fail to complete the development of our product candidates in a timely manner or fail to obtain their regulatory approval and adequate labeling, our ability to generate future revenues will be materially compromised.

We license our NAV Technology Platform to other biotechnology and pharmaceutical companies. The terms of the licenses vary, and licenses may be exclusive or non-exclusive and may be sublicensable by the licensee. Licenses may grant intellectual property rights for purposes of internal and preclinical research and development only, or may include the rights, or options to obtain future rights, to commercialize drug therapies for specific diseases using the NAV Technology Platform. License agreements generally have a term at least equal to the life of the underlying patents, but are terminable at the option of the licensee. Consideration from licensees under our license agreements may include: (i) up-front and annual fees, (ii) option fees to acquire additional licenses, (iii) milestone payments based on the achievement of certain development and sales-based milestones by licensees, (iv) sublicense fees and (v) royalties on sales of licensed products.

Royalty revenue to date consists of royalties on net sales of Zolgensma, which is marketed by AveXis, Inc. (AveXis), a wholly owned subsidiary of Novartis AG (Novartis), for use in children less than two years old with spinal muscular atrophy (SMA).

Zolgensma is a licensed product under our March 2014 license agreement, as amended, with AveXis for the development and commercialization of treatments for SMA.

Future license and royalty revenues are dependent on the successful development and commercialization of licensed products by our licensees, which is uncertain, and revenues may fluctuate significantly from period to period. Additionally, we may never receive consideration in our license agreements that is contemplated on option fees, development and sales-based milestone payments, royalties on sales of licensed products or sublicense fees, given the contingent nature of these payments. Our revenues are concentrated among a low number of licensees and licenses are terminable at the option of the licensee. The termination of our licenses by licensees may materially impact the amount of revenue we recognize in future periods. Please refer to Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of segment and geographical information regarding our revenues.

Operating Expenses

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

Cost of Revenues

Our cost of revenues consists primarily of upstream fees due to our licensors as a result of revenue generated from the licensing of our NAV Technology Platform, including sublicense fees, milestone payments and royalties on net sales of licensed products. Sublicense fees are based on a percentage of license fees received by us from NAV Technology Licensees and are recognized in the period that the underlying license revenue is recognized. Milestone payments are payable to licensors upon the achievement of specified milestones by NAV Technology Licensees and are recognized in the period the milestone is achieved or deemed probable of achievement. Royalties are based on a percentage of net sales of licensed products by NAV Technology Licensees and are recognized in the period that the underlying sales occur. Future costs of revenues are uncertain due to the nature of our license agreements and significant fluctuations in cost of revenues may occur from period to period.

Research and Development Expense

Our research and development expense primarily consists of:

- salaries and personnel-related costs, including benefits, stock-based compensation and travel, for our scientific personnel performing research and development activities;
- costs related to executing preclinical studies and clinical trials;
- costs related to acquiring, developing and manufacturing materials for preclinical studies and clinical trials;
- fees paid to consultants and other third-parties who support our product candidate development;
- other costs in seeking regulatory approval of our product candidates; and
- allocated facility-related costs, depreciation expense and other overhead.

Up-front fees incurred in obtaining technology licenses for research and development activities, as well as associated milestone payments, are expensed as incurred if the technology licensed has no alternative future use.

We plan to increase our research and development expenses for the foreseeable future as we continue development of our product candidates. Our current and planned research and development activities include the following:

- a Phase I/IIa clinical trial and a planned pivotal program to evaluate the safety and efficacy of the subretinal delivery of RGX-314 for the treatment of wet AMD;
- planned Phase II clinical trials to evaluate the safety and efficacy of the suprachoroidal delivery of RGX-314 using the SCS Microinjector for the treatment of wet AMD and DR;
- a Phase I/II clinical trial to evaluate the safety and efficacy of RGX-501 for the treatment of HoFH;

- a Phase I/II clinical trial to evaluate the safety and efficacy of RGX-121 for the treatment of MPS II;
- a Phase I clinical trial to evaluate the safety and efficacy of RGX-111 for the treatment of MPS I;
- preclinical research and development and a planned clinical trial for RGX-181 for the treatment of CLN2;
- preclinical research and development for potential product candidates to treat neurodegenerative diseases, including tauopathies and alpha-synucleinopathies, under our collaboration with Neurimmune;
- preclinical research and development for potential product candidates to treat HAE;
- preclinical research and development for potential product candidates to treat neuromuscular disorders;
- preclinical research and development for potential product candidates addressing other diseases across a range of therapeutics areas;
- continued investment in advanced manufacturing analytics and process development activities; and
- continued acquisition and manufacture of clinical trial materials in support of our anticipated clinical trials.

The following table summarizes our research and development expenses incurred during the years ended December 31, 2019, 2018 and 2017 (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Direct Expenses			
RGX-314	$ 20,713	$ 6,580	$ 5,883
RGX-501	4,823	10,849	4,394
RGX-121	3,999	4,235	5,768
RGX-111	3,028	3,130	2,847
RGX-181	7,602	4,399	—
Total direct expenses	40,165	29,193	18,892
Unallocated Expenses			
Unallocated external expenses	21,083	12,431	10,187
Personnel-related	50,164	34,275	23,377
Facilities and depreciation expense	9,511	5,816	3,547
Other unallocated	3,262	2,158	1,221
Total unallocated expenses	84,020	54,680	38,332
Total research and development	$ 124,185	$ 83,873	$ 57,224

Expenses incurred in the development of RGX-181 were included in unallocated external expenses through the second quarter of 2018. Unallocated external expenses include direct costs not identifiable with a specific lead product candidate, including costs associated with our research and development platform, process development, manufacturing analytics and preclinical research and development for prospective product candidates and new technologies. We typically utilize our employee and infrastructure resources across our development programs. We do not allocate personnel and other internal costs, such as facilities and other overhead costs, to specific product candidates or development programs.

General and Administrative Expense

Our general and administrative expense consists primarily of salaries and personnel-related costs, including employee travel, benefits and stock-based compensation, for employees performing functions other than research and development. This includes certain personnel in executive, commercial, corporate development, finance, legal, human resources, information technology and administrative support functions. Other general and administrative expenses include facility-related and overhead costs not otherwise allocated to research and development expense, professional fees for accounting, legal and advisory services, expenses associated with obtaining and maintaining patents, insurance costs, costs of our information systems and other commercial and general corporate activities. We expect that our general and administrative expense will continue to increase as we continue to develop, and potentially commercialize, our product candidates.

Other Income

Interest Income from Licensing

In accordance with our revenue recognition policy, interest income from licensing consists of imputed interest recognized from significant financing components identified in our license agreements with NAV Technology Licensees.

Investment Income

Investment income consists of interest income earned and gains and losses realized from our cash equivalents and marketable securities, as well as unrealized gains and losses on marketable equity securities. Cash equivalents are comprised of money market mutual funds and highly liquid debt securities with original maturities of 90 days or less at acquisition. Marketable securities are comprised of available-for-sale debt securities and equity securities.

Critical Accounting Policies and Significant Judgments and Estimates

This Management's Discussion and Analysis of Financial Condition and Results of Operations is based on our financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, as well as the reported revenues and expenses during the reported periods. We evaluate these estimates and assumptions on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies and recently announced accounting pronouncements, including the expected impact of such pronouncements, are fully described in Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. We believe the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements and understanding and evaluating our reported financial results.

Revenue Recognition

Effective January 1, 2018, we adopted Accountings Standards Update (ASU) 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in Accounting Standards Codification (ASC 605), *Revenue Recognition* (Topic 605). Our financial results for periods ending after January 1, 2018 are presented in accordance with the requirements of Topic 606, while prior period amounts have not been adjusted and continue to be reported in accordance with Topic 605.

Topic 606 requires entities to recognize revenue when control of the promised goods or services is transferred to customers at an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. The following five steps are performed to determine the appropriate revenue recognition for arrangements within the scope of Topic 606: (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 entity satisfies the performance obligations.

We apply the five-step model to contracts that are within the scope of Topic 606 only when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, for contracts within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations and whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to respective performance obligations when (or as) the respective performance obligations are satisfied.

We evaluate our contracts with customers for the presence of significant financing components. If a significant financing component is identified in a contract and provides a financing benefit to the customer, the transaction price for the contract is adjusted to account for the financing portion of the arrangement, which is recognized as interest income over the financing term using the effective interest method. In determining the appropriate interest rates for significant financing components, we evaluate the credit profile of the customer and prevailing market interest rates and select an interest rate in which we believe would be charged to the customer in a separate financing arrangement over a similar financing term.

License and royalty revenue

We license our NAV Technology Platform to other biotechnology and pharmaceutical companies. The terms of the licenses vary, and licenses may be exclusive or non-exclusive and may be sublicensable by the licensee. Licenses may grant intellectual

property rights for purposes of internal and preclinical research and development only, or may include the rights, or options to obtain future rights, to commercialize drug therapies for specific diseases using our NAV Technology Platform. License agreements generally have a term at least equal to the life of the underlying patents, but are terminable at the option of the licensee. Consideration payable to us under our license agreements may include: (i) up-front and annual fees, (ii) option fees to acquire additional licenses, (iii) milestone payments based on the achievement of certain development and sales-based milestones by licensees, (iv) sublicense fees and (v) royalties on sales of licensed products.

Our license agreements are accounted for as contracts with customers within the scope of Topic 606. At the inception of each license agreement, we determine the contract term for purposes of applying the requirements of Topic 606. Licenses are generally terminable at the option of the licensee with advance notice to us. For each license granted, including licenses granted upon the exercise of license options, we evaluate these termination rights to determine whether a substantive termination penalty would be incurred by the licensee upon termination. If the licensee incurs a substantive termination penalty upon termination, the contract term for revenue recognition purposes is generally equal to the stated term of the license, which is the life of the underlying licensed patents. Alternatively, if the licensee does not incur a substantive termination penalty upon termination, the contract term for revenue recognition purposes may be shorter than the stated term of the license, in which case the termination rights may be accounted for as contract renewal options. The determination of whether a substantive termination penalty is associated with the termination rights requires significant judgment. In making this determination, we consider, among other things, the nature of the intellectual property rights that would be returned to us upon termination, including the exclusivity of the licensed rights and the stage of development of the licensed products, the payment terms, including the amount and timing of non-refundable or guaranteed payments, and the business purpose of the termination rights granted to the licensee. Generally, the most significant judgment in determining whether a substantive termination penalty exists relates to the amount of any up-front or guaranteed non-refundable payments relative to the amount of annual payments that may be avoided by the licensee upon termination of the license. We consider all of the facts and circumstances relevant to each license when making this determination.

Performance obligations under our license agreements may include (i) the delivery of intellectual property licenses and (ii) options granted to licensees to acquire additional licenses to the extent the options represent material rights to the licensee. At the inception of each license agreement which contains options for the licensee to acquire additional licenses, or contract renewal options, we evaluate the options to determine whether they provide material rights to the licensee. In making this determination, we consider whether the options are priced at a discount to the standalone selling price for the underlying licenses. If an option is priced at a discount to the standalone selling price for the underlying license, the option is considered to be a material right to the licensee and is accounted for as a separate performance obligation under the current license agreement.

We evaluate the transaction price of our license agreements at the inception of each agreement and at each reporting date. The transaction price includes the fixed consideration payable to us during the contract term, as well as any variable consideration to the extent that it is probable that a significant reversal of revenue will not occur in the future. Fixed consideration under the license agreements includes up-front and annual fees payable during the contract term. Variable consideration under the license agreements includes development and sales-based milestone payments, sublicense fees and royalties on sales of licensed products. Consideration contingent upon the exercise of options by a licensee is excluded from the transaction price and not accounted for as part of the license agreement until the option is exercised.

The transaction price for each license agreement is allocated to the underlying performance obligations and recognized as revenue when the performance obligations are satisfied. Consideration allocated to performance obligations for the delivery of an intellectual property license is recognized as revenue in full upon the delivery of the license to the licensee. Consideration allocated to performance obligations for license options is recognized as revenue in full upon the earlier of the option exercise or expiration. The exercise of a license option by a licensee is accounted for as a new license for revenue recognition purposes.

Up-front and annual licenses fees payable to us over the contract term of each license are included in the transaction price, and the portion of this consideration that is allocated to the performance obligation for the delivery of the intellectual property license is recognized as revenue in full upon the delivery of the license to the licensee. If annual license fees are payable to us in periods beyond 12 months from the delivery of the license, a significant financing component is deemed to exist which provides a financing benefit to the licensee. If a significant financing component is identified, we adjust the transaction price for the license to include only the present value of the annual license fees payable to us over the contract term. The discounted portion of the license fees is recognized as interest income from licensing over the financing period of the license.

Development milestone payments are payable to us upon the achievement of specified development milestones by licensees. At the inception of each license agreement that contains development milestone payments, we evaluate whether the milestones are considered probable of achievement and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal will not occur in the future, milestone payments are included in the

transaction price and recognized as revenue upon the delivery of the license. Milestone payments contingent on the achievement of development milestones that are not within our control or the control of the licensee, such as regulatory approvals, are not considered probable of being achieved and are excluded from the transaction price until the milestone is achieved. At each reporting date, we re-evaluate the probability of achievement of each outstanding development milestone and, if necessary, adjust the transaction price for any milestones for which the probability of achievement has changed due to current facts and circumstances. Any such adjustments are recorded on a cumulative catch-up basis and recognized as revenue in the period of the adjustment.

Royalties on sales of licensed products, sales-based milestone payments and sublicense fees based on the receipt of certain fees by licensees from any sublicensees are excluded from the transaction price of each license and recognized as revenue in the period that the related sales or sublicenses occur, provided that the associated license has been delivered to the licensee.

Royalty revenue to date consists of royalties on net sales of Zolgensma, which is a licensed product under our March 2014 license agreement, as amended, with AveXis for the development and commercialization of treatments for SMA. We recognize royalty revenue from net sales of Zolgensma in the period in which the underlying products are sold by AveXis, which in certain cases may require us to estimate royalty revenue for periods of net sales which have not yet been reported to us. Sales-based milestone payments related to net sales of Zolgensma are recognized as royalty revenue in the period in which the milestone is achieved.

We receive payments from licensees based on the billing schedules established in each license agreement. Amounts recognized as revenue which have not yet been received from licensees, including unbilled royalties, are recorded as accounts receivable when our rights to the consideration are conditional solely upon the passage of time. Amounts recognized as revenue which have not yet been received from licensees are recorded as contract assets when our rights to the consideration are not unconditional. Contract assets are recorded as other current assets on the consolidated balance sheets. If a licensee elects to terminate a license prior to the end of the license term, the licensed intellectual property is returned to us and any consideration recorded as accounts receivable or contract assets which is not contractually payable by the licensee is charged off as a reduction of license revenue in the period of the termination. Amounts received by us prior to the delivery of underlying performance obligations are deferred and recognized as revenue upon the satisfaction of the performance obligations. Deferred revenue which is not expected to be recognized within 12 months from the reporting date is recorded as non-current on the consolidated balance sheets.

Accrued Research and Development Expenses

We estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing contracts and purchase orders with service providers, identifying services that have been performed on our behalf and estimating the level of service performed, the expected remaining period of performance and the associated expenses incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. Depending on the timing of payments to the service providers and the estimated expenses incurred, we may record net prepaid or accrued research and development expenses relating to these costs.

Examples of estimated accrued research and development expenses include fees paid to:

- contract research organizations in connection with preclinical development and clinical studies;
- contract manufacturing organizations and other vendors related to process development and manufacturing of materials for use in preclinical development and clinical studies; and
- service providers for professional service fees such as consulting and other research and development related services.

Our understanding of the status and timing of services performed relative to the actual status and timing may vary and may result in us reporting changes in estimates in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

Stock-based Compensation

Our stock-based awards include stock options granted to employees and nonemployees, restricted stock units and shares issued under our employee stock purchase plan.

Our stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and nonemployees with service-based vesting conditions is recognized on a straight-line basis based on the estimated grant date fair value over the requisite service period of the award, which is generally the vesting term. Compensation expense related to awards to employees and nonemployees with performance-based vesting conditions is recognized based on the

estimated grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

We have elected to not estimate forfeitures of stock-based awards and to account for forfeitures as they occur.

Determination of the Fair Value of Stock-based Awards

We estimate the fair value of our stock option awards using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including (i) the fair value of the underlying common stock, (ii) the expected stock price volatility, (iii) the expected term of the award, (iv) the risk-free interest rate and (v) expected dividends. In applying these assumptions, we consider the following factors:

- The fair value of our common stock used to determine the exercise price and fair value of our stock options is based on the closing price of our common stock on the date of the grant.
- Our common stock has only been publicly traded since September 2015 and, accordingly, we do not have sufficient historical and implied volatility data for our common stock necessary to estimate the expected the volatility of our common stock over a period of time commensurate with the expected term of our stock option awards. As a result, we estimate expected volatility based on the historical volatility of both our common stock and the common stock of a selected peer group of similar publicly traded companies for which sufficient historical volatility data is available. Due to the lack of historical volatility data for our common stock, we place a higher weight on the historical volatility of the selected peer group in estimating expected volatility. We compute the historical volatility data using the daily closing prices for the selected companies' shares during a period equivalent to the expected term of the stock option awards. For the purpose of identifying the selected peer group companies, we consider characteristics such as enterprise value, risk profiles, position within the industry and length of historical share price information. We focus our peer group company selection on companies that operate within the biotechnology industry, and specifically on companies that use gene therapy, or similar technologies, for treating diseases and/or are focused on treating diseases in our development pipeline or our licensees' pipelines. We plan to continue using historical peer group volatility data as an input to estimate expected volatility until a sufficient amount of historical volatility data for our common stock becomes available.
- We estimate the expected term of "plain vanilla" stock options granted to employees based on the simplified method in accordance with SEC Staff Accounting Bulletin Nos. 107 and 110, as our common stock has only been publicly traded since September 2015. Using the simplified method, the expected term of the award equals the arithmetic average of the vesting term and the original contractual term of the option. We expect to use the simplified method to estimate the expected term of stock options granted to employees until we have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term. For stock options granted to nonemployees, we use the contractual term of the award rather than the expected term to estimate the fair value of the award.
- We estimate the risk-free interest rates for periods within the expected term of our stock options based on the rates of U.S. Treasury securities with maturity dates commensurate with the expected term of the associated awards.
- The assumed dividend yield of zero is based on our history of not paying dividends and our expectation of not paying dividends for the foreseeable future.

We estimate the fair value of our restricted stock units based on the closing price of our common stock on the date of the grant.

Income Taxes

As of December 31, 2019, we had federal net operating loss (NOL) carryforwards of $170.4 million, U.S. state NOL carryforwards of $269.3 million and federal and state research and development credit carryforwards of $40.5 million which may be available to offset future income tax liabilities and expire at various dates through 2039.

Under the provisions of the Internal Revenue Code, the NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may be subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on our value immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. We have completed several financings since our inception which may have resulted in

a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

We account for income taxes in accordance with ASC 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

We have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets, including our NOL and credit carryforwards. Based on our history of operating losses, we believe that it is more likely than not that the benefit of our deferred tax assets will not be realized. Accordingly, we have provided a full valuation allowance for our net deferred tax assets as of December 31, 2019 and 2018.

Recent Accounting Pronouncements

See Note 2 “Recent Accounting Pronouncements” in the notes to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a full description of recent accounting pronouncements and the potential impact to our financial statements.

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

	Years Ended December 31,		
	2019	2018	Change
	(in thousands)		
Revenues			
License and royalty revenue	$ 35,233	$ 218,505	$ (183,272)
Total revenues	35,233	218,505	(183,272)
Operating Expenses			
Cost of revenues	8,241	9,640	(1,399)
Research and development	124,185	83,873	40,312
General and administrative	51,815	36,850	14,965
Other operating expenses (income)	(10)	42	(52)
Total operating expenses	184,231	130,405	53,826
Income (loss) from operations	(148,998)	88,100	(237,098)
Other Income			
Interest income from licensing	2,951	8,946	(5,995)
Investment income	48,559	7,070	41,489
Total other income	51,510	16,016	35,494
Income (loss) before income taxes	(97,488)	104,116	(201,604)
Income Tax Benefit (Expense)	2,755	(4,179)	6,934
Net income (loss)	$ (94,733)	$ 99,937	$ (194,670)

License and Royalty Revenue. License and royalty revenue decreased by $183.3 million, from $218.5 million for the year ended December 31, 2018 to $35.2 million for the year ended December 31, 2019. The decrease was primarily attributable to the following:

- $176.1 million of non-recurring license revenue recognized in 2018 under our amended March 2014 license agreement with AveXis for the development and commercialization of treatments for SMA; and
- $35.6 million of non-recurring license revenue recognized in 2018 under our November 2018 license agreement with Abeona Therapeutics Inc. (Abeona) for the development and commercialization of treatments for various diseases.

The decrease was partially offset by $20.8 million of royalty revenue recognized in 2019 related to net sales of Zolgensma. Commercial sales of Zolgensma commenced in the second quarter of 2019. We are eligible to receive a milestone payment of $80.0 million from AveXis upon the achievement of $1.0 billion in cumulative net sales of Zolgensma.

Research and Development Expense. Research and development expenses increased by $40.3 million, from $83.9 million for the year ended December 31, 2018 to $124.2 million for the year ended December 31, 2019. The increase was primarily attributable to the following:

- an increase of $15.6 million for personnel costs as a result of increased headcount of research and development personnel, including a $5.4 million increase in stock-based compensation expense;
- an increase of $8.2 million for external costs associated with clinical trial activities for our lead product candidates;
- an increase of $6.0 million for laboratory costs and facilities used by research and development personnel, including a $3.1 million increase in depreciation expense allocated to research and development functions;
- an increase of $4.4 million for external costs associated with preclinical studies and regulatory activities; and
- an increase of $3.8 million for external costs associated with manufacturing-related services.

General and Administrative Expense. General and administrative expenses increased by $15.0 million, from $36.9 million for the year ended December 31, 2018 to $51.8 million for the year ended December 31, 2019. The increase was primarily attributable to the following:

- an increase of $7.3 million for personnel costs as a result of increased headcount of general and administrative personnel, including a $4.8 million increase in stock-based compensation expense; and
- an increase of $4.2 million for professional services, including commercial, legal, accounting and other advisory services.

Interest Income from Licensing. Interest income from licensing decreased by $6.0 million, from $8.9 million for the year ended December 31, 2018 to $3.0 million for the year ended December 31, 2019. The decrease was primarily attributable to $8.0 million of interest income recognized in 2018 under our amended March 2014 license agreement with AveXis.

Investment Income. Investment income increased by $41.5 million, from $7.1 million for the year ended December 31, 2018 to $48.6 million for the year ended December 31, 2019. The increase was primarily attributable to unrealized gains of $31.8 million and realized gains of $6.0 million recognized in 2019 related to our marketable equity securities of Prevail Therapeutics Inc. (Prevail). We acquired the securities as consideration for a commercial license to the NAV Technology Platform granted to Prevail in August 2017. Prevail completed its initial public offering (IPO) in June 2019. Prior to Prevail's IPO, the securities were accounted for as non-marketable equity securities without a readily determinable fair value and had a carrying value of $0.4 million. Upon Prevail's IPO in June 2019, the securities were reclassified to marketable securities and are measured at fair value. As of December 31, 2019, the Company's marketable equity securities of Prevail had a fair value of $32.1 million. Significant fluctuations in the fair value of the securities may occur from period to period.

Comparison of the Years Ended December 31, 2018 and 2017

	Years Ended December 31,		
	2018	2017	Change
	(in thousands)		
Revenues			
License and royalty revenue	$ 218,505	$ 10,385	$ 208,120
Other revenues	—	8	(8)
Total revenues	218,505	10,393	208,112
Operating Expenses			
Cost of revenues	9,640	1,709	7,931
Research and development	83,873	57,224	26,649
General and administrative	36,850	27,229	9,621
Other operating expenses	42	116	(74)
Total operating expenses	130,405	86,278	44,127
Income (loss) from operations	88,100	(75,885)	163,985
Other Income			
Interest income from licensing	8,946	—	8,946
Investment income	7,070	2,716	4,354
Total other income	16,016	2,716	13,300
Income (loss) before income taxes	104,116	(73,169)	177,285
Income Tax Expense	(4,179)	—	(4,179)
Net income (loss)	$ 99,937	$ (73,169)	$ 173,106

License and Royalty Revenue. License and royalty revenue increased by $208.1 million, from $10.4 million for the year ended December 31, 2017 to $218.5 million for the year ended December 31, 2018. The increase was primarily attributable to the following license revenue recognized in 2018:

- $176.1 million of revenue recognized under our amended March 2014 license agreement with AveXis for the development and commercialization of treatments for SMA; and
- $35.6 million of revenue recognized under our November 2018 license agreement with Abeona for the development and commercialization of treatments for various diseases.

The increase in revenues in 2018 resulted in a $7.9 million increase in cost of revenues incurred during the period related to sublicense fees we are obligated to pay to our licensors.

Research and Development Expense. Research and development expenses increased by $26.6 million, from $57.2 million for the year ended December 31, 2017 to $83.9 million for the year ended December 31, 2018. The increase was primarily attributable to the following:

- an increase of $10.9 million for personnel costs as a result of increased headcount of research and development personnel, including a $2.5 million increase in stock-based compensation expense;
- an increase of $6.1 million for laboratory costs and facilities and equipment used by research and development personnel, including a $1.3 million increase in depreciation expense allocated to research and development functions;
- an increase of $4.5 million for external costs associated with clinical trial activities for our lead product candidates; and
- an increase of $3.5 million for external costs associated with manufacturing-related services.

General and Administrative Expense. General and administrative expenses increased by $9.6 million, from $27.2 million for the year ended December 31, 2017 to $36.9 million for the year ended December 31, 2018. The increase was primarily attributable to the following:

- an increase of $5.7 million for personnel costs as a result of increased headcount of general and administrative personnel, including a $3.6 million increase in stock-based compensation expense; and
- an increase of $2.1 million for professional services, including commercial, legal, accounting and other advisory services.

Interest Income from Licensing. Interest income from licensing increased by $8.9 million, from zero for the year ended December 31, 2017. In January 2018, we adopted new revenue recognition standards under Topic 606, the requirements of which have not been retrospectively applied to prior periods. Under Topic 606, we impute and recognize interest income related to significant financing components identified in our license agreements with NAV Technology Licensees. During the year ended December 31, 2018, we recognized $8.0 million of interest income under our amended March 2014 license agreement with AveXis and $0.4 million of interest income under our November 2018 license agreement with Abeona.

Investment Income. Investment income increased by $4.4 million, from $2.7 million for the year ended December 31, 2017 to $7.1 million for the year ended December 31, 2018. The increase was primarily attributable to the overall growth of our investment portfolio in 2018, which was largely driven by cash inflows from our licensing arrangements as well as the net proceeds received from the public offering of our common stock completed in August 2018.

Liquidity and Capital Resources

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $400.0 million, which were primarily derived from the sale of common stock as well as revenues generated from the licensing of our NAV Technology Platform. We expect that our cash, cash equivalents and marketable securities as of December 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months from the date of this report, based on our current business plan.

During the year ended December 31, 2019, we recognized total realized and unrealized gains of $37.8 million related to our marketable equity securities of Prevail. As of December 31, 2019, the Company’s marketable equity securities of Prevail had a fair value of $32.1 million. Significant fluctuations in the fair value of the securities may occur from period to period.

In August 2018, we completed a public offering of 3,105,000 shares of our common stock (inclusive of 405,000 shares pursuant to the full exercise by the underwriters of their option to purchase additional shares) at a price of $65.00 per share. The aggregate net proceeds from the offering, inclusive of the underwriters’ option exercise, were $189.1 million, net of underwriting discounts and commissions and offering expenses payable by us.

In January 2018, we amended our March 2014 license agreement (the January 2018 Amendment) with AveXis which modified its terms and conditions and provided additional intellectual property rights to AveXis. In consideration for the additional rights granted under the amended license agreement, AveXis paid us $80.0 million upon the effective date of the amendment. In addition, AveXis was obligated to pay us (i) $30.0 million on the first anniversary of the effective date of the January 2018 Amendment, (ii) $30.0 million on the second anniversary of the effective date of the January 2018 Amendment and (iii) potential sales-based milestone payments of up to $120.0 million. In the event of a change of control of AveXis, to the extent that any fee described in (i) or (ii) above, or the first $40.0 million of milestone payments described in (iii) above, had not yet been paid to us, AveXis was obligated to pay any such unpaid fee to us upon the change of control. Accordingly, when AveXis was acquired by Novartis in May 2018, AveXis paid us $100.0 million in accelerated license payments following the change of control. Pursuant to the amended license agreement, AveXis is obligated to pay us $80.0 million upon the achievement of a sales-based milestone, in addition to other regulatory milestone payments and royalties on net sales of licensed products. In May 2019, the FDA approved Zolgensma for marketing in the United States, which is a licensed product under our March 2014 license, as amended, with AveXis. Commercial sales of Zolgensma commenced in the second quarter of 2019, upon which we began recognizing royalty revenue on net sales of the licensed product. We recognized royalty revenue of $20.8 million related to net sales of Zolgensma during the year ended December 31, 2019.

In March 2017, we completed a public offering of 3,700,000 shares of our common stock at a price of $20.50 per share. In connection with the offering, we granted the underwriters an option to purchase 555,000 additional shares of common stock at the public offering price. The underwriters exercised the option in full and purchased the additional shares in April 2017. The aggregate net proceeds from the offering, inclusive of the underwriters’ option exercise, were $81.5 million, net of underwriting discounts and commissions and offering expenses payable by us.

We intend to devote the majority of our current capital to clinical development and seeking regulatory approval of our product candidates and capital expenditures to build out additional office, laboratory and manufacturing capacity. Because of the numerous risks and uncertainties associated with the development and commercialization of gene therapy product candidates, we are unable to estimate the amount of operating expenditures and capital outlays necessary to complete the development of our product candidates. Additionally, our estimates are based on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect.

Cash Flows

	Years Ended December 31,		
	2019	2018	2017
	(in thousands)		
Net cash provided by (used in) operating activities	$ (107,705)	$ 104,648	$ (57,992)
Net cash provided by (used in) investing activities	93,559	(279,358)	(4,790)
Net cash provided by financing activities	8,376	204,443	84,598
Net increase (decrease) in cash and cash equivalents and restricted cash	$ (5,770)	$ 29,733	$ 21,816

Cash Flows from Operating Activities

Our net cash used in operating activities for the year ended December 31, 2019 increased by $212.4 million from the year ended December 31, 2018. The change was primarily attributable to $180.0 million in non-recurring license payments we received in 2018 related to the amendment of our March 2014 license agreement with AveXis, as well as an increase in operating expenses in 2019. The increase in operating expenses during the period was primarily attributable to increased employee headcount and external research and development expenses as we continue the development and advancement of our lead product candidates and other research programs.

For the year ended December 31, 2019, our net cash used in operating activities of $107.7 million consisted of a net loss of $94.7 million, $7.6 million in adjustments for non-cash items and changes in working capital of $5.3 million. Adjustments for non-cash items primarily consisted of unrealized gains on our marketable equity securities of Prevail of $31.8 million, net realized gains on marketable equity securities of $6.0 million, imputed interest earned from our license agreements of $3.0 million and net accretion of discounts on marketable debt securities of $1.2 million, and were partially offset by stock-based compensation expenses of $26.9 million and depreciation and amortization expense of $7.2 million. The changes in working capital were primarily attributable to an increase in accounts receivable of $8.6 million, an increase in other assets of $2.7 million and an increase in prepaid expenses of $1.0 million, and were partially offset by increases in accounts payable and accrued expenses and other current liabilities of $8.4 million. The increase in accounts receivable was largely driven by royalties on net sales of Zolgensma during the fourth quarter of 2019 which were recorded as accounts receivable as of December 31, 2019. The increases in prepaid expenses and other assets were largely driven by the amounts we were billed by service providers in 2019 which are applicable to future periods of performance, including periods beyond 12 months from December 31, 2019. The increases in accounts payable and accrued expenses and other current liabilities were largely driven by accrued royalties to our licensors related to net sales of Zolgensma during the fourth quarter of 2019, as well as a general increase in operating expenses in 2019.

For the year ended December 31, 2018, our net cash provided by operating activities of $104.6 million consisted of net income of $99.9 million and $12.5 million in adjustments for non-cash items, offset by changes in working capital of $7.8 million. Adjustments for non-cash items primarily consisted of stock-based compensation expenses of $16.6 million, depreciation and amortization expense of $4.0 million and net amortization of premiums on marketable debt securities of $0.8 million and were partially offset by imputed interest earned from our license agreements of $8.9 million. The changes in working capital were primarily attributable to an increase in accounts receivable of $16.8 million, increases in prepaid expenses and other current assets of $2.5 million and an increase in other assets of $1.5 million, and were partially offset by an increase in accrued expenses and other current liabilities of $7.6 million, an increase in deferred revenue of $3.9 million and an increase in other liabilities of $1.7 million. The increase in accounts receivable was largely driven by $26.0 million of accounts receivable recorded as of December 31, 2018 related to the November 2018 license agreement with Abeona, and was partially offset by the imputed interest recognized upon the acceleration of license payments under our amended March 2014 license agreement with AveXis.

For the year ended December 31, 2017, our net cash used in operating activities of $58.0 million consisted of a net loss of $73.2 million, offset by $14.3 million in adjustments for non-cash items and changes in working capital of $0.9 million. Adjustments for non-cash items primarily consisted of stock-based compensation expenses of $10.6 million, depreciation and amortization expense of $2.7 million and net amortization of premiums on marketable debt securities of $1.8 million. The changes in working capital were primarily attributable to increases in accounts payable and accrued expenses and other current liabilities of $4.5 million, and were partially offset by an increase in prepaid expenses of $3.6 million.

Cash Flows from Investing Activities

For the year ended December 31, 2019, net cash provided by investing activities consisted of $296.0 million in sales and maturities of marketable securities, offset by $190.7 million to purchase marketable securities and $11.7 million to purchase property and equipment. We expect capital expenditures to increase, beginning in 2020, as a result of the buildout of our future corporate, manufacturing and research headquarters at 9800 Medical Center Drive in Rockville, Maryland.

For the year ended December 31, 2018, net cash used in investing activities consisted of $445.8 million to purchase marketable securities and $13.3 million to purchase property and equipment, offset by $179.7 million in sales and maturities of marketable securities.

For the year ended December 31, 2017, net cash used in investing activities consisted of $68.6 million to purchase marketable securities and $7.2 million to purchase property and equipment, offset by $71.0 million in sales and maturities of marketable securities.

Cash Flows from Financing Activities

For the year ended December 31, 2019, net cash provided by financing activities consisted of $8.4 million in proceeds received from the exercise of stock options and issuance of common stock under our employee stock purchase plan.

For the year ended December 31, 2018, net cash provided by financing activities consisted of $189.1 million in aggregate net proceeds from a public offering of our common stock, net of underwriting discounts and commissions and additional offering expenses we paid during the period, and $15.3 million in proceeds received from the exercise of stock options and issuance of common stock under our employee stock purchase plan.

For the year ended December 31, 2017, net cash provided by financing activities consisted of $81.5 million in aggregate net proceeds from a public offering of our common stock, net of underwriting discounts and commissions and additional offering expenses we paid during the period, and $3.0 million in proceeds received from the exercise of stock options and issuance of common stock under our employee stock purchase plan.

Future Funding Requirements

We have incurred cumulative losses since our inception and had an accumulated deficit of $177.8 million as of December 31, 2019. Our transition to recurring profitability is dependent upon achieving a level of revenues adequate to support our cost structure, which depends heavily on the successful development, approval and commercialization of our product candidates. We do not expect to achieve such revenues, and expect to continue to incur losses, for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase for the foreseeable future as we continue the development of, and seek regulatory approval for, our product candidates. Subject to obtaining regulatory approval for our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. Additionally, we expect our capital expenditures will increase significantly in the future for costs associated with building out additional office, laboratory and manufacturing capacity to further support the development of our product candidates and potential commercialization efforts. As a result, we will need significant additional capital to fund our operations, which we may obtain through one or more equity offerings, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements.

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

- the timing of enrollment, commencement and completion of our clinical trials;
- the results of our clinical trials;
- the results of our preclinical studies for our product candidates and any subsequent clinical trials;
- our planned expansion of the licensing of our NAV Technology Platform;

- the scope, progress, results and costs of drug discovery, laboratory testing, preclinical development and clinical trials for our product candidates;
- the costs associated with building out additional laboratory and manufacturing capacity;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future product sales, medical affairs, marketing, manufacturing and distribution activities for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- revenue received from commercial sales of Zolgensma and other revenue, if any, received in connection with commercial sales of our NAV Technology Licensees' products, should any of their product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- our current licensing agreements or collaborations remaining in effect;
- our ability to establish and maintain additional licensing agreements or collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Many of these factors are outside of our control. 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 regulatory and marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, and any commercial milestones or royalty payments under our licensing agreements, will be derived from or based on sales of products, the majority of which may not be commercially available for many years, if at all. In addition, revenue from our NAV Technology Platform sublicensing is dependent in part on the clinical and commercial success of our licensing partners. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

The issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline. Adequate additional financing may not be available to us on acceptable terms, or at all. We also could be required to seek funds through arrangements with partners or otherwise that may require us to relinquish rights to our intellectual property, our product candidates or otherwise agree to terms unfavorable to us.

Contractual Obligations, Commitments and Contingencies

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

Our commitments also include obligations to our licensors under our in-license agreements, which may include sublicense fees, milestones fees, royalties and reimbursement of patent maintenance costs. Sublicense fees are due to the licensors when we sublicense underlying intellectual property to third parties; the fees are based on a percentage of the license fees we receive from the sublicensees. Based on license fees we have received from sublicensees or recorded as accounts receivable as of December 31, 2019, we had accrued $2.7 million of sublicense fees payable to our licensors, of which $0.8 million was expected to be paid within 12 months and $1.8 million was expected to be paid in periods beyond 12 months. The actual amount of sublicense fees payable in future periods could differ materially if new licenses are granted to sublicensees, existing licenses are terminated by sublicensees or if certain other contingent consideration, such as milestone payments, is received from sublicensees in the future. Accordingly, the amount of sublicense fees payable in future periods is not fixed and determinable and therefore is not included in the table below. Milestone fees are payable by us upon our future achievement of certain development and regulatory milestones. Royalties are payable by us based on a percentage of net sales of licensed products. Maintenance costs are reimbursements to the licensors for maintaining licensed patents. These amounts are not fixed and determinable and therefore are not included in the table below.

We have entered into a number of long-term leases for office and laboratory space in Rockville, Maryland and New York, New York, as well as a number of laboratory and other equipment leases. The table below includes the future minimum lease payments under our lease agreements.

The following table summarizes our contractual obligations as of December 31, 2019, excluding the items discussed above related to vendor contracts, purchase commitments and license commitments:

	Total	2020	2021 and 2022	2023 and 2024	2025 and Thereafter
			(in thousands)		
Future minimum lease payments	$ 127,185	$ 2,941	$ 11,026	$ 15,869	$ 97,349
Total contractual obligations	$ 127,185	$ 2,941	$ 11,026	$ 15,869	$ 97,349

Off-Balance Sheet Arrangements

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

ITEM 7A. *QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK*

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to interest rate risk results from the cash equivalents and marketable securities in our investment portfolio. Our primary objectives in managing our investment portfolio are to preserve principal, maintain proper liquidity to meet operating needs and maximize yields. At any time, significant changes in interest rates can affect the fair value of the investment portfolio and its interest earnings. Currently, we do not hedge these interest rate exposures. As of December 31, 2019 and 2018, we had cash, cash equivalents and marketable securities of $400.0 million and $470.6 million, respectively. Our cash equivalents and marketable securities as of December 31, 2019 consisted of money market mutual funds, U.S. government and federal agency securities, certificates of deposit, corporate bonds and equity securities. If market interest rates were to increase immediately and uniformly by 100 basis points, or one percentage point, from levels at December 31, 2019, we estimate that the increase in interest rates would have resulted in a hypothetical decline of $1.9 million in the net fair value of our interest-sensitive securities.

Foreign Currency Exchange Rate Risk

We are exposed to foreign currency exchange rate risk as a result of entering into transactions denominated in currencies other than U.S. dollars, primarily including euros, British pounds, Canadian dollars and Japanese yen. All foreign currency transactions settle on the applicable spot exchange basis at the time such payments are made. Accordingly, an adverse movement in foreign exchange rates between the U.S. dollar and the aforementioned currencies could impact our results of operations and cash flows. Currently, we do not hedge these foreign currency exchange rate exposures. The effect of a hypothetical 10% change in foreign currency exchange rates applicable to our business would not materially harm our business, financial condition or results of operations.

ITEM 8. *FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA*

The financial statements and related financial statement schedules required to be filed are listed in the Index to Consolidated Financial Statements and are incorporated herein.

ITEM 9. *CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE*

None.

ITEM 9A. *CONTROLS AND PROCEDURES*

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2019, our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Under the supervision and with the participation of management, including our principal executive and financial officers, we assessed our internal control over financial reporting as of December 31, 2019, based on criteria for effective internal control over financial reporting established in *Internal Control — Integrated Framework* (2013), issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our management's opinion, we have maintained effective internal control over financial reporting as of December 31, 2019, based on criteria established in the COSO 2013 framework.

The effectiveness of our internal control over financial reporting as of December 31, 2019 has been audited by PricewaterhouseCoopers LLP, our independent registered public accounting firm, as stated in their report which accompanies our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on the Effectiveness of Controls

Control systems, no matter how well conceived and operated, are designed to provide a reasonable, but not an absolute, level of assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. Because of the inherent limitations in any control system, misstatements due to error or fraud may occur and not be detected.

ITEM 9B. *OTHER INFORMATION*

None.

PART III

ITEM 10. *DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE*

The information required by this item will be included in our proxy statement for the 2020 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2019 (2020 Proxy Statement) under the headings “Election of Directors,” “Information about our Executive Officers” “Corporate Governance” and “Delinquent Section 16(a) Reports” and is incorporated herein by reference.

We maintain a code of business conduct and ethics that qualifies as a “code of ethics” under Item 406 of the SEC’s Regulation S-K and applies to each of our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer and controller, or persons performing similar functions. The code of business conduct and ethics is available in the corporate governance section of our corporate website at www.regenxbio.com. Any amendment or waiver of the “code of ethics” provisions of the code of business conduct and ethics for an executive officer or director may be granted only by our Board of Directors or a committee thereof and must be timely disclosed as required by applicable law. We intend to satisfy the disclosure requirements regarding any such amendment or waiver applicable to any principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, in a current report filed with the SEC on Form 8-K or on our corporate website at www.regenxbio.com.

ITEM 11. *EXECUTIVE COMPENSATION*

The information required by this item will be included in our 2020 Proxy Statement under the headings “Corporate Governance,” “Director Compensation” and “Executive Compensation” and is incorporated herein by reference.

ITEM 12. *SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS*

The information required by this item will be included in our 2020 Proxy Statement under the headings “Executive Compensation” and “Security Ownership of Certain Beneficial Owners and Management” and is incorporated herein by reference.

ITEM 13. *CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE*

The information required by this item will be included in our 2020 Proxy Statement under the headings “Certain Relationships and Related Party Transactions” and “Corporate Governance” and is incorporated herein by reference.

ITEM 14. *PRINCIPAL ACCOUNTANT FEES AND SERVICES*

The information required by this item will be included in our 2020 Proxy Statement under the heading “Ratification of Appointment of Independent Registered Public Accounting Firm” and is incorporated herein by reference.

PART IV

ITEM 15. *EXHIBITS, FINANCIAL STATEMENT SCHEDULES*

(a) The following documents are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K:

1. *Financial Statements.* See Index to Consolidated Financial Statements under Item 8 of this Annual Report on Form 10-K.
2. *Financial Statement Schedules.* All schedules have been omitted because the information required to be presented in them is not applicable or is shown in the financial statements or related notes.
3. *Exhibits.* We have filed, or incorporated into this Annual Report on Form 10-K by reference, the exhibits listed on the accompanying Exhibit Index immediately following the financial statements in this Annual Report on Form 10-K.

(b) *Exhibits.* See Item 15(a)(3) above.

(c) *Financial Statement Schedules.* See Item 15(a)(2) above.

ITEM 16. *FORM 10-K SUMMARY*

Not applicable.

REGENXBIO INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of REGENXBIO Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of REGENXBIO Inc. and its subsidiaries (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations and comprehensive income (loss), of stockholders' equity, and of cash flows for each of the three years in the period ended December 31, 2019, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Changes in Accounting Principles

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019 and the manner in which it accounts for revenues from contracts with customers in 2018.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

License revenue- Substantive Termination Penalties

As described in Notes 2 and 9 to the consolidated financial statements, at the inception of each license agreement, management determines the contract term for purposes of applying the requirements of generally accepted accounting policies relevant to revenue recognition. Licenses are generally terminable at the option of the licensee with advance notice to the Company. For each license granted, including licenses granted upon the exercise of license options, management evaluates these termination rights to determine whether a substantive termination penalty would be incurred by the licensee upon termination. If the licensee incurs a substantive termination penalty upon termination, the contract term for revenue recognition purposes is generally equal to the stated term of the license, which is the life of the underlying licensed patents. Alternatively, if the licensee does not incur a substantive termination penalty upon termination, the contract term for revenue recognition purposes may be shorter than the stated term of the license, in which case the termination rights may be accounted for as contract renewal options. The determination of whether a substantive termination penalty is associated with the termination rights requires significant judgment. In making this determination, management considers, among other things, the nature of the intellectual property rights that would be returned to the Company upon termination, including the exclusivity of the licensed rights and the stage of development of the licensed products, the payment terms, including the amount and timing of nonrefundable or guaranteed payments, and the business purpose of the termination rights granted to the licensee. Generally, the most significant judgment in determining whether a substantive termination penalty exists is related to the amount of any up-front or guaranteed non-refundable payments relative to the amount of annual payments that may be avoided by the licensee upon termination of the license. Management considers all of the facts and circumstances relevant to each license when making this determination. The Company's consolidated license and royalty revenue was $35.2 million for the year ended December 31, 2019, of which license revenue makes up a significant portion.

The principal considerations for our determination that performing procedures relating to license revenue, specifically substantive termination penalties, is a critical audit matter are there was significant judgment by management in determining whether each license granted, including licenses granted upon the exercise of license options, had substantive termination penalties used to determine the contract term for revenue recognition. This in turn led to significant auditor, judgment, subjectivity and effort in performing procedures to evaluate the audit evidence obtained relating to management's determination of the existence of a substantive termination penalty in license revenue agreements.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the revenue recognition process, including controls over the determination of the existence of a substantive termination penalty in license revenue agreements. These procedures also included, among others, evaluating and testing, for a sample of license revenue contracts, management's process for determining whether a licensee incurs a substantive termination penalty upon termination, which included evaluating (i) the nature of the license, (ii) the payment terms, (iii) the business purpose of contract terms that include termination rights, and (iv) the impact of contract cancellation on other performance obligations, if any, in the contract.

/s/ PricewaterhouseCoopers LLP

McLean, Virginia
February 26, 2020

We have served as the Company's auditor since 2015.

REGENXBIO INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except per share data)

	December 31, 2019	December 31, 2018
Assets		
Current assets		
Cash and cash equivalents	$ 69,514	$ 75,561
Marketable securities	226,696	244,200
Accounts receivable	38,148	8,587
Prepaid expenses	6,475	5,734
Other current assets	4,199	3,831
Total current assets	345,032	337,913
Marketable securities	103,785	150,819
Accounts receivable	4,155	23,012
Property and equipment, net	28,973	28,702
Operating lease right-of-use assets	10,078	—
Restricted cash	1,330	1,053
Other assets	4,555	2,315
Total assets	$ 497,908	$ 543,814
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 6,409	$ 4,412
Accrued expenses and other current liabilities	24,846	17,164
Deferred revenue	—	600
Operating lease liabilities	2,421	—
Total current liabilities	33,676	22,176
Deferred revenue	3,333	3,333
Operating lease liabilities	8,874	—
Deferred rent	—	1,098
Financing lease obligations	—	5,854
Other liabilities	1,828	2,505
Total liabilities	47,711	34,966
Commitments and contingencies (Note 7)		
Stockholders' equity		
Preferred stock; $0.0001 par value; 10,000 shares authorized, and no shares issued and outstanding at December 31, 2019 and December 31, 2018	—	—
Common stock; $0.0001 par value; 100,000 shares authorized at December 31, 2019 and December 31, 2018; 36,992 and 36,120 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively	4	4
Additional paid-in capital	627,810	592,580
Accumulated other comprehensive income (loss)	205	(720)
Accumulated deficit	(177,822)	(83,016)
Total stockholders' equity	450,197	508,848
Total liabilities and stockholders' equity	$ 497,908	$ 543,814

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

REGENXBIO INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)
(in thousands, except per share data)

	Years Ended December 31,		
	2019	2018	2017
Revenues			
License and royalty revenue	$ 35,233	$ 218,505	$ 10,385
Other revenues	—	—	8
Total revenues	35,233	218,505	10,393
Operating Expenses			
Cost of revenues	8,241	9,640	1,709
Research and development	124,185	83,873	57,224
General and administrative	51,815	36,850	27,229
Other operating expenses (income)	(10)	42	116
Total operating expenses	184,231	130,405	86,278
Income (loss) from operations	(148,998)	88,100	(75,885)
Other Income			
Interest income from licensing	2,951	8,946	—
Investment income	48,559	7,070	2,716
Total other income	51,510	16,016	2,716
Income (loss) before income taxes	(97,488)	104,116	(73,169)
Income Tax Benefit (Expense)	2,755	(4,179)	—
Net income (loss)	$ (94,733)	$ 99,937	$ (73,169)
Other Comprehensive Income (Loss)			
Unrealized gain (loss) on available-for-sale securities, net	885	(5)	(682)
Total other comprehensive income (loss)	885	(5)	(682)
Comprehensive income (loss)	$ (93,848)	$ 99,932	$ (73,851)
Net income (loss) applicable to common stockholders	$ (94,733)	$ 99,937	$ (73,169)
Net income (loss) per share:			
Basic	$ (2.58)	$ 2.99	$ (2.45)
Diluted	$ (2.58)	$ 2.73	$ (2.45)
Weighted-average common shares outstanding:			
Basic	36,690	33,427	29,878
Diluted	36,690	36,648	29,878

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

REGENXBIO INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock Shares	Common Stock Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balances at December 31, 2016	26,477	$ 3	$ 276,354	$ (33)	$ (114,587)	$ 161,737
Issuance of common stock upon public offering, net of transaction costs of $5,738	4,255	—	81,489	—	—	81,489
Exercise of stock options	516	—	2,493	—	—	2,493
Issuance of common stock under employee stock purchase plan	48	—	556	—	—	556
Stock-based compensation expense	—	—	10,605	—	—	10,605
Unrealized loss on available-for-sale securities, net	—	—	—	(682)	—	(682)
Net loss	—	—	—	—	(73,169)	(73,169)
Balances at December 31, 2017	31,295	3	371,497	(715)	(187,756)	183,029
Adoption of ASU 2014-09 (Topic 606)	—	—	—	—	4,803	4,803
Issuance of common stock upon public offering, net of transaction costs of $12,728	3,105	1	189,096	—	—	189,097
Exercise of stock options	1,683	—	14,499	—	—	14,499
Issuance of common stock under employee stock purchase plan	37	—	847	—	—	847
Stock-based compensation expense	—	—	16,641	—	—	16,641
Unrealized loss on available-for-sale securities, net	—	—	—	(5)	—	(5)
Net income	—	—	—	—	99,937	99,937
Balances at December 31, 2018	36,120	4	592,580	(720)	(83,016)	508,848
Adoption of ASU 2016-02 (Topic 842)	—	—	—	—	(33)	(33)
Adoption of ASU 2018-02	—	—	—	40	(40)	—
Vesting of restricted stock units	40	—	—	—	—	—
Exercise of stock options	796	—	7,062	—	—	7,062
Issuance of common stock under employee stock purchase plan	36	—	1,314	—	—	1,314
Stock-based compensation expense	—	—	26,854	—	—	26,854
Unrealized gain on available-for-sale securities, net	—	—	—	885	—	885
Net loss	—	—	—	—	(94,733)	(94,733)
Balances at December 31, 2019	36,992	$ 4	$ 627,810	$ 205	$ (177,822)	$ 450,197

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

REGENXBIO INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2019	2018	2017
Cash flows from operating activities			
Net income (loss)	$ (94,733)	$ 99,937	$ (73,169)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities			
Stock-based compensation expense	26,854	16,641	10,605
Net amortization of premiums and accretion of discounts on marketable debt securities	(1,196)	755	1,815
Depreciation and amortization	7,152	3,982	2,686
Net realized losses (gains) on sales and maturities of marketable securities	(5,990)	39	(479)
Imputed interest income from licensing	(2,951)	(8,946)	—
Unrealized gains on marketable equity securities	(31,784)	—	—
Non-cash consideration received for licenses granted	—	—	(420)
Other non-cash adjustments	268	14	73
Changes in operating assets and liabilities			
Accounts receivable	(8,622)	(16,803)	561
Prepaid expenses	(973)	(400)	(3,559)
Other current assets	(499)	(2,069)	(402)
Operating lease right-of-use assets	2,431	—	—
Other assets	(2,694)	(1,453)	(135)
Accounts payable	1,528	(218)	2,621
Accrued expenses and other current liabilities	6,882	7,582	1,897
Deferred revenue	(600)	3,933	—
Operating lease liabilities	(2,255)	—	—
Deferred rent	—	(32)	(86)
Other liabilities	(523)	1,686	—
Net cash provided by (used in) operating activities	(107,705)	104,648	(57,992)
Cash flows from investing activities			
Purchases of marketable securities	(190,735)	(445,829)	(68,634)
Maturities of marketable securities	289,994	179,749	70,224
Sales of marketable securities	6,020	—	780
Purchases of property and equipment	(11,720)	(13,278)	(7,160)
Net cash provided by (used in) investing activities	93,559	(279,358)	(4,790)
Cash flows from financing activities			
Proceeds from exercise of stock options	7,062	14,499	2,493
Proceeds from issuance of common stock under employee stock purchase plan	1,314	847	556
Proceeds from public offerings of common stock, net of underwriting discounts and commissions	—	189,716	81,994
Issuance costs for public offerings of common stock	—	(619)	(445)
Net cash provided by financing activities	8,376	204,443	84,598
Net increase (decrease) in cash and cash equivalents and restricted cash	(5,770)	29,733	21,816
Cash and cash equivalents and restricted cash			
Beginning of period	76,614	46,881	25,065
End of period	$ 70,844	$ 76,614	$ 46,881
Supplemental cash flow information			
Cash paid for income taxes	$ 904	$ 3,443	$ —
Supplemental disclosures of non-cash investing and financing activities			
Additions to property and equipment through accounts payable and accrued expenses	$ 1,572	$ —	$ 254
Assets acquired under financing lease obligation	$ —	$ 5,854	$ —
Non-cash consideration received for licenses granted	$ —	$ —	$ 420

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

REGENXBIO INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business

REGENXBIO Inc. (the Company) is a clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy. The Company's proprietary adeno-associated virus (AAV) gene delivery platform (NAV Technology Platform) consists of exclusive rights to over 100 novel AAV vectors, including AAV7, AAV8, AAV9 and AAVrh10. The NAV® Technology Platform is being applied by the Company, as well as by third-party licensees (NAV Technology Licensees), in the development of a broad pipeline of product candidates in multiple therapeutic areas. Additionally, the NAV Technology Platform is currently being applied in one commercially available product, Zolgensma®, which is marketed by a NAV Technology Licensee. The Company was formed in 2008 in the State of Delaware and is headquartered in Rockville, Maryland.

Liquidity and Risks

As of December 31, 2019, the Company had generated an accumulated deficit of $177.8 million since inception. As the Company has incurred cumulative losses since inception, transition to recurring profitability is dependent upon achieving a level of revenues adequate to support the Company's cost structure, which depends heavily on the successful development, approval and commercialization of its product candidates. The Company may never achieve recurring profitability, and unless and until it does, the Company will continue to need to raise additional capital, to the extent possible. As of December 31, 2019, the Company had cash, cash equivalents and marketable securities of $400.0 million, which management believes is sufficient to fund operations for at least the next 12 months from the date these consolidated financial statements were issued.

The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, development by the Company or its competitors of technological innovations, risks of failure of clinical trials, dependence on key personnel, protection of proprietary technology, compliance with government regulations and ability to transition from clinical manufacturing to the commercial production of products.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (GAAP) and include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Foreign Currency Transactions

The functional currency of the Company and its consolidated subsidiaries is the U.S. dollar. Transaction gains and losses that arise from exchange rate fluctuations on transactions denominated in a currency other than the U.S. dollar are included in results of operations as incurred.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Actual results could differ materially from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these consolidated financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including: expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the consolidated financial statements. Significant estimates are used in the following areas, among others: license and royalty revenue, stock-based compensation expense, accrued research and development expenses and other accrued liabilities, income taxes and the fair value of financial instruments.

Reclassifications

Certain amounts reported in prior periods have been reclassified to conform to current period financial statement presentation. These reclassifications are not material and have no effect on previously reported financial position, results of operations and cash flows.

Segment and Geographical Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker (CODM), or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's CODM, the Chief Executive Officer, views its operations and manages its business as one operating segment.

The Company's revenues primarily consist of license and royalty revenue. For the year ended December 31, 2019, 90% of the Company's revenue was attributed to the U.S. For the year ended December 31, 2018, 99% of the Company's revenue was attributed to the U.S. For the year ended December 31, 2017, 96% of the Company's revenue was attributed to the U.S. Country of origin for license revenue is determined based on the country of domicile of the licensee. Country of origin for royalty revenue is determined based on the location of the underlying net sales of licensed products. The substantial majority of the Company's assets currently reside in the U.S.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents.

Restricted Cash

Restricted cash includes money market mutual funds used to collateralize irrevocable letters of credit as required by the Company's lease agreements. The following table provides a reconciliation of cash and cash equivalents and restricted cash as reported on the consolidated balance sheets to the total of these amounts as reported at the end of the period in the consolidated statements of cash flows (in thousands):

	December 31, 2019	December 31, 2018	December 31, 2017
Cash and cash equivalents	$ 69,514	$ 75,561	$ 46,656
Restricted cash	1,330	1,053	225
Total cash and cash equivalents and restricted cash	$ 70,844	$ 76,614	$ 46,881

Marketable Securities

Marketable securities consist of available-for-sale debt securities and equity securities and are carried at fair value. Marketable debt securities with remaining maturity dates exceeding 12 months which are not intended to be sold prior to maturity for use in current operations are classified as non-current assets. Marketable equity securities are classified as current assets.

Unrealized gains and losses on available-for-sale debt securities, net of any related tax effects, are excluded from results of operations and are included in other comprehensive income (loss) and reported as a separate component of stockholders' equity until realized. The Company uses the aggregate portfolio approach to release the tax effects of unrealized gains and losses on available-for-sale debt securities in accumulated other comprehensive income (loss). Purchase premiums and discounts on marketable debt securities are amortized or accreted into the cost basis over the life of the related security as adjustments to the yield using the effective-interest method. Interest income is recognized when earned. Unrealized gains and losses on marketable equity securities are included in results of operations as investment income. Realized gains and losses from the sale or maturity of marketable securities are based on the specific identification method and are included in results of operations as investment income.

A decline in the fair value below cost of available-for-sale debt securities that is deemed other-than-temporary is charged to results of operations, resulting in the establishment of a new cost basis for the security. The Company regularly evaluates whether declines in the fair value of its debt securities below their cost are other-than-temporary. The evaluation includes consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities and whether it is more likely than not that the Company will be required to sell the securities before the recovery of their amortized cost basis. The Company has not recorded any impairment of available-for-sale debt securities which was deemed to be to be other-than-temporary.

Concentrations of Credit Risk and Off-balance Sheet Risk

Cash and cash equivalents, marketable debt securities and accounts receivable are financial instruments that are potentially subject to concentrations of credit risk. The Company's cash and cash equivalents are deposited in accounts at multiple financial institutions, and amounts may exceed federally insured limits. The Company believes it is not exposed to significant credit risk due to the financial strength of the depository institutions in which the cash and cash equivalents are held. The Company's marketable debt securities consist of investment grade securities and may be subject to concentrations of credit risk. The Company has adopted an investment policy which limits potential concentrations of investments and establishes minimum acceptable credit ratings, thereby reducing credit risk exposure. The Company believes that it is not exposed to significant credit risk related to accounts receivable due to the credit quality and history of collections from its significant customers. The Company is unaware of any concentrations of credit risk related to accounts receivable from significant customers with deteriorated credit quality. The Company has no financial instruments with off-balance sheet risk of loss.

The following table summarizes those customers who represented at least 10% of revenue or accounts receivable, current and non-current, for the periods presented:

	Revenue			Accounts Receivable	
	Years Ended December 31,			December 31,	
	2019	2018	2017	2019	2018
Customer A	69%	81%	68%	28%	*
Customer B	*	16%	*	62%	82%
Customer C	13%	*	*	*	*
Customer D	10%	*	*	*	*

* Represented less than 10%

Accounts Receivable

Accounts receivable primarily consist of consideration due to the Company resulting from its license agreements with NAV Technology Licensees. Accounts receivable include amounts invoiced to licensees as well as rights to consideration which have not yet been invoiced, including unbilled royalties, and for which payment is conditional solely upon the passage of time. If a licensee elects to terminate a license prior to the end of the license term, the licensed intellectual property is returned to the Company and any accounts receivable from the licensee which are not contractually payable to the Company are charged off as a reduction of license revenue in the period of the termination. Accounts receivable which are not expected to be received by the Company within 12 months from the reporting date are stated net of a discount to present value and recorded as non-current assets on the consolidated balance sheets. The present value discount is recognized as a reduction of revenue in the period in which the accounts receivable are initially recorded and is accreted as interest income from licensing over the term of the receivables.

Accounts receivable are stated net of an allowance for doubtful accounts, if deemed necessary based on the Company's evaluation of collectability using specific identification of account balances, the credit profile and financial condition of its customers and historical information regarding write-offs. Account balances are charged off against the allowance when the potential for recovery is considered remote. The Company did not record an allowance for doubtful accounts as of December 31, 2019 or 2018.

Leases

Effective January 1, 2019, the Company adopted Accounting Standards Update (ASU) 2016-02, *Leases* (Topic 842) which supersedes the lease accounting requirements in Accounting Standards Codification (ASC) 840, *Leases* (Topic 840). Please refer to Recent Accounting Pronouncements below for additional information on the adoption of Topic 842 and the impact upon adoption to the Company's consolidated financial statements.

Under Topic 842, the Company classifies its leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the Company. Lease classification is evaluated at the inception of the lease agreement. Regardless of classification, the Company records a right-of-use asset and a lease liability for all leases with a term greater than 12 months. All of the Company's leases as of December 31, 2019 have been classified as operating leases. Operating lease expense is recognized on a straight-line basis over the term of the lease, with the exception of variable lease expenses which are recognized as incurred.

The Company identifies leases in its contracts if the contract conveys the right to control the use of identified property, plant or equipment for a period of time in exchange for consideration. The Company does not allocate lease consideration between lease and nonlease components and records a lease liability equal to the present value of the remaining fixed consideration under the lease. The interest rates implicit in the Company's leases are generally not readily determinable. Accordingly, the Company uses its estimated incremental borrowing rate at the commencement date of the lease to determine the present value discount of the lease liability. The Company estimates its incremental borrowing rate for each lease based on an evaluation of its expected credit rating and the prevailing market rates for collateralized debt in a similar economic environment with similar payment terms and maturity dates commensurate with the term of the lease. The right-of-use asset for each lease is equal to the lease liability, adjusted for unamortized initial direct costs and lease incentives and prepaid or accrued rent. Initial direct costs of entering into a lease are included in the right-of-use asset and amortized as lease expense over the term of the lease. Lease incentives, such as tenant improvements allowances, are recorded as a reduction of the right-of-use asset and amortized as a reduction of lease expense over the term of the lease. The Company excludes options to extend or terminate leases from the calculation of the lease liability unless it is reasonably certain the option will be exercised.

Property and Equipment

Property and equipment is stated at cost less accumulated depreciation and amortization. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation and amortization is calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

	Estimated Useful Life
Computer equipment and software	3 years
Lab equipment	5 years
Furniture and fixtures	5 years
Leasehold improvements	Shorter of lease term of estimated useful life

Certain estimated construction costs incurred and reported by the Company's landlord at 9800 Medical Center Drive through December 31, 2018 were recorded as property and equipment, with a corresponding financing lease obligation, on the consolidated balance sheets. Please refer to Note 6 for further information on the Company's lease agreements.

Impairment of Long-lived Assets

The Company evaluates its long-lived assets for impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to estimated future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets. No impairment losses were recorded during the years ended December 31, 2019, 2018 and 2017.

Non-marketable Equity Securities

The Company's non-marketable equity securities do not have readily determinable fair values and consist of equity investments in other entities in which the Company's ownership interest is below 20% and the Company does not have significant influence over the operations of the entity. The Company's non-marketable equity securities are measured at cost less impairment, adjusted for observable price changes for identical or similar investments of the same issuer. Please refer to Note 4 for further information on non-marketable equity securities.

Fair Value of Financial Instruments

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. ASC 820, *Fair Value Measurements and Disclosures*, establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.
- Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The fair values of the Company's Level 2 instruments are based on quoted market prices or broker or dealer quotations for similar assets. These investments are initially valued at the transaction price and subsequently valued utilizing third party pricing providers or other market observable data. Please refer to Note 4 for further information on the fair value measurement of the Company's financial instruments.

Revenue Recognition

Effective January 1, 2018, the Company adopted ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in ASC 605, *Revenue Recognition* (Topic 605). The Company's financial results for periods ending after January 1, 2018 are presented in accordance with the requirements of Topic 606, while prior period amounts have not been adjusted and continue to be reported in accordance with Topic 605. Please refer to Recent Accounting Pronouncements below for additional information on the adoption of Topic 606.

Topic 606 requires entities to recognize revenue when control of the promised goods or services is transferred to customers at an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. The following five steps are performed to determine the appropriate revenue recognition for arrangements within the scope of Topic 606: (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 entity satisfies the performance obligations.

The Company applies the five-step model to contracts that are within the scope of Topic 606 only when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, for contracts within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determine those that are performance obligations and whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to respective performance obligations when (or as) the respective performance obligations are satisfied.

The Company evaluates its contracts with customers for the presence of significant financing components. If a significant financing component is identified in a contract and provides a financing benefit to the customer, the transaction price for the contract is adjusted to account for the financing portion of the arrangement, which is recognized as interest income over the financing term using the effective interest method. In determining the appropriate interest rates for significant financing components, the Company evaluates the credit profile of the customer and prevailing market interest rates and selects an interest rate in which it believes would be charged to the customer in a separate financing arrangement over a similar financing term.

License and Royalty Revenue

The Company licenses its NAV Technology Platform to other biotechnology and pharmaceutical companies. The terms of the licenses vary, and licenses may be exclusive or non-exclusive and may be sublicensable by the licensee. Licenses may grant intellectual property rights for purposes of internal and preclinical research and development only, or may include the rights, or options to obtain future rights, to commercialize drug therapies for specific diseases using the Company's NAV Technology Platform. License agreements generally have a term at least equal to the life of the underlying patents, but are terminable at the option of the licensee. Consideration payable to the Company under its license agreements may include: (i) up-front and annual fees, (ii) option fees to acquire additional licenses, (iii) milestone payments based on the achievement of certain development and sales-based milestones by licensees, (iv) sublicense fees and (v) royalties on sales of licensed products.

The Company's license agreements are accounted for as contracts with customers within the scope of Topic 606. At the inception of each license agreement, the Company determines the contract term for purposes of applying the requirements of Topic 606. Licenses are generally terminable at the option of the licensee with advance notice to the Company. For each license granted, including licenses granted upon the exercise of license options, the Company evaluates these termination rights to determine whether a substantive termination penalty would be incurred by the licensee upon termination. If the licensee incurs a substantive termination penalty upon termination, the contract term for revenue recognition purposes is generally equal to the stated term of the license, which is the life of the underlying licensed patents. Alternatively, if the licensee does not incur a substantive termination penalty upon termination, the contract term for revenue recognition purposes may be shorter than the stated term of the license, in which case the termination rights may be accounted for as contract renewal options. The determination of whether a substantive termination penalty is associated with the termination rights requires significant judgment. In making this determination, the Company considers, among other things, the nature of the intellectual property rights that would be returned to the Company upon termination, including the exclusivity of the licensed rights and the stage of development of the licensed products, the payment terms, including the amount and timing of non-refundable or guaranteed payments, and the business purpose of the termination rights granted to the licensee. Generally, the most significant judgment in determining whether a substantive termination penalty exists relates to the amount of any up-front or guaranteed non-refundable payments relative to the amount of annual payments that may be avoided by the licensee upon termination of the license. The Company considers all of the facts and circumstances relevant to each license when making this determination.

Performance obligations under the Company's license agreements may include (i) the delivery of intellectual property licenses and (ii) options granted to licensees to acquire additional licenses to the extent the options represent material rights to the licensee. At the inception of each license agreement which contains options for the licensee to acquire additional licenses, or contract renewal options, the Company evaluates the options to determine whether they provide material rights to the licensee. In making this determination, the Company considers whether the options are priced at a discount to the standalone selling price for the underlying licenses. If an option is priced at a discount to the standalone selling price for the underlying license, the option is considered to be a material right to the licensee and is accounted for as a separate performance obligation under the current license agreement.

The Company evaluates the transaction price of its license agreements at the inception of each agreement and at each reporting date. The transaction price includes the fixed consideration payable to the Company during the contract term, as well as any variable consideration to the extent that it is probable that a significant reversal of revenue will not occur in the future. Fixed consideration under the license agreements includes up-front and annual fees payable during the contract term. Variable consideration under the license agreements includes development and sales-based milestone payments, sublicense fees and royalties on sales of licensed products. Consideration contingent upon the exercise of options by a licensee is excluded from the transaction price and not accounted for as part of the license agreement until the option is exercised.

The transaction price for each license agreement is allocated to the underlying performance obligations and recognized as revenue when the performance obligations are satisfied. Consideration allocated to performance obligations for the delivery of an intellectual property license is recognized as revenue in full upon the delivery of the license to the licensee. Consideration allocated to performance obligations for license options is recognized as revenue in full upon the earlier of the option exercise or expiration. The exercise of a license option by a licensee is accounted for as a new license for revenue recognition purposes.

Up-front and annual licenses fees payable to the Company over the contract term of each license are included in the transaction price, and the portion of this consideration that is allocated to the performance obligation for the delivery of the intellectual property license is recognized as revenue in full upon the delivery of the license to the licensee. If annual license fees are payable to the Company in periods beyond 12 months from the delivery of the license, a significant financing component is deemed to exist which provides a financing benefit to the licensee. If a significant financing component is identified, the Company adjusts the transaction price for the license to include only the present value of the annual license fees payable to the Company over the contract term. The discounted portion of the license fees is recognized as interest income from licensing over the financing period of the license.

Development milestone payments are payable to the Company upon the achievement of specified development milestones by licensees. At the inception of each license agreement that contains development milestone payments, the Company evaluates whether the milestones are considered probable of achievement and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal will not occur in the future, milestone payments are included in the transaction price and recognized as revenue upon the delivery of the license. Milestone payments contingent on the achievement of development milestones that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved and are excluded from the transaction price until the milestone is achieved. At each reporting date, the Company re-evaluates the probability of achievement of each outstanding development milestone and, if necessary, adjusts the transaction price for any milestones for which the probability of achievement has changed due to current facts and circumstances. Any such adjustments are recorded on a cumulative catch-up basis and recognized as revenue in the period of the adjustment.

Royalties on sales of licensed products, sales-based milestone payments and sublicense fees based on the receipt of certain fees by licensees from any sublicensees are excluded from the transaction price of each license and recognized as revenue in the period that the related sales or sublicenses occur, provided that the associated license has been delivered to the licensee.

Royalty revenue to date consists of royalties on net sales of Zolgensma, which is a licensed product under the Company's March 2014 license agreement, as amended, with AveXis, Inc. (AveXis) (a wholly owned subsidiary of Novartis AG (Novartis)) for the development and commercialization of treatments for spinal muscular atrophy (SMA). The Company recognizes royalty revenue from net sales of Zolgensma in the period in which the underlying products are sold by AveXis, which in certain cases may require the Company to estimate royalty revenue for periods of net sales which have not yet been reported to the Company. Sales-based milestone payments related to net sales of Zolgensma are recognized as royalty revenue in the period in which the milestone is achieved.

The Company receives payments from licensees based on the billing schedules established in each license agreement. Amounts recognized as revenue which have not yet been received from licensees, including unbilled royalties, are recorded as accounts receivable when the Company's rights to the consideration are conditional solely upon the passage of time. Amounts recognized as revenue which have not yet been received from licensees are recorded as contract assets when the Company's rights to the consideration are not unconditional. Contract assets are recorded as other current assets on the consolidated balance sheets. If a licensee elects to terminate a license prior to the end of the license term, the licensed intellectual property is returned to the Company and any consideration recorded as accounts receivable or contract assets which is not contractually payable by the licensee is charged off as a reduction of license revenue in the period of the termination. Amounts received by the Company prior to the delivery of underlying performance obligations are deferred and recognized as revenue upon the satisfaction of the performance obligations by the Company. Deferred revenue which is not expected to be recognized within 12 months from the reporting date is recorded as non-current on the consolidated balance sheets.

Other Revenues

Other revenues consist of grant revenue generated through research and development grant programs offered by the European Union. Grant revenue is recognized in the period in which the related costs are incurred and the related services are rendered by the Company. As of December 31, 2017, all grant programs were completed.

Cost of Revenues

Cost of revenues consists primarily of sublicense fees, milestone payments and royalties on net sales of licensed products as specified in the Company's agreements with its licensors. Sublicense fees are based on a percentage of license fees received by the Company from NAV Technology Licensees and are recognized in the period that the underlying revenue is recognized. Milestone payments are payable to licensors upon the achievement of specified milestones by NAV Technology Licensees and are recognized in the period the milestone is achieved or deemed probable of achievement. Royalties are based on a percentage of net sales of licensed products by NAV Technology Licensees and are recognized in the period that the underlying sales occur. Amounts which are payable to licensors in periods beyond 12 months from the reporting date are recorded as non-current liabilities on the consolidated balance sheets.

Research and Development Expenses

Research and development costs are expensed as incurred. Advance payments for goods or services related to research and development activities are deferred and expensed as the goods are delivered or the related services are performed. Research and development costs include salaries, benefits and other personnel costs, laboratory and facilities costs and other overhead costs allocated to research and development activities. Additionally, research and development costs include goods and services associated

with preclinical research, clinical trial activities, manufacturing-related activities, regulatory and other related services performed by third-parties. At the end of each reporting period, the Company compares payments made to third-party service providers to the estimated expenses incurred based on the services provided and progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the estimated expenses incurred, the Company may record net prepaid or accrued research and development expenses relating to these costs.

Up-front fees incurred in obtaining technology licenses, as well as milestone payments to licensors, are charged to research and development expense as incurred if the technology licensed has no alternative future use.

Collaborative Arrangements

The Company evaluates its collaboration arrangements to determine whether they are within the scope of ASC 808, *Collaborative Arrangements* (Topic 808). Such arrangements are within the scope of Topic 808 if they involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This evaluation is performed throughout the life of the arrangement based on any changes in the roles and responsibilities of the parties under the arrangement. For arrangements within the scope of Topic 808, the Company identifies the various transactions with the counterparty and determines if any unit of account is more reflective of a transaction with a customer and therefore should be accounted for within the scope of Topic 606. For transactions that are accounted for pursuant to Topic 808, an appropriate method of recognition and presentation is determined and consistently applied. Amounts that are owed to collaboration partners for development activities are recognized as research and development expenses as incurred by the collaboration partner. Amounts received from collaboration partners for development activities are recognized as a reduction of research and development expenses as incurred by the Company. The Company does not have any collaborative arrangements containing transactions with customers accounted for under Topic 606.

Stock-based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC 718, *Compensation—Stock Compensation*. ASC 718 requires all stock-based awards to employees and nonemployees to be recognized in the consolidated statement of operations and comprehensive income (loss) based on the grant date fair value of the awards. The Company's stock-based awards include stock options granted to employees and nonemployees, restricted stock units and shares issued under its employee stock purchase plan.

The Company's stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and nonemployees with service-based vesting conditions is recognized on a straight-line basis based on the estimated grant date fair value over the requisite service period of the award, which is generally the vesting term. Compensation expense related to awards to employees and nonemployees with performance-based vesting conditions is recognized based on the estimated grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

The Company has elected to not estimate forfeitures of stock-based awards and to account for forfeitures as they occur.

The Company estimates the fair value of its stock option awards using the Black-Scholes option-pricing model, which requires the input of subjective assumptions, including (i) the fair value of the underlying common stock, (ii) the expected stock price volatility, (iii) the expected term of the award, (iv) the risk-free interest rate and (v) expected dividends. The Company does not have sufficient historical and implied volatility data for its common stock necessary to estimate the expected the volatility of its common stock over a period of time commensurate with the expected term of its stock option awards. As a result, the Company estimates expected volatility based on the historical volatility of both its common stock and the common stock of a selected peer group of similar publicly traded companies for which sufficient historical volatility data is available. Due to the lack of historical volatility data for its common stock, the Company places a higher weight on the historical volatility of the selected peer group in estimating expected volatility. The Company computes the historical volatility data using the daily closing prices for the selected companies' shares during a period equivalent to the expected term of the stock option awards. For the purpose of identifying the selected peer group companies, the Company considers characteristics such as enterprise value, risk profiles, position within the industry and length of historical share price information. The Company plans to continue using historical peer group volatility data as an input to estimate expected volatility until a sufficient amount of historical volatility data for its common stock becomes available. The Company estimates the expected term of its employee stock options using the "simplified" method, whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the option due to its lack of sufficient historical data. For stock options granted to nonemployees, the Company uses the contractual term of the award rather than expected term to estimate the fair value of the award.

The Company estimates the risk-free interest rates for periods within the expected term of its options based on the rates of U.S. Treasury securities with maturity dates commensurate with the expected term of the associated awards. The Company has never paid and does not expect to pay dividends in the foreseeable future.

The Company estimates the fair value of restricted stock units based on the fair value of the Company's common stock on the date of the grant.

Income Taxes

Income taxes are recorded in accordance with ASC 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances.

The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2019 and 2018, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive income (loss).

Net Income (Loss) Per Share

Basic net income (loss) per share is calculated by dividing net income (loss) applicable to common stockholders by the weighted-average common shares outstanding during the period, without consideration for common stock equivalents. Diluted net income (loss) per share is calculated by adjusting the weighted-average common shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. Contingently convertible shares in which conversion is based on non-market-priced contingencies are excluded from the calculations of both basic and diluted net income (loss) per share until the contingency has been fully met. For purposes of the diluted net income (loss) per share calculation, common stock equivalents are excluded from the calculation of diluted net income (loss) per share if their effect would be anti-dilutive.

Comprehensive Income (Loss)

The Company's comprehensive income (loss) includes its net income (loss) as well as net unrealized gains and losses on available-for-sale securities, net of income tax effects and reclassification adjustments for realized gains and losses.

Recent Accounting Pronouncements

Adoption of ASU 2016-02, Leases

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02, *Leases* (Topic 842) which supersedes the lease accounting requirements in ASC 840, *Leases* (Topic 840). Effective January 1, 2019, the Company adopted Topic 842 using the modified retrospective transition method. Under this method, the Company applied Topic 842 to all leases in effect as of, or entered into after, January 1, 2019 and recorded the cumulative impact of the adoption as an adjustment to its accumulated deficit on January 1, 2019. The Company's consolidated financial statements for periods ending after January 1, 2019 are presented in accordance with the requirements of Topic 842, while comparative prior period amounts have not been adjusted and continue to be reported in accordance with Topic 840. Please refer to Leases above for a description of the Company's lease accounting policies upon the adoption on Topic 842.

The Company elected certain practical expedients allowed by Topic 842 for transition purposes, including the package of practical expedients which permitted the Company to not reassess lease identification, classification and initial direct costs under Topic 842 for leases that commenced prior to January 1, 2019. Additionally, the Company elected the practical expedient allowed for transition purposes to use hindsight in determining the terms of leases that commenced prior to January 1, 2019.

Upon the adoption of Topic 842, the Company recorded operating lease right-of-use assets of $7.4 million and operating lease liabilities of $8.4 million for its leases which were in effect and had commenced prior to January 1, 2019 and had original lease terms of more than 12 months. The Company also derecognized current and non-current deferred rent liabilities of $1.4 million and prepaid expenses, other current assets and other assets of $0.4 million upon the adoption of Topic 842. Additionally, upon the adoption of Topic 842, the Company derecognized $5.9 million of property and equipment and $5.9 million of financing lease obligations related to construction-in-progress at 9800 Medical Center Drive, as the Company does not control the building during the construction period under the requirements of Topic 842. The lease term for the facility at 9800 Medical Center Drive does not commence until certain construction is completed by the landlord and the building is delivered to the Company. The right-of-use assets and lease liabilities related to the facility at 9800 Medical Center Drive will not be recognized on the Company's consolidated balance sheets until the commencement date of the lease, which is expected to occur in 2020.

The cumulative impact of the adoption of Topic 842 resulted in an increase in accumulated deficit of less than $0.1 million on January 1, 2019. The adoption of Topic 842 did not have a material impact on the Company's results of operations for year ended December 31, 2019, nor does the Company believe it will have a material impact on future results of operations based on its current leasing arrangements.

Other Recently Adopted Accounting Pronouncements

In November 2018, the FASB issued ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606*. The standard clarifies that certain transactions between participants of a collaborative arrangement should be accounted for as revenue under Topic 606 when the counterparty in the collaborative arrangement is a customer in the context of a unit of account. Additionally, the standard precludes entities from presenting consideration received from a participant in a collaborative arrangement with revenue recognized under Topic 606 if the participant is not a customer. The Company early adopted this standard effective July 1, 2019 and applied the standard retrospectively to all relevant contracts that were not completed as of the date of adoption. As of July 1, 2019, the Company had no contracts within the scope of Topic 808, thus the adoption of this standard required no cumulative-effect adjustments and did not have a material impact on the Company's financial position or results of operations.

In February 2018, the FASB issued ASU 2018-02, *Income Statement—Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income*, which amends the previous guidance on comprehensive income to provide an option for an entity to reclassify the stranded tax effects of the Tax Cuts and Jobs Act of 2017 (the TCJA) that was signed into law in December 2017 from accumulated other comprehensive income directly to retained earnings. The stranded tax effects result from the remeasurement of deferred tax assets and liabilities which were originally recorded in comprehensive income but whose remeasurement is reflected in the income statement. The Company adopted this standard effective January 1, 2019, and upon adoption recorded a cumulative adjustment of less than $0.1 million to reclassify the stranded tax effects of unrealized gains and losses on available-for-sale securities from accumulated other comprehensive income (loss) to accumulated deficit. The adoption of this standard did not have a material impact on the Company's financial position or results of operations.

In April 2017, the FASB issued ASU 2017-08, *Receivables—Nonrefundable Fees and Other Costs (Subtopic 310-20)*, which amends the required amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period for the premium to the earliest call date. The Company adopted this standard effective January 1, 2019. The adoption of this standard required no cumulative-effect adjustments and did not have a material impact on the Company's financial position or results of operations.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in ASC 605, *Revenue Recognition* (Topic 605). Effective January 1, 2018, the Company adopted Topic 606 using the modified retrospective transition method. Under this method, the Company applied Topic 606 to all contracts with customers which were not completed as of January 1, 2018 and recorded the cumulative impact of the adoption as an adjustment to its accumulated deficit on January 1, 2018. The Company's financial results for periods ending after January 1, 2018 are presented in accordance with the requirements of Topic 606, while prior period amounts have not been adjusted and continue to be reported in accordance with Topic 605.

The Company recorded a net reduction in opening accumulated deficit of $4.8 million as of January 1, 2018 for the cumulative impact of adoption of Topic 606, which was primarily the result of accelerated recognition of license revenue related to annual license fees under Topic 606. Under Topic 605, annual license fees payable to the Company by licensees were recognized as license revenue annually when the amounts became fixed or determinable. Under Topic 606, the present value of aggregate annual license fees over the contract term of the license agreement are recognized as revenue upon the delivery of the license to the licensee. The impact of the accelerated recognition of license revenue upon adoption was partially offset by the accelerated recognition of licensing costs to the Company's licensors. The Company recognizes sublicense fees to its licensors in the period the underlying license revenue is recognized.

Recent Accounting Pronouncements Not Yet Adopted

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740)—Simplifying the Accounting for Income Taxes*, which simplifies the current accounting for income taxes. Among other changes, the standard removes the exception to the incremental approach for intraperiod tax allocation when there is a loss from continuing operations and income or a gain from other items such as other comprehensive income. The standard is effective for the Company beginning January 1, 2021, with early adoption permitted. The Company does not believe the application of this standard will have a material impact on its financial position or results of operations.

In August 2018, the FASB issued ASU 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*. The standard aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal-use software license). The standard is effective for the Company beginning January 1, 2020 and may be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. The Company will adopt this standard on a prospective basis and does not believe the application of this standard will have a material impact on its financial position or results of operations.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies certain disclosure requirements regarding fair value measurements. The standard is effective for the Company beginning January 1, 2020. The Company does not believe the application of this standard will have a material impact on its financial statement disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which amends the accounting for credit losses for most financial assets and certain other instruments. The standard requires that entities holding financial assets that are not accounted for at fair value through net income be presented at the net amount expected to be collected. An allowance for credit losses will be a valuation account that will be deducted from the amortized cost basis of the financial asset to present the net carrying value at the amount expected to be collected on the financial asset. The standard is effective for the Company beginning January 1, 2020. The Company does not believe the application of this standard will have a material impact on its financial position or results of operations.

3. Marketable Securities

The following tables present a summary of the Company's marketable securities, which consist solely of available-for-sale debt securities and equity securities (in thousands):

	Amortized Cost / Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2019				
U.S. government and federal agency securities	$ 62,637	$ 215	$ (5)	$ 62,847
Certificates of deposit	8,506	77	—	8,583
Corporate bonds	226,137	808	(29)	226,916
Equity securities	351	31,784	—	32,135
	$ 297,631	$ 32,884	$ (34)	$ 330,481

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2018				
U.S. government and federal agency securities	$ 103,410	$ 93	$ (37)	$ 103,466
Certificates of deposit	8,992	—	—	8,992
Corporate bonds	282,902	36	(377)	282,561
	$ 395,304	$ 129	$ (414)	$ 395,019

As of December 31, 2019 and 2018, no available-for-sale debt securities had remaining maturities greater than three years. The amortized cost of marketable debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, or to the earliest call date for callable debt securities purchased at a premium.

As of December 31, 2019 and 2018, the balance in the Company's accumulated other comprehensive income (loss) consisted solely of net unrealized gains and losses on available-for-sale debt securities, net of income tax effects and reclassification adjustments for realized gains and losses. During the years ended December 31, 2019, 2018 and 2017, the Company recognized net unrealized gains (losses) on available-for-sale securities of $1.4 million, less than $(0.1) million and $(0.2) million, respectively, and income tax expense of $0.5 million, zero and zero, respectively, in other comprehensive income (loss) for the periods. The Company recognized net realized gains (losses) of less than $0.1 million, less than $(0.1) million and $0.5 million on the sale or maturity of available-for-sale securities during the years ended December 31, 2019, 2018 and 2017, respectively, which were reclassified out of accumulated other comprehensive income (loss) during the periods and were included in investment income in the consolidated statements of operations and comprehensive income (loss).

The following tables present the fair values and unrealized losses of available-for-sale debt securities held by the Company in an unrealized loss position for less than 12 months and 12 months or greater (in thousands):

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
December 31, 2019						
U.S. government and federal agency securities	$ 12,562	$ (5)	$ —	$ —	$ 12,562	$ (5)
Corporate bonds	48,556	(29)	—	—	48,556	(29)
	$ 61,118	$ (34)	$ —	$ —	$ 61,118	$ (34)

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
December 31, 2018						
U.S. government and federal agency securities	$ 53,124	$ (37)	$ —	$ —	$ 53,124	$ (37)
Corporate bonds	245,283	(354)	12,424	(23)	257,707	(377)
	$ 298,407	$ (391)	$ 12,424	$ (23)	$ 310,831	$ (414)

As of December 31, 2019, available-for-sale debt securities held by the Company which were in an unrealized loss position consisted of 20 investment grade security positions. The Company has the intent and ability to hold such securities until recovery and has determined that none of its available-for-sale debt securities were other-than-temporarily impaired as of December 31, 2019 or 2018.

Marketable equity securities held by the Company as of December 31, 2019 consisted solely of common stock of Prevail Therapeutics Inc. (Prevail). The Company acquired the securities as consideration for a commercial license to the NAV Technology Platform granted to Prevail in August 2017. Prevail completed its initial public offering (IPO) in June 2019. Prior to Prevail's IPO, the securities were accounted for as non-marketable equity securities without a readily determinable fair value and had a carrying value of $0.4 million. Upon Prevail's IPO in June 2019, the securities were reclassified to marketable securities and are measured at fair value. During the year ended December 31, 2019, the Company recognized unrealized gains of $31.8 million and realized gains of $6.0 million related to its marketable equity securities of Prevail, which were included in investment income in the consolidated statements of operations and comprehensive income (loss).

4. Fair Value of Financial Instruments

Financial instruments reported at fair value on a recurring basis include cash equivalents and marketable securities. The following tables present the fair value of cash equivalents and marketable securities in accordance with the hierarchy discussed in Note 2 (in thousands):

	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total
December 31, 2019				
Cash equivalents:				
Money market mutual funds	$ —	$ 56,058	$ —	$ 56,058
Total cash equivalents	—	56,058	—	56,058
Marketable securities:				
U.S. government and federal agency securities	—	62,847	—	62,847
Certificates of deposit	—	8,583	—	8,583
Corporate bonds	—	226,916	—	226,916
Equity securities	32,135	—	—	32,135
Total marketable securities	32,135	298,346	—	330,481
Total cash equivalents and marketable securities	$ 32,135	$ 354,404	$ —	$ 386,539

	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total
December 31, 2018				
Cash equivalents:				
Money market mutual funds	$ —	$ 75,542	$ —	$ 75,542
Total cash equivalents	—	75,542	—	75,542
Marketable securities:				
U.S. government and federal agency securities	—	103,466	—	103,466
Certificates of deposit	—	8,992	—	8,992
Corporate bonds	—	282,561	—	282,561
Total marketable securities	—	395,019	—	395,019
Total cash equivalents and marketable securities	$ —	$ 470,561	$ —	$ 470,561

There were no transfers of financial instruments between levels of the fair value hierarchy during the years ended December 31, 2019 and 2018.

Management estimates that the carrying amounts of its current accounts receivable, accounts payable and accrued expenses and other current liabilities approximate fair value due to the short-term nature of those instruments. Accounts receivable which contain non-current portions are recorded at their present values using a discount rate that is based on prevailing market rates and the credit profile of the licensee on the date the amounts are initially recorded. Management does not believe there have been any significant changes in market conditions or credit quality that would cause the discount rates initially used to be significantly different from those that would be used as of December 31, 2019 to determine the present value of the receivables. Accordingly, management estimates that the carrying value of its non-current accounts receivable approximates the fair value of those instruments.

Non-marketable equity securities are measured at cost less impairment, adjusted for observable price changes for identical or similar investments of the same issuer. As of December 31, 2018, non-marketable equity securities had a carrying value of $0.4 million and were included in other assets on the consolidated balance sheet. The Company did not identify any observable price changes or changes in circumstances that would have had an adverse effect on the fair value of the securities as of December 31, 2018. During year ended December 31, 2019, all of the Company’s non-marketable equity securities were reclassified to marketable securities and as of December 31, 2019, the Company did not hold any non-marketable equity securities. No remeasurements or impairment losses were recorded on non-marketable equity securities during the years ended December 31, 2019, 2018 and 2017.

5. Property and Equipment, Net

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

	December 31, 2019	December 31, 2018
Lab equipment	$ 19,663	$ 14,417
Computer equipment and software	2,545	2,002
Furniture and fixtures	2,188	1,915
Leasehold improvements	18,915	11,751
Construction-in-progress	—	5,854
Total property and equipment	43,311	35,939
Accumulated depreciation and amortization	(14,338)	(7,237)
Property and equipment, net	$ 28,973	$ 28,702

Construction-in-progress reported in the table above as of December 31, 2018 consisted of certain costs incurred and reported by the Company's landlord at 9800 Medical Center Drive. Upon the adoption of Topic 842 on January 1, 2019, the Company derecognized the cumulative amount of construction costs incurred by the landlord of $5.9 million. Please refer to Note 2 for further information on the Company's adoption of Topic 842 and Note 6 for further information on the Company's lease at 9800 Medical Center Drive.

During the years ended December 31, 2019, 2018 and 2017, the Company recorded depreciation expense of $7.2 million**,** $4.0 million and $2.7 million, respectively.

6. Leases

9800 Medical Center Drive

In November 2018, the Company entered into a lease agreement, as amended in April 2019 and November 2019, for approximately 177,000 square feet of office, laboratory and manufacturing facilities in a new building to be constructed at 9800 Medical Center Drive in Rockville, Maryland (the 9800 Medical Center Drive Lease). The initial construction of the building is being conducted by the landlord and is expected to be completed in 2020, after which the leased premises will be delivered to the Company to make additional improvements to the building. Pursuant to the amended lease agreement, the Company will receive a $19.5 million tenant improvement allowance from the landlord to construct additional improvements to the leased premises. The lease expires approximately 16 years from delivery of the leased premises to the Company, subject to certain extension and termination options held by the Company. The Company has the option to extend the term of the lease for up to 10 additional years and the option to terminate the lease after 12 years from the delivery of the leased premises to the Company. If the Company elects to terminate the lease, it will be subject to a termination fee equal to the unamortized tenant improvement allowance, rent abatement and landlord commissions as of the termination date, bearing interest at 5% per annum, plus four months of base rent and operating expenses. Additionally, after the delivery of the leased premises under the 9800 Medical Center Drive Lease, the Company will have the option to terminate its lease at 9712 Medical Center Drive with six months' notice. Monthly payments under the 9800 Medical Center Drive Lease begin approximately 12 months from the delivery of the leased premises to the Company and escalate annually in accordance with the lease agreement. As required by the lease agreement, the Company has provided the landlord with an irrevocable letter of credit of $1.1 million which the landlord may draw upon in the event of any uncured default by the Company under the terms of the lease.

The Company is involved in the construction project for the leased premises at 9800 Medical Center Drive, including having the responsibility to pay for a portion of the costs of non-normal tenant improvements such as finish work, mechanical, electrical and plumbing elements of the building, among other items. As of December 31, 2018, under the requirements of Topic 840, the Company was deemed the owner of the leased premises during the construction period for accounting purposes and certain estimated construction costs incurred and reported by the landlord were recorded as property and equipment, with a corresponding financing lease obligation, on the consolidated balance sheet. The Company has determined that it does not control the building during the construction period under the requirements of Topic 842. Accordingly, upon the adoption of Topic 842 on January 1, 2019, the Company derecognized property and equipment of $5.9 million for the cumulative costs of construction incurred by the landlord as well as the associated $5.9 million financing lease obligation. As of December 31, 2019, the Company had recorded $5.4 million of costs related to the construction at 9800 Medical Center Drive, which have been recorded as leasehold improvements within property and equipment on the consolidated balance sheets.

As of December 31, 2019, the right-of-use assets and lease liabilities related to the 9800 Medical Center Drive Lease have not been recorded on the Company's consolidated balance sheets and will be measured and recognized on the commencement date of the lease, which is expected to occur in 2020 when the landlord delivers the newly constructed building to the Company.

Other Leases

In March 2015, the Company entered into an operating lease for office space at 9712 Medical Center Drive in Rockville, Maryland (the 9712 Medical Center Drive Lease). The lease term commenced in April 2015. Monthly payments under the lease began in October 2015 and escalate annually in accordance with the lease agreement.

In September 2015, November 2015, July 2017 and April 2018, the Company amended the 9712 Medical Center Drive Lease to include additional office and laboratory space at 9714 Medical Center Drive, and ultimately extend the term of the lease to September 2021. The Company has options to extend the term of the 9712 Medical Center Drive Lease for up to six additional years. Additionally, upon the commencement of the 9800 Medical Center Drive Lease, the Company will have the option to terminate the 9712 Medical Center Drive Lease with six months' notice. The Company's extension and termination options under the 9712 Medical Center Drive Lease have been excluded from the measurement of the right-of-use assets and lease liabilities for the lease as they are not reasonably certain of exercise. The Company received a $0.4 million tenant improvement allowance from the landlord which has been recorded as a reduction of the right-of-use assets for the lease and is amortized on a straight-line basis as a reduction of rent expense over the term of the lease.

In January 2016, the Company entered into an operating lease for its corporate headquarters at 9600 Blackwell Road in Rockville, Maryland (the Blackwell Road Lease). The lease commenced in February 2016 and expires in September 2023. In November 2017, the Blackwell Road Lease was amended to include additional office space for the remainder of the lease term. Monthly payments under the lease began in September 2016 and escalate annually in accordance with the lease agreement. The Company has an option to extend the term of the Blackwell Road Lease for up to five additional years and the option to terminate the lease after 67 months from the lease commencement date. If the Company elects to terminate the lease, it will be subject to a termination fee equal to the unamortized tenant improvement allowance, rent abatement and landlord costs and commissions as of the termination date, bearing interest at 8% per annum. The Company's extension and termination options under the Blackwell Road Lease have been excluded from the measurement of the right-of-use assets and lease liabilities for the lease as they are not reasonably certain of exercise. The Company received a $0.8 million tenant improvement allowance from the landlord which has been recorded as a reduction of the right-of-use assets for the lease and is amortized on a straight-line basis as a reduction of rent expense over the term of the lease.

In May 2016, the Company entered into an operating lease for office space at 400 Madison Avenue in New York, New York (the 400 Madison Lease). The lease commenced in July 2016 and monthly payments under the lease began in October 2016 and escalate annually in accordance with the lease agreement. In May 2019, the 400 Madison Lease was amended to include additional office space and extend the term of the lease from October 2020 to April 2027. The Company will receive a $0.7 million tenant improvement allowance from the landlord to construct improvements to the leased premises. As required by the lease agreement, the Company has provided the landlord with an irrevocable letter of credit of $0.2 million which the landlord may draw upon in the event of any uncured default by the Company under the terms of the lease.

As a result of the amendment in May 2019, the expiration of the lease term for the original premises under the 400 Madison Lease was adjusted from October 2020 to August 2019, the date in which the Company temporarily vacated the premises so that the landlord could perform demolition of the original leased premises. Upon the execution of the amendment in May 2019, the right-of-use assets and lease liabilities for the original premises were reduced by $0.4 million to account for the modification of the lease term. The right-of-use assets and lease liabilities related to the expanded premises for the extended lease term were measured and recognized upon the delivery of the expanded premises to the Company to make tenant improvements, which occurred in October 2019.

The Company leases additional office and laboratory facilities in Rockville, Maryland, as well as laboratory and other equipment, under operating leases with various expiration dates through 2022.

Operating Lease Information

All of the Company's leases are classified as operating leases. The following table summarizes the Company's lease costs and supplemental cash flow information related to its operating leases (in thousands):

	Year Ended December 31, 2019
Operating lease cost	$ 3,040
Variable lease cost	666
Total lease cost	$ 3,706
Cash paid for amounts included in operating lease liabilities	$ 2,724
Right-of-use assets acquired through operating lease liabilities	$ 5,114

Right-of-use assets acquired through operating lease liabilities for the year ended December 31, 2019 includes a reduction of $0.4 million related to the May 2019 amendment to the 400 Madison Lease for the adjustment of the lease term. Short-term lease expense for the year ended December 31, 2019 was not material and is included in operating lease cost in the table above. Variable lease cost under the Company's operating leases includes items such as common area maintenance, utilities, taxes and other charges.

The weighted-average remaining lease term and weighted-average discount rate of the Company's operating leases were as follows:

	As of December 31, 2019
Weighted-average remaining lease term (years)	4.6
Weighted-average discount rate	5.1%

The following table presents a reconciliation of the undiscounted future minimum lease payments remaining under the 9800 Medical Center Drive Lease and other operating leases to the amounts reported as operating lease liabilities on the consolidated balance sheet as of December 31, 2019 (in thousands):

	9800 Medical Center Drive Lease (a)	Other Operating Leases	Total Minimum Lease Payments
Undiscounted future minimum lease payments:			
2020	$ —	$ 2,941	$ 2,941
2021	1,444	3,528	4,972
2022	4,535	1,519	6,054
2023	6,401	1,427	7,828
2024	7,054	987	8,041
Thereafter	94,943	2,406	97,349
Total undiscounted future minimum lease payments	$ 114,377	$ 12,808	$ 127,185
Amount representing imputed interest		(1,513)	
Total operating lease liabilities		11,295	
Current portion of operating lease liabilities		(2,421)	
Operating lease liabilities, non-current		$ 8,874	

(a) Includes undiscounted future minimum lease payments under the 9800 Medical Center Drive Lease which are not included in the lease liabilities reported on the consolidated balance sheet as of December 31, 2019. The actual timing and amounts of these payments are subject to adjustment based on the commencement dates and actual square footage of the leased premises. Accordingly, these amounts were estimates as of December 31, 2019.

As of December 31, 2018, future minimum lease payments under Topic 840 for the 9800 Medical Center Drive Lease and other operating leases were as follows (in thousands):

	9800 Medical Center Drive Lease (a)	Other Operating Leases	Total Minimum Lease Payments
2019	$ —	$ 2,798	$ 2,798
2020	—	3,054	3,054
2021	1,329	2,391	3,720
2022	4,289	621	4,910
2023	5,156	479	5,635
Thereafter	76,420	—	76,420
Total minimum lease payments	$ 87,194	$ 9,343	$ 96,537

(a) Includes all future minimum lease payments under the 9800 Medical Center Drive Lease, including amounts recorded as financing lease obligations on the consolidated balance sheet. The actual timing and amounts of payments under the 9800 Medical Center Drive Lease are subject to adjustment based on the commencement date and actual square footage of the leased premises. Accordingly, these amounts were estimates as of December 31, 2018.

Rent expense, as recognized in accordance with Topic 840, under all leases, including additional rent charges for utilities, parking, property management, operating expenses and real estate taxes for the years ended December 31, 2018 and 2017 was $2.8 million and $1.8 million, respectively.

7. Commitments and Contingencies

Licenses and Collaborations

The Company licenses intellectual property from third-parties, primarily for technology used in its product candidates and development programs and which may be sublicensed to NAV Technology Licensees. Licenses granted to the Company may require the Company to make future payments relating to sublicense fees, milestone fees and royalties on future sales of licensed products. Additionally, the Company may be responsible for the cost of the maintenance of the intellectual property as incurred by its licensors. Up-front fees to obtain licensed technology are recorded as research and development expenses if the technology has no alternative future use. Patent maintenance costs are recorded as general and administrative expenses. Sublicense fees are based on a specified percentage of license fees earned by the Company as a result of sublicensing the technology to third-parties and are recorded as cost of revenues. Milestone fees are recorded as cost of revenues if the underlying milestone is achieved by a licensee, or as research and development expense if the underlying milestone is achieved by the Company as a result of the development of its product candidates and the technology has no alternative future use. Royalties due on sales of licensed products, including sales by NAV Technology Licensees, are recorded as cost of revenues.

The Trustees of the University of Pennsylvania

In February 2009, the Company entered into a license agreement, which has been amended from time to time, with The Trustees of the University of Pennsylvania (together with the University of Pennsylvania, Penn) for exclusive, worldwide rights to certain patents owned by Penn underlying the Company's NAV Technology Platform, as well as exclusive rights to certain data, results and other information generated in connection with the clinical trial for RGX-501, the Company's product candidate for the treatment of homozygous familial hypercholesterolemia (HoFH). Pursuant to the license agreement, the Company and is obligated to pay Penn royalties on net sales of licensed products and sublicense fees. Additionally, the Company is obligated to reimburse Penn for certain costs incurred related to the maintenance of the licensed patents.

In April 2019, the Company amended its license from Penn to include exclusive license rights to certain patent rights and know-how, including research data and other information, relating to the treatment of late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease. In consideration for the additional licensed rights, and in addition to any consideration owed under the license prior to the amendment, the Company paid Penn an up-front fee and is obligated to pay milestone fees of up to $20.5 million upon the achievement of various development and sales-based milestones and additional royalties on net sales of licensed products for the treatment of CLN2 disease. Additionally, the amendment modified the percentage of sublicense fees the Company is obligated to pay Penn on amounts the Company receives from third parties for the sublicensing of the licensed rights for the treatment of CLN2 disease.

Expenses incurred by the Company related to its license from Penn were recorded as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Cost of revenues	$ —	$ (18)	$ 211
Research and development	200	—	—
General and administrative	905	130	233
	$ 1,105	$ 112	$ 444

As of December 31, 2019 and 2018, the Company had recorded $0.1 million and $0.1 million, respectively, in expenses payable to Penn under the license agreement, which are included in accounts payable, accrued expenses and other current liabilities and other liabilities on the consolidated balance sheets.

GlaxoSmithKline LLC

In March 2009, the Company entered into a license agreement, which was amended in April 2009, with GlaxoSmithKline LLC (GSK) for exclusive, worldwide rights to certain patents underlying the Company's NAV Technology Platform which are owned by Penn and exclusively licensed to GSK. Pursuant to the license agreement, the Company is obligated to pay GSK royalties on net sales of licensed products and sublicense fees. Additionally, the Company is obligated to reimburse GSK for certain costs incurred related to the maintenance of the licensed patents. The Company was also obligated to pay $1.5 million to GSK upon the achievement of various milestones, all of which have been achieved and paid as of December 31, 2019.

Expenses incurred by the Company related to its license from GSK were recorded as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Cost of revenues:			
Royalties on net sales of licensed products	$ 5,822	$ —	$ —
Other cost of revenues	2,419	9,407	1,499
Total cost of revenues	8,241	9,407	1,499
General and administrative	928	548	509
	$ 9,169	$ 9,955	$ 2,008

As of December 31, 2019 and 2018, the Company had recorded $6.7 million and $4.1 million, respectively, in expenses payable to GSK under the license agreement, which are included in accounts payable, accrued expenses and other current liabilities and other liabilities on the consolidated balance sheets.

Neurimmune AG

In July 2019, the Company entered into a collaboration and license agreement with Neurimmune AG (Neurimmune) pursuant to which the Company and Neurimmune will jointly develop and commercialize novel gene therapies using AAV vectors from the NAV Technology Platform to deliver human antibodies for chronic neurodegenerative diseases. The Company and Neurimmune will share all research and development costs for the first two years of the agreement, after which each party will have the option, on a target-by-target basis, to: (i) continue as a 50% partner in the collaboration; (ii) receive a phase-based worldwide royalty in lieu of continued development investment; or (iii) negotiate with the other party to lead the development and commercialization of the respective program. Unless the parties agree otherwise, upon the commercialization of any product candidates, if any, it is anticipated that profits and losses will be shared equally on a worldwide basis.

The Company determined that the collaboration and license agreement with Neurimmune is a collaborative arrangement within the scope of Topic 808, and that no unit of account under the arrangement should be accounted for as a transaction with a customer within the scope of Topic 606. In accordance with the Company's accounting policies for collaborative arrangements, if Neurimmune's development costs incurred under the collaboration exceed those incurred by the Company during a reporting period, the Company will recognize research and development expense and record a liability for the amount due to Neurimmune at the end of the period. Alternatively, if the Company's development costs incurred under the collaboration exceed those incurred by Neurimmune during a reporting period, the Company will recognize a reduction of research and development expenses and record an amount due from Neurimmune at the end of the period. During the year ended December 31, 2019, the Company recognized net research and development expenses of less than $0.1 million under the collaboration and license agreement with Neurimmune.

Clearside Biomedical, Inc.

In August 2019, the Company entered into an option and license agreement with Clearside Biomedical, Inc. (Clearside) pursuant to which the Company was granted an option to exclusively license the worldwide rights to certain patents related to Clearside's proprietary, in-office SCS Microinjector™ for the delivery of RGX-314 to the suprachoroidal space to treat wet age-related macular degeneration (wet AMD), diabetic neuropathy (DR) and other diseases. The Company exercised its license option in October 2019, resulting in a payment of $1.6 million to Clearside which was recognized as research and development expense upon exercise. Additionally, the Company is obligated to pay milestone fees of up to $136.0 million upon the achievement of various development and sales-based milestones, as well as royalties on net sales of licensed products using the SCS Microinjector. Clearside is responsible for supplying the SCS Microinjector to the Company to support all preclinical, clinical and commercial needs. As of December 31, 2019, no milestones had been achieved, or were deemed probable of achievement, under the license agreement.

Other Licenses

In November 2014, the Company entered into a license agreement, which was amended in November 2016, with Regents of the University of Minnesota (Minnesota), for an exclusive license under Minnesota's interest in certain patent rights which are co-owned by Minnesota and the Company to commercialize products covered by the licensed patent rights in any country or territory in which a licensed patent has been issued and is unexpired, or a licensed patent application is pending. Pursuant to the license agreement, the Company is obligated to pay Minnesota annual maintenance fees, royalties on net sales, sublicense fees and fees upon the achievement of various milestones. Additionally, the Company is obligated to pay for certain costs incurred related to the maintenance of the licensed patents.

In August 2018, the Company entered into a license agreement with Emory University (Emory) for an exclusive license under Emory's interest in certain patent rights which are co-owned by Emory and the Company to commercialize products covered by the licensed patent rights in any country or territory. Pursuant to the license agreement, the Company is obligated to reimburse Emory for patent prosecution and maintenance expenses and pay Emory annual maintenance fees under certain circumstances, royalties on net sales, sublicense fees and fees upon the achievement of various milestones for the first licensed product.

Other Funding Commitments

In the normal course of business, the Company enters into agreements with contract research organizations, contract manufacturing organizations and other third-parties for services to be provided to the Company. Generally, these agreements provide for termination upon notice, with specified amounts due upon termination based on the timing of termination and the terms of the agreement. The actual amounts and timing of payments under these agreements are uncertain and contingent upon the initiation and completion of services to be provided to the Company.

Guarantees and Indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. The Company's potential exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2019 and 2018, the Company did not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded any related liabilities.

8. Capitalization

As of December 31, 2019 and 2018, the authorized capital stock of the Company included 100,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. The Company's restated certificate of incorporation and bylaws contain the rights, preferences and privileges of the Company's stockholders and their respective shares.

In March 2017, the Company completed a public offering of 3,700,000 shares of its common stock at a price of $20.50 per share. In connection with the offering, the Company granted the underwriters an option to purchase 555,000 additional shares of common stock at the public offering price. The underwriters exercised the option in full and purchased the additional shares in April 2017. The aggregate net proceeds received by the Company from the offering, inclusive of the underwriters' option exercise, were $81.5 million, net of underwriting discounts and commissions and offering expenses payable by the Company.

In August 2018, the Company completed a public offering of 3,105,000 shares of its common stock (inclusive of 405,000 shares pursuant to the full exercise by the underwriters of their option to purchase additional shares) at a price of $65.00 per share. The aggregate net proceeds received by the Company from the offering, inclusive of the underwriters' option exercise, were $189.1 million, net of underwriting discounts and commissions and offering expenses payable by the Company.

The Company's reserved shares of common stock for future issuance are as follows (in thousands):

	December 31, 2019	December 31, 2018
Reserved for issuance under equity incentive plans	7,607	6,999
Reserved for issuance under employee stock purchase plan	134	170
	7,741	7,169

9. License and Royalty Revenue

Effective January 1, 2018, the Company adopted Topic 606 using the modified retrospective transition method and has applied the new standard to all of its license agreements in effect as of, or entered into after, January 1, 2018. Revenue reported for periods ending after January 1, 2018 is presented in accordance with the requirements of Topic 606, while prior period amounts have not been adjusted and continue to be reported in accordance with Topic 605 and accordingly, may not be comparable.

As of December 31, 2019, the Company's NAV Technology Platform was being applied by NAV Technology Licensees in one commercial product, Zolgensma, and in the development of more than 20 product candidates. Consideration to the Company under its license agreements may include: (i) up-front and annual fees, (ii) option fees to acquire additional licenses, (iii) milestone payments based on the achievement of certain development and sales-based milestones by licensees, (iv) sublicense fees and (v) royalties on sales of licensed products. Sublicense fees vary by license and range from a mid-single digit percentage to a low-double digit percentage of license fees received by licensees as a result of sublicenses. Royalties on net sales of commercialized products vary by license and range from a mid-single digit percentage to a low double-digit percentage of net sales by licensees.

Development milestone payments are evaluated each reporting period and only included in the transaction price of each license and recognized as license revenue to the extent they are considered probable of achievement. Sales-based milestones are excluded from the transaction price of each license agreement and recognized as royalty revenue in the period of achievement. As of December 31, 2019, the Company's license agreements, excluding additional licenses that could be granted upon the exercise of options by licensees, contained unachieved milestones which could result in aggregate milestone payments to the Company of up to $0.3 million upon the submission of preclinical regulatory filings, $20.1 million upon the commencement of various stages of clinical trials, $31.0 million upon the submission of regulatory approval filings, $99.0 million upon the approval of commercial products by regulatory agencies and $207.0 million upon the achievement of specified sales targets for licensed products. To the extent the milestone payments are realized by the Company, the Company will be obligated to pay sublicense fees to licensors based on a specified percentage of the fees earned by the Company. The achievement of milestones by licensees is highly dependent on the successful development and commercialization of licensed products and it is at least reasonably possible that some or all of the milestone fees will not be realized by the Company.

The following tables present changes in the balances of the Company's receivables, contract assets and contract liabilities during the periods presented (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Year Ended December 31, 2019				
Receivables and contract assets:				
Accounts receivable, current and non-current	$ 31,599	$ 39,203	$ (28,499)	$ 42,303
Contract assets	$ 750	$ 1,000	$ (1,750)	$ —
Contract liabilities:				
Deferred revenue, current and non-current	$ 3,933	$ —	$ (600)	$ 3,333

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Year Ended December 31, 2018				
Receivables and contract assets:				
Accounts receivable, current and non-current	$ 5,850	$ 231,154	$ (205,405)	$ 31,599
Contract assets	$ 350	$ 3,000	$ (2,600)	$ 750
Contract liabilities:				
Deferred revenue, current and non-current	$ —	$ 3,933	$ —	$ 3,933

Additions to accounts receivable during the year ended December 31, 2019 primarily consisted of royalties on net sales of Zolgensma of $20.8 million, receivables recorded related to new licenses granted during the period, amounts billed upon the achievement of development milestones by licensees and interest income recognized during the period related to significant financing components. Deductions to accounts receivable during the year ended December 31, 2019 primarily consisted of amounts collected from licensees during the period.

Additions to accounts receivable during the year ended December 31, 2018 primarily consisted of amounts recorded under the January 2018 amendment to the license agreement with AveXis for the development of and commercialization of treatments for SMA, receivables recorded related to new licenses granted during the period, amounts billed upon the achievement of development milestones by licensees and interest income recognized during the period related to significant financing components. Deductions to accounts receivable during the year ended December 31, 2018 primarily consisted of amounts collected from licensees during the period.

The changes in the balances of contract assets during the years ended December 31, 2019 and 2018 consist of development milestones deemed probable of achievement by licensees during the period, offset by the subsequent achievement of such milestones and billing of associated milestone payments by the Company.

As of December 31, 2019, the Company had recorded deferred revenue of $3.3 million which represents consideration received from licensees for performance obligations that have not yet been satisfied by the Company. Unsatisfied performance obligations consist of options granted to licensees that provide material rights to the licensee to acquire additional licenses from the Company. These performance obligations will be satisfied, and underlying revenue will be recognized, upon the exercise or expiration of the options. The changes in deferred revenue during the years ended December 31, 2019 and 2018 consisted of amounts billed to licensees for new license options granted during the period, offset by revenue recognized during the period upon the exercise of license options by licensees. During the year ended December 31, 2019, the Company recognized $0.6 million of license revenue that was included in deferred revenue at the beginning of the period as a result of options exercised by licensees during the period. The Company did not recognize any license revenue during the year ended December 31, 2018 that was included in deferred revenue at the beginning of the period.

During the years ended December 31, 2019 and 2018, the Company recognized revenue of $26.7 million and $5.7 million, respectively, from licenses delivered to licensees in prior periods as a result of changes in the transaction prices of its license agreements as well as royalties on sales of licensed products and sublicense fees. Changes in the transaction prices during the periods were primarily attributable to development milestones achieved or deemed probable of achievement during the period that were previously not considered probable of achievement.

As of December 31, 2019, the Company had recorded total current and non-current accounts receivable of $42.3 million, of which $0.4 million had been billed to customers and $41.9 million was billable to customers in future periods. As of December 31, 2019, the Company had not recognized any impairment losses on its receivables or contract assets from contracts with customers.

AveXis March 2014 License and January 2018 Amendment

In March 2014, the Company entered into an exclusive license agreement (the March 2014 License) with AveXis. Under the license, the Company granted AveXis an exclusive, worldwide commercial license, with rights to sublicense, to the NAV AAV9 vector for the treatment of SMA in humans by *in vivo* gene therapy. In consideration for the license, AveXis paid the Company an up-front fee of $2.0 million, and is required to pay annual fees, development milestone payments of up to $12.3 million, mid-single to low double-digit royalties on net sales of licensed products, subject to reduction in specified circumstances, and a lower mid-double digit percentage of any sublicense fees AveXis receives from sublicensees for the licensed intellectual property rights.

In January 2018, the Company and AveXis amended the March 2014 License (the January 2018 Amendment). Under the January 2018 Amendment, the licensed intellectual property was expanded to include, in addition to the NAV AAV9 vector previously licensed, sublicenses to other third-party patents exclusively licensed by the Company as well as any other recombinant AAV vector in the Company's intellectual property portfolio during a period of 14 years from the effective date of the January 2018 Amendment, for the treatment of SMA in humans by *in vivo* gene therapy. The Company may also, in its sole discretion, provide specified collaborative services to AveXis as specified in the January 2018 Amendment.

The January 2018 Amendment also modified the assignment provision of the March 2014 License. Under the amended assignment provision, AveXis was permitted to transfer the March 2014 License, as amended, without the Company's consent in connection with a change of control of AveXis, subject to certain conditions. Under the original March 2014 License, any assignment by AveXis without the Company's prior written consent had been prohibited.

In consideration for the additional rights granted under the January 2018 Amendment, and in addition to any consideration owed under the original March 2014 License, AveXis paid to the Company a fee of $80.0 million upon entry into the January 2018 Amendment. In addition, AveXis was obligated to pay the Company (i) $30.0 million on the first anniversary of the effective date of the January 2018 Amendment, (ii) $30.0 million on the second anniversary of the effective date of the January 2018 Amendment and (iii) potential sales-based milestone payments of up to $120.0 million. In the event of a change of control of AveXis, to the extent that any fee described in (i) or (ii) above, or the first $40.0 million of sales-based milestone payments described in (iii) above, had not yet been paid to the Company, AveXis was required to pay any such unpaid fee to the Company upon the change of control. For any product developed for the treatment of SMA using the NAV AAV9 vector, AveXis will continue to be obligated to pay to the Company mid-single to low double-digit royalties on net sales as required by the March 2014 License, and for any product developed for the treatment of SMA using a licensed vector other than NAV AAV9, the Company will receive a low double-digit royalty on net sales.

In May 2018, AveXis was acquired by Novartis, which qualified as a change of control of AveXis under the January 2018 Amendment. Pursuant to the January 2018 Amendment, AveXis paid the Company $100.0 million in accelerated license payments as a result of the change of control.

In May 2019, the U.S. Food and Drug Administration (the FDA) approved Zolgensma for marketing in the United States, which is a licensed product under the March 2014 License, as amended, with AveXis. Upon its commercial launch in the second quarter of 2019, the Company began recognizing royalty revenue on net sales of Zolgensma.

Accounting Analysis

The January 2018 Amendment was accounted for under Topic 606 as a modification of the license agreement resulting in a new and separate contract from the original March 2014 License for revenue recognition purposes. The Company determined that a substantive termination penalty is associated with AveXis' termination rights under the amended license agreement, and therefore the contract term for revenue recognition purposes is equal to the stated term of the license. The only material performance obligation of the Company under the January 2018 Amendment is for the delivery of the modified license, which occurred upon the execution of the amendment in January 2018.

As of December 31, 2019, the transaction price of the original March 2014 License was $11.0 million. The transaction price includes (i) the up-front payment in March 2014 of $2.0 million, (ii) the present value of aggregate annual fees payable to the Company over the term of the license and (iii) payments for development milestones achieved to date or which are deemed probable of achievement. The discounted portion of the annual fees represents the financing benefit provided to AveXis and is recognized as interest income from licensing over the term of the license. Variable consideration under the original March 2014 License, which has been excluded from the transaction price, includes $3.5 million in payments for remaining development milestones that had not yet been achieved and were not considered probable of achievement, as well as any potential sublicense fees or royalties on sales of licensed products, which will be recognized in the period of the underlying sales or sublicenses. The transaction price of the original March 2014 License increased by $3.5 million during the year ended December 31, 2019 as a result of development milestones achieved during the period which were previously excluded from the transaction price.

Upon its execution, the transaction price of the January 2018 Amendment was $132.1 million, which was fully recognized as license revenue upon the delivery of the modified license in January 2018. In May 2018, as a result of the acquisition of AveXis by Novartis, the transaction price was increased by $40.0 million to account for the acceleration of the sale-based milestone which was previously excluded from the transaction price. The $40.0 million increase in the transaction price was recognized as license revenue upon the completion of the change of control in May 2018 since the amended license had been fully delivered to AveXis. Additionally, due to the acceleration of the two $30.0 million payments originally due in January 2019 and January 2020, the

Company recognized $6.1 million of interest income from licensing upon the completion of the change of control of AveXis, which represents the remaining present value discount on such payments as of the date of the change of control. As of December 31, 2019, the transaction price of the January 2018 Amendment was $172.1 million, which includes: (i) the $80.0 million payment in January 2018, (ii) the present value, as of the date of the January 2018 Amendment, of the two $30.0 million payments originally due in January 2019 and January 2020 and (iii) the $40.0 million sales-based milestone which was accelerated upon the change of control in May 2018. Variable consideration under the January 2018 Amendment, which has been excluded from the transaction price, includes the remaining sales-based milestone payment of $80.0 million, as well as any potential sublicense fees or royalties on sales of licensed products, which will be recognized in the period of the underlying sales or sublicenses. There were no increases in the transaction price of the January 2018 Amendment during the year ended December 31, 2019.

The Company recognized the following amounts under the amended March 2014 License, as amended, with AveXis (in thousands):

	Years Ended December 31,		
	2019	2018	2017
License revenue	$ 3,500	$ 176,066	$ 1,050
Zolgensma royalty revenue	20,829	—	—
Total license and royalty revenue	$ 24,329	$ 176,066	$ 1,050
Interest income from licensing	$ 29	$ 7,966	$ —

As of December 31, 2019, the Company had recorded $11.0 million of accounts receivable from AveXis under the March 2014 License, as amended, of which $10.8 million were included in current assets and $0.2 million were included in non-current assets. As of December 31, 2018, the Company had recorded $0.2 million of accounts receivable from AveXis under the March 2014 License, as amended, of which less than $0.1 million were included in current assets and $0.2 million were included in non-current assets.

AveXis June 2017 License

In June 2017, the Company entered into an exclusive license agreement (the June 2017 License) with AveXis. Under the license, the Company granted AveXis an exclusive, worldwide commercial license, with rights to sublicense, to the NAV AAV9 vector for the treatment of Rett Syndrome and amyotrophic lateral sclerosis (ALS) caused by mutations in the gene that produces the copper zinc superoxide dismutase 1 (SOD1) in humans by *in vivo* gene therapy. In consideration for the license, AveXis paid the Company an up-front fee of $6.0 million, and is required to pay annual fees, development milestone payments of up to $36.0 million, a low double-digit royalty percentage on net sales of licensed products, subject to reduction in specified circumstances, and a lower mid-double digit percentage of any sublicense fees AveXis receives from sublicensees for the licensed intellectual property rights.

During the years ended December 31, 2019, 2018 and 2017 the Company recognized license revenue of zero, zero and $6.0 million, respectively, under the June 2017 License. As of December 31, 2019, the Company had recorded $0.7 million of accounts receivable from AveXis under the June 2017 License, of which $0.1 million were included in current assets and $0.6 million were included in non-current assets. As of December 31, 2018, the Company had recorded $0.8 million of accounts receivable from AveXis under the June 2017 License, of which less than $0.1 million were included in current assets and $0.7 million were included in non-current assets.

Abeona Therapeutics Inc.

In November 2018, the Company entered into an exclusive license agreement, as amended, (the November 2018 License) with Abeona. Under the license, the Company granted Abeona an exclusive, worldwide commercial license (subject to certain non-exclusive rights previously granted by the Company), with rights to sublicense, to the NAV AAV9 vector for the treatment of Mucopolysaccharidosis Type IIIA (MPS IIIA), also known as Sanfilippo Syndrome Type A, Mucopolysaccharidosis Type IIIB (MPS IIIB), also known as Sanfilippo Syndrome Type B, Neuronal Ceroid Lipfuscinosis-1 (CLN1 disease), also known as infantile Batten Disease, and Neuronal Ceroid Lipfuscinosis-3 (CLN3 disease), also known as juvenile Batten Disease, by *in vivo* gene therapy.

In November 2019, the November 2018 License was amended to increase the total amount of license fees payable to the Company by $1.0 million and modify the timing of the first required annual payment under the license. In consideration for the license, as amended, Abeona is obligated to pay up-front and annual fees to the Company totaling up to $121.0 million, payable as follows: (i) $10.0 million upon the execution of the license agreement, (ii) $3.0 million within 12 months of the effective date of the license agreement, (iii) $8.0 million by April 1, 2020 and (iv) $100.0 million payable in five annual installments of $20.0 million beginning on the second anniversary of the effective date of the license agreement, which are subject to reduction should Abeona

terminate some but not all of the licensed indications. Any unpaid portion of the first $41.0 million of up-front and annual fees described above shall become payable upon termination of the license agreement. In the event of a change of control of Abeona, any remaining unpaid portion of the $121.0 million of up-front and annual fees described above shall become payable upon the change of control. Additionally, Abeona is obligated to pay the Company up to $60.0 million upon the achievement of specified sales-based milestones, low double-digit royalties on net sales of licensed products, subject to reduction in specified circumstances, and a lower mid-double-digit percentage of any sublicense fees Abeona receives from sublicensees for the licensed intellectual property rights.

Accounting Analysis

The Company determined that the November 2018 License has an initial contract term of three years for revenue recognition purposes due to the lack of a substantive termination penalty for license periods beyond three years from the date of the license agreement. The annual payments due under the agreement beginning in November 2021 represent contract renewal options granted to Abeona for revenue recognition purposes, and therefore are not accounted for under the current license agreement. The Company determined that the contract renewal options do not represent material rights granted to Abeona, and the only material performance obligations of the Company under the current license agreement are for the delivery of the initial intellectual property licenses, which occurred upon the execution of the license agreement in November 2018.

Upon its execution, the transaction price of the November 2018 License was $35.6 million, which was fully recognized as license revenue upon the delivery of the licenses in November 2018. As a result of the November 2019 amendment to the license, the transaction price was increased by $0.6 million to account for the modifications to the amount and timing of annual fees under the license. As of December 31, 2019, the transaction price of the November 2018 License, as amended, was $36.3 million, which includes the following fixed consideration payable to the Company over the initial contract term of three years: (i) the $10.0 million payment in November 2018 and (ii) the present value, as of the date of the license agreement, of the $3.0 million payment due in November 2019, the $8.0 million payment due in April 2020 and the $20.0 million payment due in November 2020. The discounted portion of the annual payments represents the financing benefit provided to Abeona and is recognized as interest income from licensing over the financing term of two years. Variable consideration under the license agreement, which has been excluded from the transaction price, includes the sales-based milestone payments of $60.0 million, as well as any potential sublicense fees or royalties on sales of licensed products, which will be recognized in the period of the underlying sales or sublicenses. The annual payments due under the agreement beginning in November 2021 represent contract renewal options granted to Abeona for revenue recognition purposes, and therefore are excluded from the transaction price. If renewed by Abeona, each of these payments will be recognized as revenue on the first day of the license renewal period for which the payment relates to, which is the date the payments are due under the agreement.

During the years ended December 31, 2019 and 2018, the Company recognized license revenue of $0.6 million and $35.6 million, respectively, and interest income from licensing of $2.6 million and $0.4 million, respectively under the November 2018 License. As of December 31, 2019, the Company had recorded $26.3 million of accounts receivable from Abeona under the November 2018 License, all of which was included in current assets. As of December 31, 2018, the Company had recorded $26.0 million of accounts receivable from Abeona under the November 2018 License, of which $7.5 million were included in current assets and $18.5 million were included in non-current assets.

10. Stock-based Compensation

In September 2014, the Board of Directors adopted the 2014 Stock Plan (2014 Plan). In June 2015, the Board of Directors adopted the 2015 Equity Incentive Plan (2015 Plan), which became effective upon the Company’s initial public offering in September 2015. The 2015 Plan replaced the 2014 Plan, and as of the effective date of the 2015 Plan, no further awards may be issued under the 2014 Plan. Any options or awards outstanding under the 2014 Plan as of the effective date of the 2015 Plan remained outstanding and effective. The number of authorized shares under the 2015 Plan automatically increases annually on the first business day of each fiscal year, by the lesser of (i) 4% of the total number of shares of common stock outstanding on December 31 of the prior year, or (ii) a number of common shares determined by the Board of Directors. As of December 31, 2019, the total number of shares of common stock authorized for issuance under the 2015 Plan and 2014 Plan was 10,933,221, of which 2,063,061 remained available for future grants under the 2015 Plan. In January 2020, the Board of Directors authorized an additional 1,479,696 shares to be issued under the 2015 Plan.

The 2014 Plan and 2015 Plan provide for the issuance of stock options, stock appreciation rights, restricted and unrestricted stock and unit awards, and performance cash awards to employees, members of the Board of Directors and consultants of the Company. Since the inception of the plans, the Company has issued only stock options and restricted stock units under the plans. Stock options under the 2014 Plan and 2015 Plan generally expire 10 years following the date of grant. Options typically vest over a four-year period, but vesting provisions can vary by award based on the discretion of the Board of Directors. Certain stock option

awards granted by the Company include performance conditions that must be achieved in order for vesting to occur. Stock options under the 2014 Plan and 2015 Plan have an exercise price at least equal to the estimated fair value of the Company's common stock on the date of grant. Restricted stock units vest in accordance with the underlying award agreements and, upon vesting, are settled in common stock of the Company.

Shares of common stock underlying awards previously issued under the 2014 Plan and 2015 Plan which are reacquired by the Company, withheld by the Company in payment of the purchase price, exercise price or withholding taxes, expired, cancelled due to forfeiture or otherwise terminated other than by exercise or settlement, are added to the number of shares of common stock available for issuance under the 2015 Plan. Shares available for issuance under the 2015 Plan may be either authorized but unissued shares of the Company's common stock or common stock reacquired by the Company and held in treasury. The 2015 Plan expires in June 2025, 10 years from the date it was adopted by the Board of Directors, unless earlier terminated.

Stock-based Compensation Expense

The Company's stock-based compensation expense by award type was as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Stock options	$ 25,964	$ 15,960	$ 10,031
Restricted stock units	257	275	275
Employee stock purchase plan	633	406	299
	$ 26,854	$ 16,641	$ 10,605

As of December 31, 2019, the Company had $63.8 million of unrecognized stock-based compensation expense related to stock options and the 2015 Employee Stock Purchase Plan (the 2015 ESPP), which is expected to be recognized over a weighted-average period of 2.7 years.

The Company has recorded aggregate stock-based compensation expense in the consolidated statements of operations and comprehensive income (loss) as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Research and development	$ 13,031	$ 7,612	$ 5,128
General and administrative	13,823	9,029	5,477
	$ 26,854	$ 16,641	$ 10,605

Stock Options

The following table summarizes stock option activity under the 2014 Plan and 2015 Plan (in thousands, except per share data):

	Shares	Weighted-average Exercise Price	Weighted-average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (a)
Outstanding at December 31, 2018	4,855	$ 19.31	7.6	$ 118,185
Granted	1,751	$ 46.91		
Exercised	(797)	$ 8.88		
Cancelled or forfeited	(265)	$ 34.87		
Outstanding at December 31, 2019	5,544	$ 28.79	7.5	$ 86,509
Exercisable at December 31, 2019	2,944	$ 16.73	6.4	$ 74,766
Vested and expected to vest at December 31, 2019	5,544	$ 28.79	7.5	$ 86,509

(a) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair value of the common stock for the options that were in the money at the dates reported.

The weighted-average grant date fair value per share of options granted during the years ended December 31, 2019, 2018 and 2017 was $31.19, $27.49 and $13.87, respectively. During the years ended December 31, 2019, 2018 and 2017, the total number of stock options exercised was 796,847, 1,684,522 and 515,916, respectively, resulting in total proceeds of $7.1 million, $14.5 million and $2.5 million, respectively. The total intrinsic value of options exercised during the years ended December 31, 2019, 2018 and 2017 was $30.8 million, $68.2 million and $11.1 million, respectively.

The fair values of options granted were estimated at each grant date using the Black-Scholes valuation model with the following weighted-average assumptions:

	Years Ended December 31,		
	2019	2018	2017
Expected volatility	74%	75%	77%
Expected term (in years)	6.1	6.0	6.2
Risk-free interest rate	2.3%	2.6%	2.1%
Expected dividend yield	0.0%	0.0%	0.0%

The weighted-average assumptions in the table above for the year ended December 31, 2017 exclude options granted to nonemployee advisors, except for members of the Company's Board of Directors. For the year ended December 31, 2017, the Company recognized $0.5 million of stock-based compensation expense related to stock options granted to these nonemployees. Effective July 1, 2018, upon the Company's adoption of ASU 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-based Payment Accounting*, options to nonemployees are measured at the estimated grant date value of the awards. Prior to the adoption of ASU 2018-07, stock options granted to nonemployees were remeasured at their fair values at each reporting date until vested. There was no impact to the Company's financial statements upon the adoption of ASU 2018-07 on July 1, 2018, because as of that date, there were no unvested stock options outstanding which were considered probable of achievement. The weighted-average assumptions in the table above for the years ended December 31, 2019 and 2018 include all options granted to employees and nonemployees during the periods.

Restricted Stock Units

The following table summarizes restricted stock unit activity under the 2015 Plan (in thousands, except per share data):

	Shares	Weighted-average Grant Date Fair Value
Unvested balance at December 31, 2018	40	$ 20.90
Granted	—	$ —
Vested	(40)	$ 20.90
Forfeited	—	$ —
Unvested balance at December 31, 2019	—	$ —

The total intrinsic values of restricted stock units vested during the year ended December 31, 2019 was $1.8 million. No restricted stock units vested during the years ended December 31, 2018 and 2017.

Employee Stock Purchase Plan

In June 2015, the Company's Board of Directors adopted the 2015 ESPP, which became effective upon the Company's initial public offering in September 2015. The number of authorized shares reserved for issuance under the 2015 ESPP automatically increases on the first business day of each fiscal year by the lesser of (i) 1% of the shares of common stock outstanding on the last business day of the prior fiscal year; or (ii) the number of shares determined by the Company's Board of Directors. Unless otherwise determined by the administrator of the 2015 ESPP, two offering periods of six months' duration will begin each year on January 1 and July 1. As of December 31, 2019, the total number of shares of common stock authorized for issuance under the 2015 ESPP was 254,000, of which 133,586 remained available for future issuance. During the years ended December 31, 2019, 2018 and 2017, 35,994, 36,700 and 47,720 shares of common stock, respectively, were issued under the 2015 ESPP. In January 2020, the Board of Directors authorized an additional 369,924 shares to be issued under the 2015 ESPP.

11. Retirement Plan

The Company sponsors a defined-contribution retirement plan under Section 401(k) of the Internal Revenue Code (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. The Company matches employee deferrals up to a specified percentage of eligible compensation. For the years ended December 31, 2019, 2018 and 2017, the Company incurred expenses of $1.8 million, $1.3 million and $1.0 million, respectively, for matching contributions to the 401(k) Plan.

12. Income Taxes

The components of income (loss) before income taxes were as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
United States	$ (97,435)	$ 104,181	$ (73,138)
Foreign	(53)	(65)	(31)
Total income (loss) before income taxes	$ (97,488)	$ 104,116	$ (73,169)

The components of the provision for income tax expense (benefit) were as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Current:			
Federal	$ —	$ —	$ —
State	(2,288)	4,179	—
Foreign	—	—	—
Total current	(2,288)	4,179	—
Deferred:			
Federal	(284)	—	—
State	(183)	—	—
Foreign	—	—	—
Total deferred	(467)	—	—
Total income tax expense (benefit)	$ (2,755)	$ 4,179	$ —

The TCJA was signed into law in December 2017 and, among other changes, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, elimination, reduction or limitation of certain domestic deductions and credits, limitation of the deduction for net operating losses (NOLs) to 80% of current year taxable income, elimination of NOL carrybacks, one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain significant exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modification or repeal of many business deductions and credits, including the orphan drug tax credit. Most of the changes resulting from the TCJA were effective beginning in 2018.

In December 2017, the SEC staff issued Staff Accounting Bulletin No. 118 (SAB 118), which allowed the Company to record provisional amounts for the effects of the TCJA in the period it was enacted for a measurement period not extend beyond one year from the enactment date. Under SAB 118, the Company recorded a provisional reduction in its deferred tax assets and associated valuation allowance of $17.9 million in 2017 for the effects of the TCJA, which was primarily attributable to the reduction in federal tax rates. The Company completed its assessment of the final impact of the TCJA within the required measurement period under SAB 118 and determined that there were no material adjustments to the provisional amounts previously recorded.

A reconciliation of income tax expense (benefit) computed at the statutory federal income tax rate of 21% for the years ended December 31, 2019 and 2018, and 34% for the year ended December 31, 2017, to income tax expense (benefit) as reflected in the financial statements for such periods is as follows (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Federal income tax expense (benefit) at statutory rate	$ (20,473)	$ 21,862	$ (24,876)
State income tax expense (benefit), net of federal tax effect	(15,323)	9,691	(7,756)
Research and development credits	(11,075)	(7,847)	(6,297)
Stock-based compensation expense for incentive stock options and employee stock purchase plan	(2,134)	(6,493)	(3,012)
Other non-deductible expenses and reconciling items	144	139	(26)
Change in corporate tax rates	130	(729)	16,598
Change in valuation allowance	45,976	(12,444)	25,369
Total income tax expense (benefit)	$ (2,755)	$ 4,179	$ —

The significant components of the Company's net deferred tax assets are as follows (in thousands):

	December 31, 2019	December 31, 2018
Deferred tax assets:		
Net operating loss carryforwards	$ 53,841	$ 15,468
Research and development tax credits	40,365	28,984
Step-up in assets upon conversion to C-corporation	648	729
Stock-based compensation expense for non-qualified stock options and restricted stock units	10,224	5,462
Unrealized losses on marketable securities	—	101
Lease liabilities	3,916	—
Deferred rent	—	495
Depreciation	26	—
Accruals and other	4,131	2,772
Total deferred tax assets before valuation allowance	113,151	54,011
Valuation allowance	(97,511)	(51,533)
Total deferred tax assets	15,640	2,478
Deferred tax liabilities:		
Unrealized gains on marketable securities	(11,344)	—
Right-of-use assets	(3,467)	—
Depreciation	—	(1,207)
Other	(829)	(1,271)
Total deferred tax liabilities	(15,640)	(2,478)
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, including a three-year cumulative loss position as of December 31, 2019, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for its net deferred tax assets as of December 31, 2019 and 2018. The valuation allowance increased (decreased) by $46.0 million and $(14.1) million during the years ended December 31, 2019 and 2018, respectively. The increase in the valuation allowance during the year ended December 31, 2019 was due primarily to federal and state NOLs and research and development credits generated during the period, stock-based compensation expense and other increases in deferred tax assets during the period, the impact of which was partially offset by an increase in deferred tax liabilities resulting from unrealized gains on marketable securities recognized during the period. The decrease in the valuation allowance during the year ended December 31, 2018 was due primarily to the utilization of federal and state NOLs and increases in deferred tax liabilities during the period, the impact of which was partially offset by research and development credits, stock-based compensation expense and other increases in deferred tax assets during the period.

As of December 31, 2019 and 2018, the Company had U.S. federal NOL carryforwards of approximately $170.4 million and $56.1 million, respectively, which may be available to offset future income tax liabilities and expire at various dates though 2039. As of December 31, 2019 and 2018, the Company also had U.S. state NOL carryforwards of approximately $269.3 million and $56.2 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2039.

As of December 31, 2019 and 2018, the Company had U.S. federal and state research and development and orphan drug tax credit carryforwards of approximately $40.5 million and $29.1 million, respectively, which may be available to reduce future income tax liabilities and expire at various dates through 2039. The calculation of these credits requires assumptions to be made by the Company to estimate qualified research expenses. The Company conducts formal studies to document the qualified activities and expenses used to calculate these credits, however a portion of these credits may be subject to future studies which have not yet occurred, the results of which may result in an adjustment to the Company's credit carryforwards. The Company accounts for uncertain tax positions in accordance with the requirements of ASC 740, and accordingly, recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. As of December 31, 2019 and 2018, the Company had total unrecognized tax benefits of $0.1 million and $0.2 million, respectively, which were reserved against the credit carryforwards as uncertain tax positions. No reserve for uncertain tax positions has been placed against qualified expenses for which a study has not been conducted. However, a full valuation allowance has been provided against the net credit carryforwards and, if an adjustment is required upon the completion of the study, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Under the provisions of the Internal Revenue Code, the Company's NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may be subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

The Company and its subsidiaries file income tax returns in the United States, at the federal level and in various states, and foreign jurisdictions. The U.S. federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2015 onward. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. The Company's U.S. federal tax return for the year ended December 31, 2015 was examined by the Internal Revenue Service. The Internal Revenue Service completed its examination and made no changes to the amounts reported by the Company.

13. Related Party Transactions

FOXKISER LLP

Since 2016, the Company has been party to professional services agreements with FOXKISER LLP (FOXKISER), an affiliate of certain stockholders of the Company and an affiliate of a member of the Company's Board of Directors, pursuant to which the Company pays a fixed monthly fee in consideration for certain strategic services provided by FOXKISER. Effective January 2019, the Company entered into a new professional services agreement with FOXKISER with similar terms and conditions as the previous agreements. The agreement was amended effective June 2019 to expand the scope of the services provided and increase the monthly fee, and the amended agreement expires in December 2020. Expenses incurred under the agreements with FOXKISER for the years ended December 31, 2019, 2018 and 2017 were $4.1 million, $2.1 million and $1.5 million, respectively, and were recorded as research and development expenses in the consolidated statements of operations and comprehensive income (loss).

14. Net Income (Loss) Per Share

The computations of basic and diluted net income (loss) per share are as follows (in thousands, except per share data):

	Years Ended December 31,		
	2019	2018	2017
Basic net income (loss) per share:			
Net income (loss) applicable to common stockholders	$ (94,733)	$ 99,937	$ (73,169)
Shares used in computation:			
Weighted-average common shares outstanding	36,690	33,427	29,878
Basic net income (loss) per share	$ (2.58)	$ 2.99	$ (2.45)
Diluted net income (loss) per share:			
Net income (loss) applicable to common stockholders	$ (94,733)	$ 99,937	$ (73,169)
Shares used in computation:			
Weighted-average common shares outstanding	36,690	33,427	29,878
Stock options	—	3,186	—
Restricted stock units	—	32	—
Employee stock purchase plan	—	3	—
Weighted-average diluted common shares	36,690	36,648	29,878
Diluted net income (loss) per share	$ (2.58)	$ 2.73	$ (2.45)

For periods in which the Company incurred net losses applicable to common stockholders, common stock equivalents are excluded from the calculation of diluted net loss per share as their effect would be anti-dilutive, and accordingly, basic and diluted net loss per share are the same for such periods. Outstanding stock options with exercise prices greater than the average market price of common stock are excluded from the calculation of diluted net income (loss) per share as their effect would be anti-dilutive. The following potentially dilutive common stock equivalents outstanding at the end of the period were excluded from the computations of weighted-average diluted common shares for the periods indicated as their effects would be anti-dilutive (in thousands):

	Years Ended December 31,		
	2019	2018	2017
Stock options issued and outstanding	5,544	928	5,468
Unvested restricted stock units outstanding	—	—	40
Employee stock purchase plan	17	—	20
	5,561	928	5,528

15. Supplemental Disclosures

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

	December 31, 2019	December 31, 2018
Accrued personnel costs	$ 10,903	$ 9,484
Accrued external research and development expenses	5,791	4,274
Accrued sublicense fees and royalties	4,542	1,617
Accrued external general and administrative expenses	2,053	773
Accrued purchases of property and equipment	1,328	221
Accrued income taxes payable	—	726
Other accrued expenses and current liabilities	229	69
	$ 24,846	$ 17,164

Other liabilities of $1.8 million and $2.5 million reported as of December 31, 2019 and 2018, respectively, consist of accrued sublicense fees payable to licensors in periods beyond 12 months from the reporting date.

16. Selected Quarterly Financial Information (Unaudited)

The following tables contain quarterly financial information for the years ended December 31, 2019 and 2018. Management believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period. Amounts in the following table are in thousands, except per share data.

	Quarters Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Total revenues	$ 884	$ 7,881	$ 14,700	$ 11,768
Cost of revenues	$ 29	$ 1,927	$ 2,494	$ 3,791
Research and development expense	$ 25,203	$ 29,483	$ 35,692	$ 33,807
General and administrative expense	$ 11,558	$ 13,405	$ 12,402	$ 14,450
Total operating expenses	$ 36,790	$ 44,753	$ 50,596	$ 52,092
Net income (loss)	$ (32,228)	$ (1,457)	$ (34,584)	$ (26,464)
Basic net income (loss) per share	$ (0.89)	$ (0.04)	$ (0.94)	$ (0.72)
Diluted net income (loss) per share	$ (0.89)	$ (0.04)	$ (0.94)	$ (0.72)

	Quarters Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Total revenues	$ 132,391	$ 40,031	$ 5,306	$ 40,777
Cost of revenues	$ 2,408	$ 3,872	$ 517	$ 2,843
Research and development expense	$ 19,550	$ 21,486	$ 18,508	$ 24,329
General and administrative expense	$ 8,380	$ 8,318	$ 9,008	$ 11,144
Total operating expenses	$ 30,366	$ 33,681	$ 28,031	$ 38,327
Net income (loss)	$ 104,239	$ 10,594	$ (19,202)	$ 4,306
Basic net income (loss) per share	$ 3.30	$ 0.33	$ (0.56)	$ 0.12
Diluted net income (loss) per share	$ 3.04	$ 0.30	$ (0.56)	$ 0.11

EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference			Filed or Furnished Herewith
		Form	Exhibit Number	Filing Date	
3.1	Restated Certificate of Incorporation	8-K	3.1	9/22/15	
3.2	Amended and Restated Bylaws	8-K	3.2	9/22/15	
4.1	Specimen stock certificate evidencing the shares of common stock	S-1	4.1	8/17/15	
4.2	Amended and Restated Investors' Rights Agreement dated as of May 15, 2015	S-1	4.2	8/17/15	
4.3	Description of Securities				X
10.1	Form of Indemnity Agreement for directors and officers	S-1	10.1	8/17/15	
10.2*	2014 Stock Plan, as amended	S-1	10.2	8/17/15	
10.3*	2015 Equity Incentive Plan and form of option agreement thereunder	S-1/A	10.3	9/15/15	
10.4*	2015 Employee Stock Purchase Plan	S-1/A	10.4	9/8/15	
10.5*	Employment Agreement effective as of June 30, 2015 between the Registrant and Kenneth T. Mills	S-1	10.5	8/17/15	
10.6*	Employment Agreement effective as of June 30, 2015 between the Registrant and Vittal Vasista	S-1	10.7	8/17/15	
10.7*	Employment Agreement effective as of February 16, 2016 between the Registrant and Curran Simpson	10-K	10.34	3/3/16	
10.8*	Employment Agreement effective as of August 18, 2016 between the Registrant and Patrick J. Christmas	10-Q	10.37	11/9/16	
10.9*	Employment Agreement effective as of March 27, 2017 between the Registrant and Olivier Danos, Ph.D.	10-Q	10.1	5/9/17	
10.10*	Employment Agreement effective as of April 17, 2019 between the Registrant and Steve Pakola, M.D.	10-Q	10.1	5/7/19	
10.11*	Compensation Program for Non-Employee Directors				X
10.12*	Management Cash Incentive Plan	S-1	10.29	8/17/15	
10.13†	License Agreement effective February 24, 2009 between the Registrant and The Trustees of the University of Pennsylvania	S-1/A	10.9	9/15/15	
10.14†	First Amendment to License Agreement dated March 6, 2009 between the Registrant and The Trustees of the University of Pennsylvania	S-1	10.10	8/17/15	
10.15†	Second Amendment to License Agreement effective September 9, 2014 between the Registrant and The Trustees of the University of Pennsylvania	S-1/A	10.11	9/15/15	
10.16†	Third Amendment to License Agreement effective April 29, 2016 between the Registrant and The Trustees of the University of Pennsylvania	10-Q/A	10.36	12/23/16	
10.17†	Fourth Amendment to License Agreement effective April 4, 2019 between the Registrant and The Trustees of the University of Pennsylvania	10-Q	10.2	5/7/19	

Exhibit Number	Description	Incorporated by Reference			Filed or Furnished Herewith
		Form	Exhibit Number	Filing Date	
10.18†	License Agreement dated March 6, 2009 between the Registrant and SmithKline Beecham Corporation d/b/a GlaxoSmithKline	S-1/A	10.12	9/15/15	
10.19	Amendment to License Agreement dated April 15, 2009 between the Registrant and SmithKline Beecham Corporation d/b/a GlaxoSmithKline	S-1	10.13	8/17/15	
10.20†	License Agreement dated March 21, 2014 between the Registrant and AveXis, Inc.	S-1/A	10.16	9/15/15	
10.21†	First Amendment to License Agreement dated January 8, 2018 between the Registrant and AveXis, Inc.	10-K	10.24	3/6/18	
10.22†	License Agreement dated November 4, 2018 between the Registrant and Abeona Therapeutics Inc.	10-K	10.22	2/27/19	
10.23†	First Amendment to License Agreement dated November 4, 2019 between the Registrant and Abeona Therapeutics Inc.				X
10.24	Lease dated March 6, 2015 between the Registrant and BMR-Medical Center Drive LLC	S-1	10.26	8/17/15	
10.25	First Amendment to Lease dated September 30, 2015 between the Registrant and BMR-Medical Center Drive LLC	10-K	10.31	3/3/16	
10.26	Second Amendment to Lease dated November 23, 2015 between the Registrant and BMR-Medical Center Drive LLC	10-K	10.32	3/3/16	
10.27	Third Amendment to Lease dated July 21, 2017 between the Registrant and BMR-Medical Center Drive LLC	10-Q	10.1	8/8/17	
10.28	Fourth Amendment to Lease dated April 20, 2018 between the Registrant and BMR-Medical Center Drive LLC	10-Q	10.1	5/8/18	
10.29	Lease dated May 16, 2016 between the Registrant and DS400OWNER, LLC, as successor-in-interest to 400 Madison Holdings, LLC	8-K	10.1	6/3/19	
10.30	First Amendment to Lease dated May 28, 2019 between the Registrant and DS400OWNER, LLC	8-K	10.2	6/3/19	
10.31	Lease dated January 28, 2016 between the Registrant and TNREF III 9600 Blackwell, LLC	10-K	10.33	3/3/16	
10.32	First Amendment to Lease dated November 3, 2017 between the Registrant and 9600 Blackwell II LLC, as successor in interest to TNREF III 9600 Blackwell, LLC	10-Q	10.1	11/8/17	
10.33	Lease dated November 1, 2018 between the Registrant and ARE-Maryland No. 24, LLC	10-Q	10.1	11/7/18	
10.34	Letter Agreement to Lease dated April 12, 2019 between the Registrant and ARE-Maryland No. 24, LLC	10-Q	10.3	5/7/19	
10.35	First Amendment to Lease dated April 23, 2019 between the Registrant and ARE-Maryland No. 24, LLC	10-Q	10.4	5/7/19	

Exhibit Number	Description	Incorporated by Reference			Filed or Furnished Herewith
		Form	Exhibit Number	Filing Date	
10.36	Second Amendment to Lease dated November 4, 2019 between the Registrant and ARE-Maryland No. 24, LLC	10-Q	10.1	11/5/19	
21.1	Subsidiaries of the Registrant				X
23.1	Consent of PricewaterhouseCoopers LLP, independent registered accounting firm				X
31.1	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002				X
31.2	Certification of the Chief Financial Officer as required by Section 302 of the Sarbanes-Oxley Act of 2002				X
32.1	Certifications of the Chief Executive Officer and Chief Financial Officer as required by 18 U.S.C. 1350				X
101	The following materials from the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 formatted in Inline XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets (ii) Consolidated Statements of Operations and Comprehensive Income (Loss) (iii) Consolidated Statements of Stockholders' Equity (iv) Consolidated Statements of Cash Flows (v) Notes to Consolidated Financial Statements				X
104	The cover page from the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 formatted in Inline XBRL (included in Exhibit 101)				

* Management contract or compensatory plan or arrangement.
† Portions of this exhibit have been omitted.

The certifications attached as Exhibit 32.1 that accompany this Annual Report on Form 10-K are not deemed filed with the SEC and are not to be incorporated by reference into any filing of REGENXBIO Inc. under the Securities Act or the Exchange Act, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on February 26, 2020.

REGENXBIO INC.

By: /s/ Kenneth T. Mills
Kenneth T. Mills,
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Kenneth T. Mills Kenneth T. Mills	President, Chief Executive Officer and Director (Principal Executive Officer)	February 26, 2020
/s/ Vittal Vasista Vittal Vasista	Chief Financial Officer (Principal Financial and Accounting Officer)	February 26, 2020
/s/ Donald J. Hayden, Jr. Donald J. Hayden, Jr.	Chairman of the Board of Directors	February 26, 2020
/s/ Daniel J. Abdun-Nabi Daniel J. Abdun-Nabi	Director	February 26, 2020
/s/ Luke M. Beshar Luke M. Beshar	Director	February 26, 2020
/s/ Allan M. Fox Allan M. Fox	Director	February 26, 2020
/s/ Alexandra Glucksmann Alexandra Glucksmann	Director	February 26, 2020
/s/ A.N. “Jerry” Karabelas A.N. “Jerry” Karabelas	Director	February 26, 2020
/s/ David C. Stump David C. Stump	Director	February 26, 2020
/s/ Daniel Tassé Daniel Tassé	Director	February 26, 2020

EXHIBIT 4.3

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2019, REGENXBIO Inc. has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended: our common stock, par value $0.0001 per share. The following is a general summary of the terms of shares of our common stock. The description below does not include all of the terms of the shares of common stock and should be read together with our restated certificate of incorporation and amended and restated bylaws, each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part. Unless the context otherwise requires, throughout this document, the words "REGENXBIO," "we," or "us" refer to REGENXBIO Inc.

Description of Common Stock

Authorized Capital Stock

Our authorized capital stock consists of 110,000,000 shares, with a par value of $0.0001 per share, of which 100,000,000 shares are designated as common stock and 10,000,000 shares are designated as preferred stock. The outstanding shares of our common stock are fully paid and non-assessable.

Dividend Rights

Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time.

Preemptive and Conversion Rights

Holders of common stock have no preemptive or conversion rights or other subscription rights.

Redemption and Sinking Fund Rights

There are no redemption or sinking fund provisions applicable to our common stock.

Liquidation Rights

Upon our liquidation, dissolution or winding-up, the holders of common stock are entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any outstanding preferred stock.

Voting Rights

Each holder of common stock is entitled to one vote per share on all matters submitted to a vote of stockholders. Notwithstanding the previous sentence, unless otherwise provided by law holders of common stock are not entitled to vote on any amendment to our restated certificate of incorporation that relates solely to the terms of any preferred stock if the holders of such preferred stock are entitled to vote on such amendment.

We have not provided for cumulative voting in the election of directors.

The General Corporation Law of the State of Delaware, or the Delaware General Corporation Law, provides that holders of a class of stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of the holders of that class of stock for proposals that adversely affect such holders.

Anti-Takeover Effects of Delaware Law and Our Restated Certificate of Incorporation and Amended and Restated Bylaws

Delaware law, our restated certificate of incorporation and our amended and restated bylaws contain provisions that could make it more difficult to effect an acquisition of us by means of a tender offer, proxy contest or otherwise, or to remove our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish, or could deter, transactions that stockholders otherwise consider to be in our or their best interest, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unsolicited or unfriendly proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Delaware Business Combination Statute

We are subject to Section 203 of the Delaware General Corporation Law. Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years following the time of the transaction in which the person or entity became an interested stockholder, unless:

- prior to that time, either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder is approved by the board of directors of the corporation;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the outstanding voting stock of the corporation, excluding for this purpose shares owned by persons who are directors and also officers of the corporation and by specified employee benefit plans; or
- at or after such time, the business combination is approved by the board of directors of the corporation and by the affirmative vote, and not by written consent, of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

For the purposes of Section 203, a "business combination" is broadly defined to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder, subject to limited exceptions;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

An "interested stockholder" is a person who, together with affiliates and associates, owns or within the immediately preceding three years did own 15% or more of the corporation's voting stock.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. The existence of authorized but unissued shares of preferred stock may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Action by Written Consent; Stockholder Meetings

Our restated certificate of incorporation and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting. As a result, a holder controlling a majority of our capital stock would not be able to amend our bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws. Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board or president, or by a resolution adopted by a majority of our board of directors. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors. 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.

Staggered Board

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of holders of at least two-thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Board of Directors Vacancies

Our restated certificate of incorporation and amended and restated bylaws authorize our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors is set only by resolution adopted by a majority vote of our entire board of directors. These provisions will prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.

Stockholders Not Entitled to Cumulative Voting

Our restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least two-thirds of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Choice of Forum

Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our restated certificate of incorporation or amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. Additionally, if the subject matter of any action within the scope of the preceding sentence is filed in a court other than a court located with the State of Delaware, or is a "foreign action" (as defined in our restated certificate of incorporation), in the name of any stockholder, such stockholder shall be deemed to have consented to (i) the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to enforce the preceding sentence and (ii) having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the foreign action as agent for such stockholder. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable.

Indemnification

Our restated certificate of incorporation includes provisions that limit the liability of our directors for monetary damages for breach of their fiduciary duty as directors, except for liability that cannot be eliminated under the Delaware General Corporation Law. Accordingly, our directors will not be personally liable for monetary damages for breach of their fiduciary duty as directors, except for liabilities:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for unlawful payments of dividends or unlawful stock repurchases or redemptions, as provided under Section 174 of the Delaware General Corporation Law; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment or repeal of these provisions will require the approval of the holders of shares representing at least two-thirds of the shares entitled to vote in the election of directors, voting as one class.

Our restated certificate of incorporation and amended and restated bylaws also provide that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. Our restated certificate of incorporation and amended and restated bylaws also permit us to purchase insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions as our officer, director, employee or agent, regardless of whether Delaware law would permit indemnification. We have entered into separate

indemnification agreements with our directors, including affiliates of the selling stockholders, and officers that require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors and to advance their expenses incurred as a result of any proceeding against them as to which they could be indemnified. We believe that the limitation of liability provision in our restated certificate of incorporation and the indemnification agreements facilitate our ability to continue to attract and retain qualified individuals to serve as directors and officers. The limitation of liability and indemnification provisions in our restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Stock Exchange Listing

Our common stock is listed on The Nasdaq Global Select Market under the symbol "RGNX."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

REGENXBIO INC.
COMPENSATION PROGRAM FOR NON-EMPLOYEE DIRECTORS

(as adopted by the Board of Directors on September 22, 2015, amended as of October 29, 2019 and effective as of January 1, 2020)

A. Cash Compensation

1. Board retainer: $40,000 per year for each non-employee director, paid in quarterly installments in arrears.

2. Chairman of the Board retainer: $30,000 per year, paid in quarterly installments in arrears.

3. Committee chair retainer: $18,000 per year for the Audit Committee chair, $15,000 per year for the Compensation Committee chair, and $8,500 per year for the Nominating and Corporate Governance Committee chair, paid in quarterly installments in arrears.

4. Committee member retainer: $9,000 per year for each non-chair member of the Audit Committee, $6,000 per year for each non-chair member of the Compensation Committee, and $5,000 per year for each non-chair member of the Nominating and Corporate Governance Committee, paid in quarterly installments in arrears.

B. Equity Compensation

1. Initial stock option grant: stock option for each non-employee director to purchase 20,000 shares of REGENXBIO Inc. (the "Company") common stock. The per share price of each option shall equal 100% of the Fair Market Value (as defined in the 2015 Equity Incentive Plan (the "EIP")) of a share of common stock of the Company on the date the option is granted. The option shall vest in equal monthly installments over the 36 months following the grant date, with immediate full vesting in the event of a Change in Control (as defined in the EIP). The option will be granted by the Compensation Committee under the EIP in conjunction with the director's initial appointment or election to the Board.

2. Annual stock option grant: stock option for each non-employee director to purchase 10,000 shares of the Company's common stock. The per share price of each option shall equal 100% of the Fair Market Value of a share of common stock of the Company on the date the option is granted. The option shall vest in equal monthly installments over the 12 months following the grant date, with immediate full vesting in the event of a Change in Control. The option will be granted by the Compensation Committee under the EIP following the election of such director at the Company's annual meeting of stockholders.

C. **Other Items**

1. Non-employee directors will be reimbursed for reasonable out-of-pocket expenses incurred to attend Board and Committee meetings.

2. Customary director and officer insurance is provided for non-employee directors.

Certain identified information has been excluded from this exhibit pursuant to Item 601(b)(10)(iv) of Regulation S-K because such information both (i) is not material and (ii) would likely cause competitive harm if publicly disclosed. Excluded information is indicated with brackets and asterisks.

FIRST AMENDMENT TO LICENSE AGREEMENT

This First Amendment to License Agreement (the "First Amendment") is made as of November 4, 2019 (the "First Amendment Effective Date") by and between REGENXBIO Inc., a corporation organized under the laws of the State of Delaware, with offices at 9600 Blackwell Road, Suite 210, Rockville, MD 20850 ("Licensor"), and Abeona Therapeutics Inc., a corporation organized under the laws of the State of Delaware, with offices at 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019 ("Licensee"). Licensor and Licensee are hereinafter referred to individually as a "Party" and collectively as the "Parties."

WHEREAS, the Parties entered into that certain License Agreement dated November 4, 2018 (the "License Agreement");

WHEREAS, the Parties desire to amend certain provisions of the License Agreement relating to the timing of certain fees Licensee shall pay Licensor under the License Agreement; and

WHEREAS, pursuant to Section 10.9 of the License Agreement, the License Agreement may be amended, provided that such amendment is in writing and signed by duly authorized representatives of both Parties.

NOW, THEREFORE, in consideration of the promises and covenants contained in this First Amendment, and intending to be legally bound, the Parties hereby agree as follows:

1. Section 3.1 of the License Agreement is hereby deleted in its entirety and replaced with the following:

> "3.1 Initial Fee. In partial consideration of the rights and licenses granted to Licensee under this Agreement, Licensee shall pay Licensor an initial fee of $21,000,000, which shall be payable as follows: (a) $10,000,000 within [****] after the Effective Date; (b) $3,000,000 within twelve (12) months of the Effective Date; and (c) $8,000,000 no later than April 1, 2020, provided that any unpaid portion of the initial fee (including (a), (b) and (c)) shall be immediately payable upon termination of this Agreement or a Change of Control."

2. This First Amendment amends the terms of the License Agreement and is deemed incorporated into, and governed by all other terms of, the License Agreement. To the extent that the License Agreement is explicitly amended by this First Amendment, the terms of this First Amendment will control where the terms of the License Agreement are contrary to, or conflict with, the terms of this First Amendment. All other terms and conditions of the License Agreement not explicitly amended by this First Amendment shall remain in full force and effect.

The License Agreement, shall, together with this First Amendment, be read and construed as a single instrument.

3. Signatures on this First Amendment may be communicated by facsimile or e-mail transmission and shall be binding upon the Parties upon receipt by transmitting the same by facsimile or e-mail transmission, which signatures shall be deemed originals. If executed in counterparts, this First Amendment shall be effective as if simultaneously executed.

[Remainder of page intentionally left blank.]

IN WITNESS WHEREOF, the Parties, intending to be legally bound, have caused this First Amendment to be executed by their duly authorized representatives.

REGENXBIO INC.

By:/s/ Kenneth T. Mills
Name:Kenneth T. Mills
Title:President and Chief Executive Officer
Date:November 1, 2019

ABEONA THERAPEUTICS INC.

By:/s/ Joao Siffert
Name:Joao Siffert
Title:CEO
Date:1-Nov-2019

EXHIBIT 21.1

Subsidiaries of REGENXBIO Inc.

Name of Subsidiary	Jurisdiction of Incorporation or Organization
REGENXBIO EU Limited	Ireland

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-226691) and Form S-8 (No. 333-229910, 333-223466, 333-216508, 333-209899, 333-206984) of REGENXBIO Inc. of our report dated February 26, 2020 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
McLean, Virginia
February 26, 2020

EXHIBIT 31.1

CERTIFICATION

I, Kenneth T. Mills, certify that:

1. I have reviewed this Annual Report on Form 10-K of REGENXBIO Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2020

/s/ Kenneth T. Mills

Kenneth T. Mills
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION

I, Vittal Vasista, certify that:

1. I have reviewed this Annual Report on Form 10-K of REGENXBIO Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2020

/s/ Vittal Vasista

Vittal Vasista
Chief Financial Officer
(Principal Financial and Accounting Officer)

EXHIBIT 32.1

CERTIFICATION

In connection with the Annual Report of REGENXBIO Inc. (the "Registrant") on Form 10-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Kenneth T. Mills, President, Chief Executive Officer and Director of the Registrant, and Vittal Vasista, Chief Financial Officer of the Registrant, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to their respective knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

Date: February 26, 2020

/s/ Kenneth T. Mills

Kenneth T. Mills
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 26, 2020

/s/ Vittal Vasista

Vittal Vasista
Chief Financial Officer
(Principal Financial and Accounting Officer)

This certification is made solely for the purposes of 18 U.S.C. Section 1350, subject to the knowledge standard contained therein, and not for any other purpose. A signed original of this written statement required by Section 906 has been provided to the Registrant and will be retained by the Registrant and furnished to the United States Securities and Exchange Commission or its staff upon request.

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933 or the Securities Exchange Act of 1934 (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.