REGENXBIO Inc.
Form 10-K
February 27, 2019
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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, 2018

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:

Common Stock, $0.0001 par value per share	The Nasdaq Stock Market LLC
(Title of each class)	(Name of each exchange on which registered)

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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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 Exchange 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, 2018, the last business day of the registrant's most recently completed second quarter, was $1,624,447,767.

As of February 22, 2019, there were 36,418,716 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 proxy statement with respect to the registrant's 2019 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, 2018, are incorporated by reference into Part III of this Annual Report on 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 v 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 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 ability to obtain and maintain regulatory approval of our product candidates, and the labeling for any approved 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 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 product candidates;
- 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 and the rules of the SEC, we do not undertake any obligation, and specifically decline any obligation, to update or revise 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.

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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.

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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 genes to cells to address genetic defects or to enable cells in the body to produce therapeutic proteins or antibodies 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.

Our product candidate RGX 314 is being developed for the treatment of wet age-related macular degeneration (wet AMD), a leading cause of total and partial vision loss in the United States, Europe and Japan. We began enrollment in the Phase I/IIa clinical trial for RGX 314 for the treatment of wet AMD in May 2017. Thirty total subjects have been dosed in the RGX-314 Phase I/IIa clinical trial, including six subjects in each of the first three dose cohorts and 12 subjects in the fourth dose cohort. We previously reported that as of December 3, 2018:

- RGX-314 had been well-tolerated across all cohorts, with no drug-related serious adverse events (SAEs) reported. The most common adverse events (AEs) had been assessed as mild and there had been no observed immune responses, drug-related ocular inflammation or post-surgical inflammation beyond what is expected following a routine vitrectomy.
- 50% of subjects (3 of 6) in the third dose cohort remained anti-vascular endothelial growth factor (VEGF) rescue injection-free at nine months with persistent clinical durability of effect observed in best corrected visual acuity (BCVA) and central retinal thickness (CRT). Mean BCVA improved by +13 Early Treatment Diabetic Retinopathy Study (ETDRS) letters and mean CRT decreased by -37 microns from baseline in these subjects at nine months.

We expect to expand to a fifth dose cohort in the RGX-314 Phase I/IIa clinical trial for the treatment of wet AMD over the course of 2019. We also expect to present top-line data from the Phase I/IIa clinical trial in wet AMD and initiate a Phase IIb clinical trial in wet AMD by the end of 2019. We expect to file an investigational new drug application (IND) for a Phase II clinical trial for RGX-314 in an additional chronic retinal condition where anti-VEGF therapy is the current standard of care in the second half of 2019.

We are also developing product candidates to address the neurological symptoms of three severe genetic lysosomal storage diseases: 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 iduronate 2 sulfatase (IDS), MPS I is caused by deficiency of -l-iduronidase (IDUA) and CLN2 disease is caused by deficiency of tripeptidyl peptidase 1 (TPP1), all of which are enzymes that are responsible for breakdown of cellular waste products. 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. The first subject in the RGX-121 Phase I/II clinical trial was dosed in late 2018. As of December 4, 2018, the subject had completed an initial eight-week safety assessment, and RGX-121 had been well-tolerated with no SAEs reported.
- RGX-111 for the treatment of MPS I. The IND for RGX 111 is active. We expect to begin enrollment in a Phase I clinical trial for RGX 111 in mid 2019.
- RGX-181 for the treatment of CLN2 disease. We expect to file an IND for RGX-181 in the second half of 2019.

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. We began enrollment in the Phase I/II clinical trial for RGX 501 in March 2017. As of December 31, 2018, we had dosed three subjects in the first cohort and three subjects in the second cohort of the

RGX-501 Phase I/II clinical trial. An amendment to the Phase I/II clinical trial protocol has been submitted to health authorities to allow for the enrollment of additional subjects at the second cohort dose using corticosteroid prophylaxis. We expect to present interim data from second dose cohort with steroid prophylaxis from the Phase I/II clinical trial in the second half of 2019.

In addition to the 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 leading academic institutions and will continue to seek partnerships with innovative institutions to develop novel NAV gene therapy product candidates.

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Our gene therapy product candidates deliver genes to cells using adeno-associated virus (AAV) vectors, which are non-replicating viral delivery vehicles that are not known to cause disease. Our product candidates all utilize viral vectors from our proprietary gene delivery platform, which we call our NAV Technology Platform. Our NAV Technology Platform consists of exclusive rights to AAV7, AAV8, AAV9, AAVrh10 and over 100 other novel AAV vectors (NAV Vectors). We currently have exclusive rights to over 100 patents and patent applications worldwide covering our NAV Vectors, including composition of matter claims for AAV7, AAV8, AAV9 and AAVrh10, as well as methods for their manufacture and therapeutic uses. We believe this patent portfolio forms a strong foundation for our current programs and with our ongoing research and development, we expect to continue to expand this robust patent portfolio.

The foundation of our NAV Technology Platform was discovered in an effort to identify next generation AAV vectors that could overcome the limitations of earlier generation AAV vectors (AAV1 through AAV6). We believe the key benefits of NAV Vectors over earlier generation AAV vectors include:

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

In addition to our internal product development efforts, we also selectively sublicense our NAV Vectors to other biotechnology companies, which we refer to as NAV Technology Licensees. As of December 31, 2018, our NAV Technology Platform was being applied in the development of more than 20 partnered product candidates by our NAV Technology Licensees.

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Our internal and partnered product development program pipeline is shown below.

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Our partnered development pipeline benefits from the disease-specific expertise of 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.

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 for monogenic diseases with sub-optimal or non-existent therapies because of its potential to correct an underlying genetic defect, rather than just treating a patient's symptoms. In diseases not caused by a single gene defect, in vivo gene therapy has the potential to replace the need for frequent treatments by enabling the body to produce therapeutic proteins or antibodies consistently to impact the course of disease. We believe our NAV Technology Platform is proving to be a significant advancement over earlier AAV vectors in delivering these therapies. Based on data derived from our clinical studies and animal models using our NAV Vectors, as well as third-party clinical trials and animal models using our NAV Vectors, we believe our NAV Technology Platform possesses unique, beneficial properties that are not seen in earlier generation AAVs. We believe that our NAV Technology Platform, which underpins our internal development programs and the programs of our NAV Technology Licensees, will enable us and our partners to develop best-in-class gene therapy candidates for a wide range of disease targets.
- Rapidly advance our RGX-314 program for wet AMD and other chronic retinal conditions that respond to anti-VEGF therapy. Wet AMD and several other chronic retinal conditions are currently treated with frequent intraocular injections of anti-VEGF therapy. We believe our RGX-314 product candidate has the potential to provide long-term anti-VEGF therapy for patients via a single administration, relieving significant treatment burden for patients, physicians and caregivers, while potentially improving patient outcomes by providing consistent, sustained levels of anti-VEGF in the eye. We are conducting a Phase I/IIa clinical trial for RGX-314 for the treatment of wet AMD and plan to expand to a larger, randomized, controlled Phase IIb clinical trial for wet AMD in late 2019. In addition, we plan to expand to additional chronic retinal conditions that respond to anti-VEGF therapy. We plan to file the first IND for an additional Phase II clinical trial in a condition beyond wet AMD in the second half of 2019. If we are successful in further establishing safety and efficacy in these Phase II clinical trials, we will pursue further development, including registration trials and commercialization of such product candidates
- Aggressively progress our internal lead proprietary development programs in neurodegenerative and metabolic diseases. MPS II, MPS I, CLN2 disease and HoFH are all diseases with high unmet clinical need and current treatments that are sub-optimal. Our neurodegenerative disease franchise leverages a platform approach by using our NAV AAV9 vector and an intracisternal route of administration across our three neurodegenerative disease programs. The first subject was dosed in 2018 in the Phase I/II clinical trial for RGX 121 for the treatment of MPS II

and we expect to continue enrollment in the RGX-121 clinical trial throughout 2019. The IND for RGX 111 for the treatment of MPS I is active and we expect to initiate a Phase I clinical trial for RGX 111 in mid 2019. We are progressing preclinical studies for RGX-181 for the treatment of CLN2 disease and we plan to file an IND in the second half of 2019. Additionally, as of December 31, 2018, we had enrolled six subjects in a Phase I/II clinical trial for RGX 501 and we expect to present interim data from the Phase I/II clinical trial in the second half of 2019 on additional subjects in the second dose cohort treated with steroid prophylaxis. If we are successful in achieving proof-of-concept in the Phase I or Phase I/II clinical trials for these neurodegenerative and metabolic diseases, we will pursue further development, including registration trials and commercialization of such product candidates.

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- Establish gene therapy franchises in and beyond our current core therapeutic areas of retinal, metabolic and neurodegenerative diseases. After human proof-of-concept is achieved in a disease, we believe we will be able to apply what we have learned and use our NAV Technology Platform to more rapidly develop new product candidates for many similar diseases. Once an appropriate vector and route of administration for a particular disease type have been established, we believe a new gene can be inserted into the appropriate vector and the established route of administration can be used for other similar diseases. To date, our strategy of focusing on retinal, neurodegenerative and metabolic diseases has been informed by significant animal, and in some cases human clinical, data that indicate specific NAV Vectors are particularly effective in the cells where these types of diseases manifest. Targeting tissues where diseases manifest is critical to impacting the course of diseases with our NAV gene therapy treatments (NAV Gene Therapy). This approach underpins our strategy for our neurodegenerative disease franchise, where we applied knowledge from the IND-enabling studies for RGX 111 for MPS I to enable a rapid follow-on IND filing for RGX 121, our MPS II program, and we continue to apply these learnings as we progress our RGX-181 program for CLN2 disease. We believe that this approach is also applicable to retinal and metabolic diseases, as well as many other therapeutic areas and tissue targets, such as the muscle, and will allow us to efficiently generate product candidates for diseases in and beyond our current areas of therapeutic focus.
- Leverage the NAV Technology Platform in the expression of therapeutic proteins, antibodies and gene editing. Our treatment for wet AMD involves the novel, one-time administration of our NAV AAV8 vector encoding a gene for a monoclonal antibody fragment, which has the potential to enable a subject's retinal cells to continuously produce therapeutic antibodies. To maintain efficacy, the current standard of care for the treatment of wet AMD requires repetitive and inconvenient intraocular injections of marketed therapeutic proteins or antibodies, typically ranging from every four to eight weeks in frequency. There are many diseases where the existing standard of care involves frequent administration of marketed therapeutic proteins or antibodies and we believe there are other patient populations that would benefit from NAV-based treatments designed to enable different cells in the body of patients to produce therapeutic proteins or antibodies. In addition, it has been demonstrated by several researchers that our NAV Technology Platform can be efficiently adapted to deliver different genome editing components to address the specific treatment needs of many disease targets. We may aim to invest in research and development in these areas or explore collaborations with strategic partners that have capabilities in the development of therapeutic antibodies, proteins and gene editing.
- Further grow the potential of our NAV Technology Platform through strategic in-licensing and sublicensing of new programs. We plan to grow the potential of our NAV Technology Platform through licensing. For example, we pursue in-licensing for programs we deem to be promising research programs using our NAV Vectors from time to time. We intend to continue to selectively sublicense our NAV Technology Platform for specific vector and indication combinations to additional NAV Technology Licensees. Strategic sublicensing allows us to maintain our internal product development focus in 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.
- 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. We have licensed exclusive rights to a broad portfolio of certain fundamental AAV gene therapy patents and patent applications. In securing these rights, we have focused on obtaining robust rights for those intellectual property assets 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.

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We believe that gene therapy has the potential to become a new and 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 any human protein 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 of 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.

RGX 314 for the Treatment of Wet AMD

We are developing RGX 314 for the treatment of wet AMD. Wet AMD is characterized by loss of vision due to excess fluid accumulation from new blood vessel formation. Fluid leakage following this excess 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. Wet AMD is a leading cause of total and partial vision loss in the United States, Europe and Japan. As indicated by the name, the risk for developing wet AMD increases with age and we anticipate the diagnosis rate will continue to increase as the population continues to trend towards an aging population.

Anti-VEGF therapies are the standard of care in wet AMD due to their ability to reduce fluid accumulation and, on average, improve vision in the majority of patients with wet AMD. Currently, there are three anti-VEGFs that are commonly used for the treatment of wet AMD. All of these therapies, however, require repetitive and inconvenient intraocular injections, typically ranging from every four to eight weeks in frequency, to maintain efficacy. Patients often experience vision loss with reduced frequency of treatment and due to a variety of factors, including inconvenience and discomfort associated with frequent injections in the eye, patient compliance is a significant concern with anti-VEGF therapies.

RGX 314 is being developed as a novel, one-time subretinal treatment for wet AMD 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.

Clinical Development of RGX 314 for the Treatment of Wet AMD

Enrollment in the Phase I/IIa clinical trial of subretinally administered RGX 314 in the United States in subjects with wet AMD began in May 2017. The trial design allows for enrollment of up to 42 subjects across five dose levels. Subjects enrolled in the clinical trial must have a documented need and history of response to anti-VEGF

therapies. Primary endpoints include AEs, certain laboratory measures (including immunological parameters), evaluation of BCVA, change in 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 purpose of the clinical trial is to evaluate the safety and tolerability of RGX 314 at 24 weeks after a single dose of RGX 314 administered by subretinal delivery. Following completion of the primary study period, it is expected that subjects will enter the follow-up period and will continue to be assessed for long-term safety and durability of effect until week 106.

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In August 2018, we announced positive interim safety and efficacy data from the RGX-314 Phase I/IIa clinical trial in wet AMD. As of July 27, 2018, RGX-314 was well-tolerated by all subjects with no reported drug-related AEs or SAEs. There had been no observed immune responses, drug-related ocular inflammation or any post-surgical inflammation beyond what is expected following routine vitrectomy. Dose-dependent protein expression levels as measured from aqueous samples by electrochemiluminescence immunoassay (ECL), dose-dependent reduction in anti-VEGF injections and maintenance of CRT measured by SD-OCT had been reported across all cohorts. Additionally, through month six, BCVA assessments for subjects in the third dose cohort had a mean improvement in visual acuity of eight ETDRS letters. As of July 27, 2018, 50% of subjects (three subjects) from the third dose cohort were free of anti-VEGF injections for six months since the administration of RGX-314.

In October 2018, we provided an update on RGX-314 protein expression levels in the third dose cohort six months after administration of RGX-314. At six months post RGX-314 administration, mean and median RGX-314 protein levels measured from aqueous samples by ECL in the third dose cohort were higher than at one month post RGX-314 administration. Mean and median protein expression levels in the third dose cohort were higher both in the group of subjects who had been free of anti-VEGF injections since the administration of RGX-314 and those who had received anti-VEGF rescue injections.

In January 2019, we provided an additional update on the RGX-314 Phase I/IIa clinical trial. As of December 3, 2018, RGX-314 continued to be well-tolerated across all cohorts, with no drug-related SAEs and no observed immune responses, drug-related ocular inflammation or post-surgical inflammation beyond what is expected following a routine vitrectomy. 50% of subjects (3 of 6) in the third dose cohort continued to remain anti-VEGF rescue injection-free at nine months post-RGX-314 administration with persistent clinical durability of effect observed on BCVA and CRT. Mean BCVA improved by +13 ETDRS letters and mean CRT decreased by -37 microns from baseline in these subjects at nine months.

30 total subjects have been dosed in the RGX-314 Phase I/IIa clinical trial, including six subjects in each of the first three dose cohorts and 12 subjects in the fourth dose cohort.

We expect to present top-line data from the RGX 314 Phase I/IIa clinical trial by the end of 2019, and initiate a larger, randomized, controlled Phase IIb clinical trial for RGX-314 in wet AMD in late 2019.

RGX-314 for the Treatment of Additional Retinal Conditions

Anti-VEGF therapy is the standard of care in several chronic retinal conditions beyond wet AMD, including but not limited to diabetic retinopathy, diabetic macular edema and retinal vein occlusion. While these and other chronic retinal conditions respond to anti-VEGF therapy, we believe these patient populations could benefit from an improved, long-term anti-VEGF treatment solution that RGX-314 may be able to provide. We plan to file INDs and conduct clinical trials for RGX-314 in additional chronic retinal conditions in the future, including to further evaluate the potential benefit of RGX-314 as a one-time anti-VEGF treatment in an additional chronic retinal condition in the second half of 2019.

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 IDS. IDS is an enzyme responsible for the breakdown of polysaccharides heparan sulfate and dermatan sulfate in the lysosomes of cells, 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. Many patients develop symptoms related to GAG storage in the central nervous system (CNS), which can include excessive accumulation of fluid in the brain, spinal cord compression and cognitive impairment. 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, recombinant IDS (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 IDS reconstitution in the CNS for MPS II patients experiencing neurological complications.

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RGX 121 is designed to use the AAV9 vector to deliver the human IDS gene to the CNS. Delivery and expression of the enzyme that is deficient within cells in the CNS could provide a permanent source of secreted IDS 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 IDS 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 based gene delivery via CNS administration in subjects with MPS II began in the second half of 2018. The trial design calls for enrollment of up to six subjects 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.

We expect to provide an interim data update from the RGX-121 Phase I/II clinical trial in the second half of 2019.

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 heparan sulfate and dermatan sulfate 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 over 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. In addition, clinical trials to evaluate direct administration of ERT into the CNS for the treatment of MPS II and CLN2 disease have been initiated in an effort to find approaches that treat the CNS manifestations of lysosomal storage diseases. These approaches, however, do not address the underlying cause of these neurodegenerative diseases and we believe that if such products receive regulatory approval, the need for frequent (bi-weekly or monthly) administration into the CNS is likely to lead to patient compliance issues, further reducing the treatment potential of this method of ERT.

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.

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

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

The IND for RGX 111 is active and we plan to initiate a Phase I clinical trial of RGX 111 based gene delivery via CNS administration in mid 2019 in subjects with MPS I. The primary endpoint will be a safety assessment. The secondary endpoints include the effect of RGX 111 on biomarkers of IDUA activity in the CSF, serum and urine and the effect of RGX 111 on neurocognitive deficits, as well as other outcome measures.

We expect to begin enrollment in the RGX-111 Phase I clinical trial in mid-2019.

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 enzymatic 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 represents 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, 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 intend to file an IND in the second half of 2019 to support the initiation of a dose-escalation clinical trial of RGX-181 based gene delivery via CNS administration in subjects with CLN2 disease. Potential endpoints include a safety assessment, evaluation of biomarkers and clinical outcomes.

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.

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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. 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.

As of December 31, 2018, a total of six subjects had been enrolled in two dose cohorts of the Phase I/II trial for RGX-501 for the treatment of HoFH. Four SAEs had been reported, two of which were reported as drug-related. All three subjects enrolled at the dose of 7.5 x 10^12 GC/kg body weight (Cohort 2) experienced elevation in transaminases four to six weeks post-dosing, were asymptomatic and responded rapidly to the initiation of corticosteroids followed by a slow taper, with normalization of the transaminases. At 12 weeks, the three subjects in the first dose cohort did not show a clinically meaningful change in LDL-C levels. We believe that the ability to assess LDL-C levels at 12 weeks in the three subjects in the second dose cohort may be confounded by the potential effects on the liver and the resulting steroid therapy.

In November 2018, we entered into a new clinical trial agreement with the University of Pennsylvania (Penn), the original RGX-501 trial sponsor, which allowed us to become the trial sponsor following the required activities with regulatory authorities to effectuate the transfer of sponsorship. We believe this will allow for enhanced visibility and

control over the RGX-501 trial. In the United States, the RGX-501 IND application was transferred in November 2018. Transfer of the Clinical Trial Applications for all other participating countries was ongoing.

In parallel, an amendment to the Phase I/II clinical trial protocol has been submitted to health authorities to allow for the enrollment of additional subjects at the second dose cohort dose level using corticosteroid prophylaxis. Trial recruitment has resumed. While we have assumed sponsor responsibilities, Penn will continue to support this study both as a scientific collaborator and as the principal dosing site.

We expect to provide an interim data update from the second dose cohort with steroid prophylaxis from the RGX-501 Phase I/II clinical trial in the second half of 2019.

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Other Preclinical Programs

In addition to our lead product candidate programs, 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 in and beyond our current retina, neurodegenerative and metabolic franchise areas. We have partnered with a number of leading academic institutions and will continue to seek partnerships with innovative institutions to remain at the leading edge of the gene therapy field.

Commercial Licenses to NAV Technology Licensees

We 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. 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 proof-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 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, 2018, our NAV Technology Platform was being applied in the development of more than 20 partnered product candidates by 11 NAV Technology Licensees, 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. As of December 31, 2018, our NAV Technology Licensees had 13 clinical stage programs using NAV Vectors.

Process Development and Manufacturing

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 at commercial quantity.

AAV Vector Production

We have invested significantly in our internal capabilities and infrastructure, including the establishment of our advanced manufacturing and analytics lab, which has been recently expanded to also accommodate a larger, 200 liter scale of operation and 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. We have established internal capability to produce NAV Vectors across multiple platforms and at a scale of up to 200 liters.

We have also entered into agreements with multiple leading biologics contract manufacturing organizations (CMOs) for production of material under current Good Manufacturing Practice (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 our CMOs are capable of meeting global regulatory standards for clinical and commercial material supply. We believe partnering with multiple leading 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.

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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 global 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 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. However, 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.

Gene Therapy Overview and History of Earlier Generation AAV

Historically, the primary challenge for gene therapy has been the 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.

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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 whose normal life-cycle relies 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.

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

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Our Proprietary NAV Technology Platform for Gene Delivery

Our NAV Technology Platform has been used in a number of clinical trials conducted by us, our partners and third-party investigators. 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.

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 over 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 in the pages that follow.

Higher Gene Expression

NAV Vectors have been shown to generate higher levels of gene expression in animals than earlier generation AAV vectors such as AAV2. In mice livers, one of our NAV Vectors, 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. NAV Vectors have demonstrated stable expression in animals for over eight years. Moreover, AAV8 vectors have demonstrated stable expression for over seven years in

clinical trials for hemophilia B patients.

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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. In the CNS, AAV9 has emerged as a vector that enables efficient gene delivery when directly injected into the brain. This was aided by the ability of AAV9 to be transported throughout the brain, enabling broader delivery with a single injection.

NAV Gene Therapy has demonstrated novel tissue selectivity for the CNS when delivered intravenously. Intravenous delivery of AAV9 resulted in efficient gene expression in the brain and spinal cord, and this route of administration produced results in both small and large animals, including non-human primates. This was the first time a gene therapy vector was demonstrated to cross the blood-brain barrier. This route of administration has recently been used clinically by one of our NAV Technology Licensees to treat SMA Type I.

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 50% of certain human populations have a high level of neutralizing antibodies (NAbs) for the earlier generation vector AAV2. This represents a major obstacle to the effective use of these earlier generation AAV vectors due to the inhibition of gene delivery via particle neutralization in circulation, meaning pre-existing antibodies neutralize the vector with the transgene before it can reach the target cells. By contrast, frequency of neutralizing antibodies for AAV8 is consistently lower than for AAV2. In a French study, for example, AAV2 NAbs occurred at a frequency of 59% compared to 19% for AAV8. Thus, AAV8 is a candidate for liver-directed gene delivery in a higher proportion of the population than AAV2.

Additionally, reduced effect from the generation and reactivity of T-cells to NAV Vectors has been demonstrated, relative to earlier generation AAV vectors. Activation of T-cells to the capsid of AAV2 vectors has been implicated in liver toxicity in a clinical trial for the treatment of hemophilia B. A patient in this clinical trial developed an elevation

of liver enzymes and subsequently lost expression. This led to a hypothesis that capsid protein antigens and memory T-cell activation may lead to clearance of AAV-transduced cells. To further investigate this kind of toxicity, scientists reported a study that evaluated T-cell responses to AAV vectors after administration to mice and nonhuman primates. In this study, 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 more recent clinical trial for the treatment of hemophilia B, using AAV8, there was less of an effect from T-cells generated and reactive with AAV8. We believe this is likely a function of the lower doses that can be used as well as the structure of the vector itself.

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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, metabolic and neurodegenerative 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 and April 2016. 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 prior to September 2014;
- are related to the AAV technology platform discovered by Dr. Wilson at Penn prior to February 2009 or pursuant to a sponsored research agreement or subsequent amendment to a sponsored research agreement; and
- are owned by Penn and available for licensing.

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.

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The Penn license agreement, as amended, also provides us with a non-exclusive, worldwide license to use all data and information generated in the performance of clinical research relating to the RGX-501 clinical trial and 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 pursuant to the 2009 SRA, the 2014 SRA, the 2013 SRA or subsequent amendment to a sponsored research agreement; 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:

- 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.

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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, $0.5 million of which have been accrued or paid as of December 31, 2018;
- 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, the Company is 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, the Company is 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.

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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, 2018, in addition to the patents related to our NAV Technology described below, our patent portfolio included a total of three issued U.S. patents, eight pending International Patent applications filed pursuant to the Patent Cooperation Treaty (PCTs) and eight 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 one pending PCT for which any issued U.S. or European patent would expire in 2038;
- RGX-501: One issued U.S. patent that will expire in 2026, including patent term adjustment, one PCT that has entered national stage for which any issued U.S. or European patent would expire in 2036 and one pending PCT for which any issued U.S. or European patent would expire in 2038;
- RGX-111: Two issued U.S. patents that will expire in 2034, including patent term adjustment;
- RGX-111/RGX-121: Five PCTs that have entered national stage and five pending PCTs for which any issued U.S. or European patents would expire in 2034, 2036, 2037 or 2038; and
- RGX-181: One pending U.S. non-provisional patent application for which any issued U.S. patent would expire in 2034 and one pending PCT for which any issued U.S. or European patent would expire in 2038.

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, 2018, our licensed patent portfolio included 10 issued U.S. patents and four 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.

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.

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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, 2018, 2017 and 2016 consisted primarily of license revenue. Two customers (AveXis Inc. (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. Two customers accounted for approximately 68% of our total revenue for the year ended December 31, 2016. No other customer accounted for more than 10% of revenue in 2016. We expect future license revenue to be derived from a limited number of licensees. Future license 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

The biotechnology and pharmaceutical industries, including in the field of gene therapy, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property. While we believe that our NAV Technology Platform, strong intellectual property portfolio and scientific expertise in the gene therapy field provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical and biotechnology companies, new market entrants and new technologies.

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, Sangamo Therapeutics, Inc., Sanofi Genzyme, Sarepta Therapeutics, Inc., Solid Biosciences Inc., Spark 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.

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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. Marketed competition for wet AMD largely consists of anti-VEGF therapies developed by Roche/Genentech, Inc. (Lucentis, Avastin) and Regeneron Pharmaceuticals, Inc. (Eylea).
- 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).
- MPS I. There is one principal competitor with a marketed product for the treatment of MPS I, Sanofi Genzyme (Aldurazyme).
- MPS II. The principal marketed competition for MPS II is a systemic enzyme replacement therapy, which is marketed by Shire plc (Elaprase).
- CLN2 Disease. There is one principal competitor with a marketed product for the treatment of CLN2 Disease, BioMarin (Brineura).

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 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.

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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.

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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.

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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.

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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.

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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.

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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;

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- 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.

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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 corruptly 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 the company's 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.

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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 the United Kingdom, 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.

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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 31 January 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 is expected to be adopted as new legislation within the next three years.

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.

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 22, 2019, we employed 192 full-time employees, of which 144 were engaged in research and development activities, including preclinical, manufacturing and clinical study related functions, and 48 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.

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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). The risks described below are not the only risks facing us. 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.

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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, if any, 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.

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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.

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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 certain of those functions;

- delays in having subjects complete participation in a trial or return for post-treatment follow-up;

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- 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.

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 strategy;
- 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.

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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.

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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 different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, 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.

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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.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. 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. 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.

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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 sublicensing 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, no NAV Technology Licensee has an approved or commercialized gene therapy product based on such licensing program. We expect to normally generate only limited revenue, if any, from our current NAV Technology Licensees and any future NAV Technology Licensees in the near term. 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 sublicensing 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.

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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. We expect that our cash, cash equivalents and marketable securities as of the end of the period to which this filing relates 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.

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, if any;
- 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 sale of our products, should any of our product candidates receive marketing approval;
    - the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- 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 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.

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We have generated non-recurring revenue from our NAV Technology Platform sublicensing and may not successfully expand our licensing activities.

Our ability to generate revenue from our NAV Technology Platform sublicensing 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. We do not anticipate generating revenues from product sales for the next several years, if ever, as described elsewhere in these risk factors. To date, a significant portion of our revenues have been generated from the sublicensing of rights to our NAV Technology Platform. Our ability to generate future revenues from our NAV Technology Platform sublicensing depends on many factors, including:

- our NAV Technology Licensees successfully developing gene therapy products using our NAV Technology Platform;
- 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.

We have never generated revenue from product candidate sales and have only generated limited revenue from reagent sales.

Our ability to generate revenue from product candidate sales depends on our ability, alone or with partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. All of our revenues to date have been from sublicensing our NAV Technology Platform, the sale of licensed reagents to third-parties for use in research and development and grant revenue generated through research and development grant programs offered by the U.S. federal government and the European Union. We expect grant revenue to be minimal in future periods, as we currently do not expect to receive any new grant awards. We do not dedicate resources to sales efforts for reagents. Accordingly, future revenue from reagent sales is uncertain and may fluctuate significantly from period to period. Our ability to generate future revenues from product candidate sales depends heavily on our, or our NAV Technology Licensees', success in:

- completing research studies and preclinical and clinical development of product candidates and identifying new gene therapy product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which clinical trials are completed;
- launching and 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 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;

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- addressing any competing technological and market developments;
- 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.

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 the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

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 you make 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 accounting standards and disagreements and differing views by the SEC, the Financial Accounting Standards Board (FASB) or various other bodies with respect to the interpretations, estimates and judgments required for the preparation of our financial statements could result in the restatement of our financial statements or other potential adverse effects.

We are subject to complex tax laws, regulations, accounting principles and interpretations thereof. The preparation of our financial statements requires us to interpret accounting principles and guidance and make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our interpretations, estimates and judgments are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for the preparation of our financial statements. U.S. generally accepted accounting principles are subject to interpretation by the SEC,

FASB and various other bodies formed to interpret and create appropriate accounting principles and guidance. In the event that these rules change with respect to a matter that is or may become relevant to our business, such as revenue recognition, asset impairment and fair value determinations, inventories, business combinations and intangible asset valuations, leases and litigation, or in the event that one of these bodies disagrees with our accounting recognition, measurement or disclosure or any of our accounting interpretations, estimates or assumptions, it may have a significant effect on our reported results and may retroactively affect previously reported results. The need to restate our financial results could, among other potential adverse effects, result in us incurring substantial costs, affect our ability to timely file our periodic reports until such restatement is completed, divert the attention of our management and employees from managing our business, result in material changes to our historical and future financial results, result in investors losing confidence in our operating results, subject us to securities class action litigation, and cause our stock price to decline.

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If we are unable to maintain effective internal control over financial reporting, investors may lose confidence in the accuracy of our financial reports.

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal controls. Section 404 of the Sarbanes-Oxley Act of 2002 (Section 404) requires that we evaluate and determine the effectiveness of our internal control over financial reporting and provide a management report on internal control over financial reporting. As of January 1, 2019, we are no longer an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act), and our management report on internal control over financial reporting must be attested to by our independent registered public accounting firm.

If we have, or fail to identify, a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis, the accuracy and timing of our financial reporting may be adversely affected and our financial statements may be materially misstated. In addition, our internal control over financial reporting will not prevent or detect all errors and fraud. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If there are material weaknesses or failures in our ability to meet any of the requirements related to the maintenance and reporting of our internal controls, investors may lose confidence in the accuracy and completeness of our financial reports and that could cause the price of our common stock to decline. In addition, we could become subject to investigations by Nasdaq, the SEC or other regulatory authorities, which could require additional management attention and which could adversely affect our business.

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 are subject to taxation at the U.S. federal, state and local levels and in foreign jurisdictions. Our future tax rates and cash flows could be affected by changes in statutory rates and other legislative changes, changes in the valuation of our deferred tax assets and liabilities, changes in the composition of earnings in jurisdictions with differing tax rates, changes in determinations regarding the jurisdictions in which we are subject to taxation, and our ability to repatriate earnings from foreign jurisdictions. From time to time, governments may make substantive changes to their tax rules and the application thereof, which could result in materially higher corporate taxes than would be incurred under existing tax laws and could otherwise adversely affect our financial condition or results of operations.

We are subject to periodic tax audits. An unfavorable outcome from any tax audit could result in higher tax costs, penalties or interest, or adjustments to our tax credits or net operating losses (NOLs), which could 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 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.

In December 2017, the Tax Cuts and Jobs Act of 2017 (the TCJA) was signed into law, which 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.

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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;

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- 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.

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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, natural disasters, disruption in utility services, human error or disruptions in the operations of suppliers.

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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, 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 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 do not currently plan to independently manufacture most of the material for our planned preclinical and clinical programs. 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.

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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; 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 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 raw materials and other components required in our manufacturing process are derived from biologic sources, and we normally rely on suppliers to provide raw materials and other components. Such raw materials are difficult to procure and may be subject to contamination or recall. Certain raw materials, 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. 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.

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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.

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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.

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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. 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.

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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, 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 or natural disasters including earthquakes, floods and fires.

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.

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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.

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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. For example, the TCJA repealed the tax penalty linked to the individual mandate of PPACA, which may reduce the number of individuals covered by health benefits. We cannot predict the ultimate content, timing or effect of any potential PPACA modification, repeal or replacement or any other healthcare reform legislation, or the effect of such potential changes 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.

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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.

In the United States, the research, manufacturing, distribution, sale and promotion of drugs and biologics are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including CMS, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice offices of the U.S. Attorney, and state and local governments.

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; and

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- 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 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.

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

The collection and use of personal health data in the European Union is governed by the General Data Protection Regulation (GDPR) and Member States' national data protection laws. GDPR imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and using third party processors in connection with the processing of the personal data. GDPR also imposes strict rules on the transfer of personal data out of the European Union, including to the United States. Failure to comply with the requirements of GDPR and the applicable national data protection laws of the European Union Member States may result in fines and other administrative penalties. GDPR includes substantial fines for breaches of the data protection rules. GDPR may increase our responsibility and liability in relation to personal data that we process. To comply with the data protection rules imposed by GDPR, we may be required to put in place additional mechanisms ensuring compliance. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

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.

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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.

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

Our results of operations could be harmed by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for our product candidates or our NAV Technology Licensees' product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our future collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could harm our business.

Additionally, in June 2016, a majority of United Kingdom (UK) voters voted for the UK to exit the European Union (Brexit) and in March 2017, the UK government provided official legal notification to the European Union that the UK will exit the European Union. The timing and completion of Brexit is subject to judicial and parliamentary developments in the UK, as well as any legal challenges. The economic effects of Brexit will depend on any agreements the UK makes to retain access to European Union markets either during a transitional period or more permanently. Brexit could adversely affect European and worldwide economic or market conditions and could contribute to instability in global financial markets. Brexit is likely to lead to legal uncertainty and potentially divergent national laws and regulations as the UK determines which European Union laws to replace or replicate. Any of these effects of Brexit, and any other effects we cannot anticipate, could adversely affect our business, business opportunities, results of operations, financial condition and cash flows.

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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 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. 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.

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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 revenue for the years ended December 31, 2018 and 2017 consisted primarily of license revenue. Two customers accounted for approximately 97% of our total revenue for the year ended December 31, 2018. One customer 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 for the year ended December 31, 2017. We expect future license revenue to be derived from a limited number of licensees. Future license 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.

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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.

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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.

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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.

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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.

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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 of the United States (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.

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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;

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- 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.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion in the application of our cash and cash equivalents. Because of the number and variability of factors that will determine our use of our cash and cash equivalents, their ultimate use may vary substantially from their currently intended use. Our management might not apply our cash and cash equivalents in ways that ultimately increase the value of your investment. The failure by our management to apply our cash and cash equivalents effectively could harm our business. Pending their use, we may invest our cash and cash equivalents in a variety of capital preservation investments, including short-term, interest-bearing, investment-grade instruments and U.S. government securities. These investments may not yield a favorable return to our stockholders.

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

We have never declared or paid cash dividends on our common stock, and we currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. Therefore, our stockholders are not likely to receive any dividends on our common stock for the foreseeable future or at all and their ability to receive a return on their

investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our stockholders have purchased it.

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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 a 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.

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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.

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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 shareholder 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 67,000 square feet of office and laboratory space at a number of other locations in Rockville, Maryland and New York, New York under leases that expire at various dates through 2023, some of which are renewable for additional years. In November 2018, we entered into a lease agreement for approximately 132,000 square feet of office and laboratory space in a new facility to be constructed in Rockville, Maryland, which will serve as our future corporate, manufacturing and research headquarters. The construction of the new facility is being performed by the landlord and is expected to be completed in 2020, and we expect to make 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 construction-in-progress, are 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.

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PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED SHAREHOLDER 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 22, 2019, the last reported sale price for our common stock on The Nasdaq Global Select Market was $46.50 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, 2018, with the cumulative total return of (a) the Nasdaq Biotechnology Index (^NBI) and (b) the Nasdaq Composite Index (^IXIC), 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.

Holders

As of February 22, 2019, 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.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

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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 financial data for the years ended December 31, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. We derived the consolidated financial data for the years ended December 31, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016, 2015 and 2014 from our audited consolidated financial statements that are not included elsewhere 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,				
	2018 (a)	2017	2016	2015	2014
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenues					
License revenue	$218,505	$10,385	$4,303	$7,025	$4,575
Other revenues	—	8	286	563	1,545
Total revenues	218,505	10,393	4,589	7,588	6,120
Operating Expenses					
Costs of revenues					
Licensing costs	9,640	1,703	861	1,405	885
Other	—	6	98	98	122
Research and development	83,873	57,224	45,482	17,279	4,961
General and administrative	36,850	27,229	23,590	11,912	3,851
Other operating expenses (income)	42	116	(102)	31	(17)
Total operating expenses	130,405	86,278	69,929	30,725	9,802
Income (loss) from operations	88,100	(75,885)	(65,340)	(23,137)	(3,682)
Other Income (Expense)					
Interest income from licensing	8,946	—	—	—	—
Investment income	7,070	2,716	1,938	346	—
Interest expense	—	—	—	(20)	(321)
Total other income (expense)	16,016	2,716	1,938	326	(321)
Income (loss) before income taxes	104,116	(73,169)	(63,402)	(22,811)	(4,003)
Income Tax Benefit (Expense)	(4,179)	—	435	—	—
Net income (loss)	$99,937	$(73,169)	$(62,967)	$(22,811)	$(4,003)
Net income (loss) per share:					
Basic	$2.99	$(2.45)	$(2.38)	$(2.59)	$(1.82)
Diluted	$2.73	$(2.45)	$(2.38)	$(2.59)	$(1.82)
Weighted-average common shares outstanding:					
Basic	33,427	29,878	26,409	9,173	2,643
Diluted	36,648	29,878	26,409	9,173	2,643

(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 financial data presented for the year ended December 31, 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 and the impact to our consolidated financial statements.

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	December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$75,561	$46,656	$24,840	$54,116	$1,121
Marketable securities	395,019	129,738	134,126	162,251	—
Working capital (deficit)	315,737	153,560	83,702	113,809	(6,158)
Total assets	543,814	198,677	172,732	221,380	3,491
Non-current liabilities	12,790	1,211	1,326	233	—
Total liabilities	34,966	15,648	10,995	4,572	9,189
Convertible preferred stock	—	—	—	—	12,593
Common stock and additional paid-in capital	592,584	371,500	276,357	269,147	10,518
Total stockholders' equity (deficit)	508,848	183,029	161,737	216,808	(18,291)

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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 an internal pipeline of product candidates across the therapeutic areas of retinal, metabolic and neurodegenerative diseases.

- RGX-314: Our lead product candidate RGX-314 is for the treatment of wet age-related macular degeneration (wet AMD), a leading cause of total and partial vision loss in the United States, Europe and Japan. We began enrollment in the Phase I/IIa clinical trial for RGX-314 for the treatment of wet AMD in May 2017 and have completed dosing of 30 total subjects in four cohorts, including six subjects in each of the first three cohorts and 12 subjects in the fourth cohort. We expect to initiate a Phase IIb trial in late 2019.
- 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 with a similar phenotype to MPS I. MPS II is caused by deficiency of iduronate-2-sulfatase (IDS), an enzyme that is also responsible for breakdown of cellular waste products. We have begun dosing subjects in the Phase I/II clinical trial for RGX-121 and we expect to continue enrollment and site activation in 2019.
- 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 -l-iduronidase (IDUA), an enzyme required for breakdown of cellular waste products. The investigational new drug (IND) application filed with the U.S. Food and Drug Administration (the FDA) for RGX-111 for the treatment of MPS I is active, we have submitted an application to the Brazilian Health Surveillance Agency (ANVISA) to proceed with a Phase I clinical trial evaluating RGX-111 for treatment of MPS I and we expect to begin enrollment in a Phase I clinical trial in mid-2019.
- 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 low-density lipoprotein receptor. Enrollment in the Phase I/II clinical trial for RGX-501 began in March 2017. We have completed dosing of the first cohort of three subjects and have dosed three subjects in the second cohort, a total of six subjects. We have amended the clinical trial protocol and expect to enroll additional subjects using steroid prophylaxis.
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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 plan to submit an IND application for RGX-181 for the treatment of CLN2 to the FDA in the second half of 2019 to enable initiation of a first-in-human clinical trial.

In addition to our lead product candidates, 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.

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Overview of Our NAV Technology Platform

In addition to our internal product development efforts, we also selectively sublicense our proprietary adeno-associated virus gene therapy delivery platform (NAV Technology Platform) to other leading biotechnology companies, which we refer to as NAV Technology Licensees. As of December 31, 2018, our NAV Technology Platform was being applied in the development of more than 20 partnered product candidates by our NAV Technology Licensees. 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 proof-of-concept for our NAV Technology Platform, and creating potential additional revenue.

Financial Overview

Revenues

To date, we have primarily generated revenues through the licensing of our NAV Technology Platform to NAV Technology Licensees. We have not generated any revenues from the sale of approved products. If we fail to complete the development of our product candidates in a timely manner, or fail to obtain their regulatory approval, our ability to generate future revenues will be materially compromised.

We license our NAV Technology Platform to other biotechnology and pharmaceutical companies. As of December 31, 2018, our NAV Technology Platform was being applied in the development of more than 20 partnered product candidates by 11 NAV Technology Licensees. 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. To date we have not recognized any revenue from the achievement of sales-based milestones or royalties on sales of licensed products.

Future license revenue is highly dependent on the successful development and commercialization of licensed products by our licensees, which is uncertain, and revenue 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 license revenue is 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 license 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 license revenue.

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). We adopted Topic 606 using the modified retrospective transition method and have applied the new standard to all of our license agreements in effect as of January 1, 2018. License

revenue 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.

Operating Expenses

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

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Costs of Revenue

Costs of revenue consist primarily of sublicense fees to licensors as a result of revenues generated from the licensing of our NAV Technology Platform. Sublicense fees are based on a percentage of license fees we receive from licensees as specified in the agreements with our licensors. We recognize sublicense fees in the period that the underlying license revenue is recognized. Future costs of revenue are uncertain due to the nature of our license agreements and significant fluctuations in costs of revenue 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 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 Phase IIb clinical trial to evaluate the safety and efficacy of our RGX-314 program for the treatment of wet AMD, and a planned Phase II clinical trial to evaluate the safety and efficacy of our RGX-314 program for the treatment of an additional retinal condition;
- a Phase I/II clinical trial to evaluate the safety and efficacy of our RGX-121 program for the treatment of MPS II;
- a Phase I clinical trial to evaluate the safety and efficacy of our RGX-111 program for the treatment of MPS I;
- a Phase I/II clinical trial to evaluate the safety and efficacy of our RGX-501 program for the treatment of HoFH;
- preclinical research and development for our RGX-181 program for the treatment of CLN2;
- preclinical research and development for additional product candidates addressing other diseases in the retinal, metabolic and neurodegenerative therapeutic 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.

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The following table summarizes our research and development expenses incurred during the years ended December 31, 2018, 2017 and 2016 (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Direct Expenses			
RGX-314	$6,580	$5,883	$7,798
RGX-121	4,235	5,768	4,196
RGX-111	3,130	2,847	6,074
RGX-501	10,849	4,394	5,868
RGX-181	4,399	—	—
Total direct expenses	29,193	18,892	23,936
Unallocated Expenses			
Unallocated external expenses	12,431	10,187	6,216
Personnel-related	34,275	23,377	13,225
Facilities and depreciation expense	5,816	3,547	1,255
Other unallocated	2,158	1,221	850
Total unallocated expenses	54,680	38,332	21,546
Total research and development	$83,873	$57,224	$45,482

Expenses incurred in the development of RGX-181 were included in unallocated external expenses through the second quarter of 2018. 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

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 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 policies described below and in Note 2 to the accompanying audited financial statements, 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. 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 fixed income debt 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.

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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 ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes the revenue recognition requirements in ASC 605, Revenue Recognition (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 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 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 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 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. For each license, 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. We consider all of the facts and circumstances relevant to each license when making this determination.

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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 in the consolidated statements of operations 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 outstanding development milestones 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. To date we have not recognized any revenue from royalties on sales of licensed products or the achievement of sales-based milestones.

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 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 from licensees 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.

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Impact of Adoption of Topic 606

We 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 us 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 our licensors. We recognize sublicense fees to our licensors in the period the underlying license revenue is recognized.

Accrued Research and Development Expenses

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

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

- 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.

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

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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 is zero is based on our history of not paying dividends and 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.

On July 1, 2018, we adopted ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-based Payment Accounting. Prior to the adoption of this standard, compensation expense for our stock-based awards to nonemployees was based on the then-current fair value of the awards at each reporting date prior to the measurement date, which is generally the vesting date. Upon the adoption of ASU 2018-07, these awards will no longer be remeasured and any new stock-based awards granted to nonemployees after the adoption of the new standard will be measured at the estimated grant date fair value of the awards.

Income Taxes

As of December 31, 2018, we had federal net operating loss (NOL) carryforwards of $56.1 million, U.S. state NOL carryforwards of $56.2 million and federal research and development credit carryforwards of $29.1 million which may be available to offset future income tax liabilities and expire at various dates through 2038.

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 shareholders 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, 2018 and 2017.

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The Tax Cuts and Jobs Act of 2017 (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 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 us 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, we recorded a provisional reduction in our 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. We have completed our 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.

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.

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02, Leases (Topic 842) which supersedes ASC 840, Leases (Topic 840) and provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. We will adopt the standard effective January 1, 2019 using a modified retrospective transition method and will apply Topic 842 to leases in effect as of, or entered into after, the adoption date. The cumulative impact of adoption will be recorded as an adjustment to accumulated deficit on January 1, 2019 and prior periods will not be adjusted. This adoption approach will result in a consolidated balance sheet that may not be comparable to prior periods in the first year of adoption. Upon adoption, we expect to recognize right-of-use assets and lease liabilities on our consolidated balance sheet related to our operating leases for office and laboratory facilities and equipment. The right-of-use assets and related liabilities may be material. Additionally, upon adoption, we expect to derecognize $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 we do not control the building during the construction period under the requirements of Topic 842. We do not expect the adoption of Topic 842 to have a material impact on our results of operations. Please refer to Note 2 to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further information regarding our adoption of Topic 842.

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Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

	Years Ended December 31,		
	2018	2017	Change
	(in thousands)		
Revenues			
License revenue	$218,505	$10,385	$208,120
Other revenues	—	8	(8)
Total revenues	218,505	10,393	208,112
Operating Expenses			
Costs of revenues			
Licensing costs	9,640	1,703	7,937
Other	—	6	(6)
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 Revenue. License 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 during 2018:

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

The increase in license revenue during the year ended December 31, 2018 also resulted in a $7.9 million increase in licensing costs incurred during the period related to the sublicense fees we are obligated to pay to our licensors.

Due to the non-recurring license revenue recognized in 2018 under the AveXis and Abeona licenses discussed above, we currently expect 2019 revenues to be substantially lower than 2018 revenues. In January 2019, Novartis AG (Novartis), which acquired AveXis in May 2018, announced that it expects to launch ZOLGENSMA® in 2019,

pending approval by regulatory authorities. If approved, ZOLGENSMA will be the first approved product under our amended March 2014 license agreement with AveXis. Upon its approval and launch, we will begin recognizing royalty revenue on net sales of ZOLGENSMA.

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 externally sourced manufacturing-related and process development services.

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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 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.

Comparison of the Years Ended December 31, 2017 and 2016

	Years Ended December 31,		
	2017	2016	Change
	(in thousands)		
Revenues			
License revenue	$10,385	$4,303	$6,082
Other revenues	8	286	(278)
Total revenues	10,393	4,589	5,804
Operating Expenses			
Costs of revenues			
Licensing costs	1,703	861	842
Other	6	98	(92)
Research and development	57,224	45,482	11,742
General and administrative	27,229	23,590	3,639
Other operating expenses (income)	116	(102)	218
Total operating expenses	86,278	69,929	16,349
Loss from operations	(75,885)	(65,340)	(10,545)
Other Income			
Investment income	2,716	1,938	778
Total other income	2,716	1,938	778
Loss before income taxes	(73,169)	(63,402)	(9,767)
Income Tax Benefit	—	435	(435)

Net loss	$(73,169)	$(62,967)	$(10,202)

License Revenue. License revenue increased by $6.1 million, from $4.3 million for the year ended December 31, 2016 to $10.4 million for the year ended December 31, 2017. The increase was primarily attributable to $6.0 million of revenue recognized under our June 2017 license agreement with AveXis for the development and commercialization of treatments for Rett Syndrome and amyotrophic lateral sclerosis (ALS) caused by mutations in the gene that produces the copper zinc superoxide dismutase 1 (SOD1).

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Research and Development Expense. Research and development expenses increased by $11.7 million, from $45.5 million for the year ended December 31, 2016 to $57.2 million for the year ended December 31, 2017. The increase was primarily attributable to the following:

- an increase of $10.2 million for personnel costs as a result of increased headcount of research and development personnel, including a $2.4 million increase in stock-based compensation expense;
- an increase of $2.5 million for laboratory costs and externally sourced manufacturing-related and process development services; and
- an increase of $2.3 million for facilities and equipment used by research and development personnel, including a $1.9 million increase in depreciation expense allocated to research and development functions, primarily as a result of our advanced manufacturing and analytics laboratory which opened in early 2017.

The increase in research and development expenses was partially offset by a decrease of $4.0 million for externally sourced preclinical research and development services related to our lead product candidates and the advancement of our technology and other potential product candidates.

General and Administrative Expense. General and administrative expenses increased by $3.6 million, from $23.6 million for the year ended December 31, 2016 to $27.2 million for the year ended December 31, 2017. The increase was primarily attributable to the following:

- an increase of $2.3 million for personnel costs as a result of increased headcount of general and administrative personnel, including a $1.2 million increase in stock-based compensation expense; and
- an increase of $0.6 million for professional services, primarily attributable to commercial consulting services.

Liquidity and Capital Resources

As of December 31, 2018, we had cash, cash equivalents and marketable securities of $470.6 million, which were primarily derived from the sale of common stock, as described below. Additionally, we have supplemented our cash flows with fees received from granting commercial licenses to our proprietary technology to other biotechnology and pharmaceutical companies. We expect that our cash, cash equivalents and marketable securities as of December 31, 2018, will enable us to fund our operating expenses and capital expenditure requirements for at the least the next 12 months from the date of this report, based on our current business plan.

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.

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. In May 2018, AveXis was acquired by Novartis. 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 January 2019, Novartis announced that it expects to launch ZOLGENSMA in 2019, pending approval by regulatory authorities. If approved, ZOLGENSMA which will be the first approved product under the amended March 2014 license agreement.

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We have incurred cumulative losses since our inception and had an accumulated deficit of $83.0 million as of December 31, 2018. Our transition to recurring profitability is dependent upon the successful development, approval and commercialization of our product candidates and achieving a level of revenues adequate to support our cost structure. 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. Additionally, we expect our capital expenditures will increase significantly in the future for costs associated with building out additional office, laboratory and manufacturing capacity. As a result, we will need significant additional capital to fund our operations, which we may obtain through one or more equity offerings, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements.

Cash Flows

	Years Ended December 31,		
	2018	2017	2016
	(in thousands)		
Net cash provided by (used in) operating activities	$104,648	$(57,992)	$(48,558)
Net cash provided by (used) in investing activities	(279,358)	(4,790)	19,388
Net cash provided by financing activities	204,443	84,598	119
Net increase (decrease) in cash and cash equivalents and restricted cash	$29,733	$21,816	$(29,051)

Operating Activities

Our net cash provided by operating activities for the year ended December 31, 2018 increased by $162.6 million from the year ended December 31, 2017. The increase was primarily attributable to $180.0 million in license payments received in 2018 related to the amendment of our March 2014 license agreement with AveXis, and was partially offset by an increase in operating expenses during the period. Net cash used in operating activities increased by $9.4 million during the year ended December 31, 2017 from the year ended December 31, 2016. The increase was primarily attributable to an increase in operating expenses during the period. The increases in operating expenses during the periods were primarily attributable to increased employee headcount and increases in external research and development expenses as we continue the development and advancement of our lead product candidates.

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 change in working capital was primarily attributable to an increase in accounts receivable of $16.8 million, an increase in prepaid expenses and other current assets of $2.5 million and an increase in other assets of $1.5 million, and was 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 increased in other liabilities of $1.7 million. The increase in accounts receivable is largely driven by $26.0 million of accounts receivable recorded as of December 31, 2018

related to the November 2018 license with Abeona, and was partially offset by the imputed interest recognized upon the acceleration of license payments under our amended license agreement with AveXis. The increase in accrued expenses and other current liabilities is largely driven by increases in accrued personnel costs, accrued external research and development expenses and accrued licensing costs as of December 31, 2018. The increase in deferred revenue is largely driven by consideration received from licensees during the period for license options which represent unsatisfied performance obligations as of December 31, 2018.

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 change in working capital was primarily attributable to an increase in accounts payable and accrued expenses and other current liabilities of $4.5 million, and was partially offset by an increase in prepaid expenses of $3.6 million.

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For the year ended December 31, 2016, our net cash used in operating activities of $48.6 million consisted of a net loss of $63.0 million, offset by $9.2 million in adjustments for non-cash items and changes in working capital of $5.2 million. Adjustments for non-cash items primarily consisted of stock-based compensation expenses of $7.0 million and net amortization of premiums on marketable debt securities of $2.0 million. The change in working capital was primarily attributable to an increase in accounts payable and accrued expenses and other current liabilities of $4.1 million, an increase in deferred rent of $1.3 million and a decrease in accounts receivable of $1.1 million, and was partially offset by an increase in prepaid expenses and other current assets of $0.9 million.

Investing Activities

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.

For the year ended December 31, 2016, net cash provided by investing activities consisted of $72.6 million in sales and maturities of marketable securities, partially offset by $45.1 million to purchase marketable securities and $8.1 million to purchase property and equipment.

Financing Activities

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.

For the year ended December 31, 2016, net cash provided by financing activities primarily consisted of $0.2 million in proceeds received from the exercise of stock options.

Future Funding Requirements

To date, we have primarily generated revenue through license agreements with strategic partners for research, development and commercialization of product candidates using our proprietary technology. We do not expect to generate significant recurring revenue unless and until we obtain regulatory approval for and commercialize our product candidates. In addition, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue to expand the research, development and clinical trials of, and seek regulatory approval for, our product candidates. In addition, subject to obtaining regulatory approval for our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing

operations.

We expect that our cash, cash equivalents and marketable securities as of December 31, 2018 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. We intend to devote the majority of our current capital to clinical development and seeking regulatory approval of our product candidates. Because of the numerous risks and uncertainties associated with the development and commercialization of gene therapy product candidates, we are unable to estimate the amount of increased capital outlays and operating expenditures 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.

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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, if any;
- 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 sale of our products, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- 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 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.

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Our commitments 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, 2018, we have accrued $4.1 million of sublicense fees payable to our licensors, of which $1.6 million is expected to be paid in 2019 and $2.5 million is expected to be paid in periods beyond 2019. 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. Royalty fees are 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, 2018, excluding the items discussed above:

	Total	Less Than 1 Year	Years 1-3	Years 3-5	More Than 5 Years
	(in thousands)				
Future minimum lease payments	$96,537	$2,798	$6,774	$10,545	$ 76,420
Total contractual obligations	$96,537	$2,798	$6,774	$10,545	$ 76,420

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.

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ITEM 7A. QUALITATIVE AND QUANTITATIVE 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, 2018 and 2017, we had cash, cash equivalents and marketable securities of $470.6 million and $176.4 million, respectively. Our cash equivalents and marketable securities as of December 31, 2018 consisted of money market mutual funds, U.S. government and federal agency securities, certificates of deposit and corporate bonds. If market interest rates were to increase immediately and uniformly by 100 basis points, or one percentage point, from levels at December 31, 2018, we estimate that the increase in interest rates would have resulted in a hypothetical decline of $2.9 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, 2018. 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, 2018, our disclosure controls and procedures were effective at a reasonable assurance level.

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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, 2018, 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, 2018, based on criteria established in the COSO 2013 framework.

The effectiveness of our internal control over financial reporting as of December 31, 2018 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, 2018 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.

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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 2019 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2018 (2019 Proxy Statement) under the headings “Election of Directors,” “Executive Officers,” “Corporate Governance” and “Section 16(a) Beneficial Ownership Reporting Compliance” and is incorporated herein by reference.

We maintain a code of business conduct 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 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 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 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 2019 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 2019 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 2019 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 2019 Proxy Statement under the heading “Ratification of Appointment of Independent Registered Public Accounting Firm” and is incorporated herein by reference.

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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.

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REGENXBIO INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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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, 2018 and 2017, 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, 2018, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 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, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for revenue 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.

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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.

/s/ PricewaterhouseCoopers LLP

McLean, Virginia

February 27, 2019

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

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REGENXBIO INC.

CONSOLIDATED BALANCE SHEETS

(in thousands, except per share data)

	December 31, 2018	December 31, 2017
Assets		
Current assets		
Cash and cash equivalents	$75,561	$46,656
Marketable securities	244,200	114,122
Accounts receivable	8,587	473
Prepaid expenses	5,734	5,334
Other current assets	3,831	1,412
Total current assets	337,913	167,997
Marketable securities	150,819	15,616
Accounts receivable	23,012	—
Property and equipment, net	28,702	13,977
Restricted cash	1,053	225
Other assets	2,315	862
Total assets	$543,814	$198,677
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$4,412	$4,832
Accrued expenses and other current liabilities	17,164	9,605
Deferred revenue	600	—
Total current liabilities	22,176	14,437
Deferred revenue	3,333	—
Deferred rent, net of current portion	1,098	1,211
Financing lease obligation	5,854	—
Other liabilities	2,505	—
Total liabilities	34,966	15,648
Commitments and contingencies (Note 6)		
Stockholders' equity		
Preferred stock; $0.0001 par value; 10,000 shares authorized, and no shares issued and outstanding at December 31, 2018 and December 31, 2017	—	—
Common stock; $0.0001 par value; 100,000 shares authorized at December 31, 2018 and December 31, 2017; 36,120 and 31,295 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	4	3
Additional paid-in capital	592,580	371,497
Accumulated other comprehensive loss	(720)	(715)

Accumulated deficit	(83,016)	(187,756)
Total stockholders' equity	508,848	183,029
Total liabilities and stockholders' equity	$543,814	$198,677

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

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REGENXBIO INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)

(in thousands, except per share data)

	Years Ended December 31,		
	2018	2017	2016
Revenues			
License revenue	$218,505	$10,385	$4,303
Other revenues	—	8	286
Total revenues	218,505	10,393	4,589
Operating Expenses			
Costs of revenues			
Licensing costs	9,640	1,703	861
Other	—	6	98
Research and development	83,873	57,224	45,482
General and administrative	36,850	27,229	23,590
Other operating expenses (income)	42	116	(102)
Total operating expenses	130,405	86,278	69,929
Income (loss) from operations	88,100	(75,885)	(65,340)
Other Income			
Interest income from licensing	8,946	—	—
Investment income	7,070	2,716	1,938
Total other income	16,016	2,716	1,938
Income (loss) before income taxes	104,116	(73,169)	(63,402)
Income Tax Benefit (Expense)	(4,179)	—	435
Net income (loss)	$99,937	$(73,169)	$(62,967)
Other Comprehensive Income (Loss)			
Unrealized gain (loss) on available-for-sale securities, net of reclassifications and income tax expense	(5)	(682)	686
Total other comprehensive income (loss)	(5)	(682)	686
Comprehensive income (loss)	$99,932	$(73,851)	$(62,281)
Net income (loss) applicable to common stockholders	$99,937	$(73,169)	$(62,967)
Net income (loss) per share:			
Basic	$2.99	$(2.45)	$(2.38)
Diluted	$2.73	$(2.45)	$(2.38)
Weighted-average common shares outstanding:			
Basic	33,427	29,878	26,409
Diluted	36,648	29,878	26,409

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

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REGENXBIO INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands)

	Common Shares	Stock Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balances at December 31, 2015	26,313	$ 3	$ 269,144	$ (719)	$ (51,620)	$ 216,808
Exercise of stock options	163	—	179	—	—	179
Stock-based compensation expense	—	—	7,031	—	—	7,031
Unrealized gain on available-for-sale securities, net of reclassifications and income tax expense	—	—	—	686	—	686
Net loss	—	—	—	—	(62,967)	(62,967)
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 of reclassifications and income tax expense	—	—	—	(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 ASC 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 of reclassifications and income tax expense	—	—	—	(5)	—	(5)
Net income	—	—	—	—	99,937	99,937

Balances at December 31, 2018	36,120	$ 4	$ 592,580	$ (720)	$ (83,016)	$ 508,848

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

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REGENXBIO INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Years Ended December 31,		
	2018	2017	2016
Cash flows from operating activities			
Net income (loss)	$99,937	$(73,169)	$(62,967)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities			
Stock-based compensation expense	16,641	10,605	7,031
Net amortization of premiums and accretion of discounts on marketable debt securities	755	1,815	2,004
Depreciation and amortization	3,982	2,686	544
Net realized losses (gains) on sales and maturities of marketable securities	39	(479)	—
Imputed interest income from licensing	(8,946)	—	—
Non-cash consideration received for licenses granted	—	(420)	—
Other non-cash adjustments	14	73	(399)
Changes in operating assets and liabilities			
Accounts receivable	(16,803)	561	1,073
Prepaid expenses	(400)	(3,559)	(755)
Other current assets	(2,069)	(402)	(159)
Other assets	(1,453)	(135)	(139)
Accounts payable	(218)	2,621	186
Accrued expenses and other current liabilities	7,582	1,897	3,873
Deferred revenue	3,933	—	—
Advance payments	—	—	(127)
Deferred rent	(32)	(86)	1,277
Other liabilities	1,686	—	—
Net cash provided by (used in) operating activities	104,648	(57,992)	(48,558)
Cash flows from investing activities			
Purchases of marketable securities	(445,829)	(68,634)	(45,072)
Maturities of marketable securities	179,749	70,224	72,586
Sales of marketable securities	—	780	23
Purchases of property and equipment	(13,278)	(7,160)	(8,149)
Net cash provided by (used) in investing activities	(279,358)	(4,790)	19,388
Cash flows from financing activities			
Proceeds from exercise of stock options	14,499	2,493	179
Proceeds from issuance of common stock under employee stock purchase plan	847	556	—
Proceeds from public offerings of common stock, net of underwriting discounts	189,716	81,994	—

and commissions			
Issuance costs for public offerings of common stock	(619)	(445)	(60)
Net cash provided by financing activities	204,443	84,598	119
Net increase (decrease) in cash and cash equivalents and restricted cash	29,733	21,816	(29,051)
Cash and cash equivalents and restricted cash			
Beginning of period	46,881	25,065	54,116
End of period	$76,614	$46,881	$25,065
Supplemental cash flow information			
Cash paid for income taxes	$3,443	$—	$—
Supplemental disclosures of non-cash investing and financing activities			
Purchases of property and equipment in accounts payable and accrued expenses	$—	$254	$1,181
Assets acquired under financing lease obligation	$5,854	$—	$—
Non-cash consideration received for licenses granted	$—	$420	$—
Issuance costs for public offerings of common stock in accounts payable and accrued expenses	$—	$—	$33

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

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REGENXBIO INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business

REGENXBIO Inc. (the Company) is a leading 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 Company's NAV® Technology Platform is being applied by the Company, as well as by third-party licensees (NAV Technology Licensees), in the development of product candidates for a variety of diseases with unmet needs. The Company was formed in 2008 in the State of Delaware and is headquartered in Rockville, Maryland.

Liquidity and Risks

As of December 31, 2018, the Company had generated an accumulated deficit of $83.0 million since inception. As the Company has incurred cumulative losses since inception, transition to recurring profitability is dependent upon the successful development, approval and commercialization of its product candidates and achieving a level of revenues adequate to support the Company's cost structure. The Company may never achieve recurring profitability, and unless and until it does, the Company will continue to need to raise additional capital. As of December 31, 2018, the Company had cash, cash equivalents and marketable securities of $470.6 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). The accompanying consolidated financial statements 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: revenue, stock-based compensation expense, accrued research and development expenses and other accrued liabilities, income taxes and the fair value of financial instruments.

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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 revenue primarily consists of license revenue. For the year ended December 31, 2018, 99% of the Company's revenue was generated from customers located in the U.S. For the year ended December 31, 2017, 96% of the Company's revenue was generated from customers located in the U.S. For the year ended December 31, 2016, 90% of the Company's revenue was generated from customers located in the U.S. Country of origin for license revenue is determined based on the country of domicile of the licensee. 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, 2018	December 31, 2017	December 31, 2016
Cash and cash equivalents	$ 75,561	$ 46,656	$ 24,840
Restricted cash	1,053	225	225
Total cash and cash equivalents and restricted cash	$ 76,614	$ 46,881	$ 25,065

Marketable Securities

Marketable securities consist of debt securities and are classified as available-for-sale and carried at fair value. Marketable 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. Unrealized gains and losses, 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. Purchase premiums and discounts 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. 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.

A decline in the fair value below cost of available-for-sale 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 investments 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 securities which was deemed to be to be other-than-temporary.

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Concentrations of Credit Risk and Off-balance Sheet Risk

Cash and cash equivalents, marketable 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 securities consist of investment grade debt 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 Years Ended December 31,			Accounts Receivable December 31,	
	2018	2017	2016	2018	2017
Customer A	81%	68%	*	*	*
Customer B	16%	*	*	82%	*
Customer C	*	*	24%	*	*
Customer D	*	*	*	*	42%
Customer E	*	*	*	*	32%
Customer F	*	*	44%	*	*
Customer G	*	*	*	*	21%

*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 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, 2018 or 2017.

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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:

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

Certain estimated construction costs incurred and reported by the Company's landlord at 9800 Medical Center Drive are 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 reviews long-lived assets 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 have been recorded during the years ended December 31, 2018, 2017 and 2016.

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. Prior to January 1, 2018, non-marketable equity securities were accounted for using the cost method and measured at cost less impairment. Beginning January 1, 2018, upon the Company's adoption of Accounting Standards Update (ASU) 2016-01, Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities, 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.

Declines in the fair value of non-marketable equity securities below their carrying values that are deemed to be other-than-temporary are charged to results of operations as realized losses. In estimating other-than-temporary impairment losses, management considers, among other things, the length of time and the extent to which the fair value has been less than cost, the financial condition and near-term prospects of the issuer and the intent and ability of the Company to retain its investments in the issuer for a period of time sufficient to allow for the anticipated recovery in fair value. The Company has not recorded any other-than-temporary impairment losses on its 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. Accounting Standards Codification (ASC) Topic 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.

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- 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). Please refer to Recent Accounting Pronouncements below for additional information on the adoption of Topic 606 and the impact upon adoption to the Company's financial position and results of operations.

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 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 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.

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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, 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. 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 in the consolidated statements of operations 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 outstanding development milestones 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.

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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. To date the Company has not recognized any revenue from royalties on sales of licensed products or the achievement of sales-based milestones.

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 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 sales of licensed reagents to third parties for use in research and development and grant revenue generated through research and development grant programs offered by the European Union. Revenue from reagent sales is recognized when control of the licensed reagents is transferred to the customer. 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.

Costs of Revenues

Licensing costs consist of sublicense fees to licensors as a result of license revenues generated by the Company. Sublicense fees are based on a percentage of license fees received by the Company from licensees as specified in the Company's agreements with its licensors. The Company recognizes sublicense fees in the period that the underlying license revenue is recognized. Sublicense fees payable by the Company to licensors in periods beyond 12 months from the reporting date are recorded as non-current liabilities on the consolidated balance sheets.

Other costs of revenue consist of royalties to licensors as a result of the sales of licensed reagents by the Company. The Company recognizes royalties on sales of licensed reagents in the period that the underlying sales occur.

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.

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.

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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 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.

On July 1, 2018, the Company adopted ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-based Payment Accounting. Prior to the adoption of this standard, compensation expense for the Company's stock-based awards to nonemployees was based on the then-current fair value of the awards at each reporting date prior to the measurement date, which is generally the vesting date. Upon the adoption of ASU 2018-07, these awards will no longer be remeasured and any new stock-based awards granted to nonemployees after the adoption of the new standard will be measured at the estimated grant date fair value of the awards.

For the year ended December 31, 2016, the Company was also required to estimate forfeitures of stock-based awards at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from its estimates. For all periods through December 31, 2016, a forfeiture rate of zero was used to calculate stock-based compensation expense due to the lack of historical information necessary to estimate forfeitures. To the extent that actual forfeitures differed from the Company's estimates, the differences were recorded as a cumulative adjustment in the period the estimates were revised. On January 1, 2017, the Company adopted ASU 2016 09, Compensation—Stock

Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. Upon the adoption of this standard, the Company elected to no longer estimate forfeitures of stock-based awards and to account for forfeitures as they occur. The adoption of this standard required retrospective application, however, since the Company had previously assumed a forfeiture rate of zero on all stock-based awards there was no impact to the consolidated financial statements as a result of the adoption of this standard.

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.

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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 will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2018 and 2017, 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 2014-09, Revenue from Contracts with Customers

In May 2014, the Financial Accounting Standards Board (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. Please refer to Revenue Recognition above for additional information on Topic 606, including a description of the Company's revenue recognition policies upon adoption.

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.

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The cumulative adjustment for the adoption of Topic 606 had the following effects on the Company's consolidated balance sheet as of January 1, 2018 (in thousands):

	Balance at December 31, 2017	Cumulative Adjustment for Adoption of Topic 606	Balance at January 1, 2018
Consolidated Balance Sheet			
Assets:			
Accounts receivable, current	$ 473	$ 527	$ 1,000
Accounts receivable, non-current	$ —	$ 4,850	$ 4,850
Other current assets	$ 1,412	$ 350	$ 1,762
Liabilities:			
Accrued expenses and other current liabilities	$ 9,605	$ 105	$ 9,710
Other liabilities	$ —	$ 819	$ 819
Stockholders Equity:			
Accumulated deficit	$ (187,756)	$ 4,803	$ (182,953)

The following tables present the effects of the adoption of Topic 606 on each financial statement line item of the Company's consolidated financial statements as of and for the year ended December 31, 2018 (in thousands, except per share data):

	As of December 31, 2018		
	As Reported	Impact of Adoption of Topic 606	Results Without Adoption of Topic 606
Consolidated Balance Sheet			
Assets:			
Accounts receivable, current	$8,587	$ (1,803)	$10,390
Accounts receivable, non-current	$23,012	$ 3,012	$20,000
Prepaid expenses	$5,734	$ 60	$5,674
Other current assets	$3,831	$ 750	$3,081
Other assets	$2,315	$ 267	$2,048
Liabilities:			
Accrued expenses and other current liabilities	$17,164	$ (580)	$17,744
Deferred revenue, current	$600	$ 600	$—
Deferred revenue, non-current	$3,333	$ 3,333	$—

Other liabilities	$2,505	$ 705	$1,800
Stockholders Equity:			
Accumulated deficit	$(83,016)	$ (1,772)	$(81,244)

	Year Ended December 31, 2018		
	As Reported	Impact of Adoption of Topic 606	Results Without Adoption of Topic 606
Consolidated Statement of Operations			
Revenues:			
License revenue	$218,505	$(16,647)	$235,152
Operating Expenses:			
Licensing costs	$9,640	$(396)	$10,036
Other Income:			
Interest income from licensing	$8,946	$8,946	$—
Income Tax Expense	$(4,179)	$730	$(4,909)
Net Income	$99,937	$(6,575)	$106,512
Net Income Per Share:			
Basic	$2.99	$(0.20)	$3.19
Diluted	$2.73	$(0.18)	$2.91

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	Year Ended December 31, 2018		
	As Reported	Impact of Adoption of Topic 606	Results Without Adoption of Topic 606
Consolidated Statement of Cash Flows			
Cash Flows from Operating Activities:			
Net income	$99,937	$(6,575)	$106,512
Imputed interest income from licensing	$(8,946)	$(8,946)	$—
Changes in accounts receivable	$(16,803)	$13,114	$(29,917)
Changes in prepaid expenses	$(400)	$(60)	$(340)
Changes in other current assets	$(2,069)	$(400)	$(1,669)
Changes in other assets	$(1,453)	$(267)	$(1,186)
Changes in accrued expenses and other current liabilities	$7,582	$(685)	$8,267
Changes in deferred revenue	$3,933	$3,933	$—
Changes in other liabilities	$1,686	$(114)	$1,800

The most significant effects that the adoption of Topic 606 had on the results of operations for the year ended December 31, 2018, as compared to what results would have been if Topic 605 had continued to be applied, were (i) the amount of revenue and interest income from licensing recognized as a result of significant financing components identified within the Company's license agreements, and (ii) the amount of revenue recognized from license options granted during the period. Under Topic 606, if a significant financing component is identified within a license agreement, the Company is required to adjust the amount of revenue recognized upon the delivery of the license to the present value of the underlying consideration. The discounted portion of the consideration is recognized as interest income from licensing over the financing term of the license agreement. Under Topic 605, the amount of revenue recognized from the delivery of licenses is not adjusted for significant financing components. During the year ended December 31, 2018, the Company recognized $8.9 million of interest income from licensing as a result of significant financing components identified in its license agreements. Under Topic 605, the Company would not have recognized any interest income from significant financing components during the period, and would have recognized $12.4 million of additional license revenue during the period related to its March 2014 license agreement, as amended, with AveXis, Inc. (AveXis) and its November 2018 license agreement with Abeona Therapeutics Inc. (Abeona). Additionally, under Topic 606, the Company recorded deferred revenue of $3.9 million as of December 31, 2018 for consideration received during the period related to license options granted to licensees which were deemed material rights to the licensee to acquire additional licenses in the future. Under Topic 605, the Company would have recognized the $3.9 million of consideration received as license revenue during the period as the options would have been considered substantive and excluded from the contract for accounting purposes until exercised.

Other recently adopted accounting pronouncements

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-based Payment Accounting which supersedes the existing guidance for accounting for stock-based awards to nonemployees under ASC 505-50, Equity—Equity-based Payments to Nonemployees. The new

guidance expands the scope of ASC 718 to include stock-based awards to nonemployees for goods or services. Consequently, the accounting for stock-based awards to employees and nonemployees will be substantially aligned. The Company elected to early adopt this standard effective July 1, 2018, which required the Company to remeasure all of its outstanding stock-based awards to nonemployees which do not yet have established measurement dates to the estimated fair value on the adoption date. These awards, which consisted solely of stock options granted to third-party advisors with performance-based vesting conditions, will no longer be remeasured and any new stock-based awards granted to nonemployees after the adoption of the new standard will be measured at the estimated grant date fair value of the awards. The new standard requires the cumulative effect of the adoption on the adoption date to be presented as an adjustment to retained earnings as of the beginning of the year of adoption. On the adoption date, the Company had no unvested stock-based awards to nonemployees which were probable of vesting. Accordingly, the adoption of this standard required no retrospective adjustment and did not have a material impact on the Company’s financial position or results of operations.

In May 2017, the FASB issued ASU 2017-09, Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when modification accounting should be applied for changes to terms or conditions of a stock-based award. The Company adopted this standard effective January 1, 2018. The adoption of this standard did not have a material impact on the Company’s financial position or results of operations.

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In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The standard requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents and restricted cash. As a result, amounts generally described as restricted cash should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company adopted this standard effective January 1, 2018 and applied it retrospectively to each period presented in the financial statements. The adoption of this standard did not have a material impact on the Company's consolidated statements of cash flows.

In January 2016, the FASB issued ASU 2016-01, Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities, which modifies the current guidance on the recognition, measurement, presentation and disclosure of financial instruments. In February 2018, the FASB issued ASU 2018-03, Technical Corrections and Improvements to Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities, which clarifies the guidance in ASU 2016-01. The Company adopted these standards effective January 1, 2018. Upon the adoption of these standards, the Company elected to measure its non-marketable equity securities without readily available fair values at cost less impairment, adjusted for observable price changes for identical or similar investments of the same issuer. Prior to the adoption of these standards, the Company measured these investments at cost less impairment. The adoption of these standards did not have a material impact on the Company's financial position or results of operations.

Recent accounting pronouncements not yet adopted

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, with early adoption permitted upon issuance. The Company does not believe the application of this standard will have a material impact on the Company's disclosures.

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 current 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 standard is effective for the Company beginning January 1, 2019, with early adoption permitted upon issuance. The Company does not believe the application of this standard will 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 standard is effective for the Company beginning January 1, 2019, with early adoption permitted upon issuance, and is to be applied on a modified retrospective basis through a cumulative-effect adjustment directly to retained earnings as of the beginning of the period of adoption. The Company does not believe the application of this standard will have a material impact on the Company's financial position or results of operations.

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 and net investment in leases 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, with early adoption permitted for annual and interim periods beginning January 1, 2019. The Company does not believe the application of this standard will have a material impact on the Company’s financial position or results of operations.

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In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842) which supersedes ASC 840, Leases (Topic 840) and provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of classification. If elected, leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. The Company will adopt the standard effective January 1, 2019 using a modified retrospective transition method and will apply Topic 842 to leases in effect as of, or entered into after, the adoption date. The cumulative impact of adoption will be recorded as an adjustment to accumulated deficit on January 1, 2019 and prior periods will not be adjusted. This adoption approach will result in a consolidated balance sheet that may not be comparable to prior periods in the first year of adoption. The Company plans to elect certain practical expedients allowed by Topic 842 for transition purposes which will permit the Company to not reassess lease identification, classification and initial direct costs under Topic 842 for leases that commenced prior to January 1, 2019, and will allow the Company to use hindsight in determining the terms of such leases. The Company will also elect to account for leases with a term of 12 months or less as operating leases similar to existing guidance. The Company has substantially completed the process of analyzing and extracting relevant data from its lease contracts and is finalizing its evaluation of Topic 842 and the impact of adoption on the Company's financial statements and related disclosures. Upon adoption, the Company expects to recognize right-of-use assets and lease liabilities on its consolidated balance sheet related to its operating leases for office and laboratory facilities and equipment. The right-of-use assets and related liabilities may be material. Please refer to Note 6 for information regarding future minimum lease payments for the Company's operating leases as of December 31, 2018, which, in all material respects, approximate the undiscounted payments that will be used to calculate the present value of lease payments to be recorded as lease liabilities upon the adoption of Topic 842. Upon adoption, the Company expects to derecognize $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 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. Accordingly, the lease payments for 9800 Medical Center Drive disclosed in the table of future minimum lease payments in Note 6 will not be included in the right-of-use assets and lease liabilities that will be recorded upon the adoption of Topic 842. The Company does not expect the adoption of Topic 842 to have a material impact on the Company's results of operations. The Company is finalizing the implementation of a new lease accounting software system and updating its internal controls and processes to support the adoption and subsequent accounting and disclosure requirements of Topic 842.

3. Marketable Securities

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

	Amortized	Unrealized	Unrealized

	Cost	Gains	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

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2017				
Corporate bonds	$ 130,018	$ 2	$ (282)	$ 129,738
	$ 130,018	$ 2	$ (282)	$ 129,738

As of December 31, 2018 and 2017, no marketable securities had remaining maturities greater than three years.

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The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. As of December 31, 2018 and 2017, the balance in the Company's accumulated other comprehensive loss consisted solely of net unrealized gains and losses on available-for-sale securities, net of income tax effects and reclassification adjustments for realized gains and losses. During the years ended December 31, 2018, 2017 and 2016, the Company recognized net unrealized gains (losses) on available-for-sale securities of less than $(0.1) million, $(0.2) million and $1.1 million, respectively, and income tax expense of zero, zero and $0.4 million, respectively, in other comprehensive income (loss). The Company recognized net realized gains (losses) of less than $(0.1) million, $0.5 million and less than $(0.1) million on the sale or maturity of available-for-sale securities during the years ended December 31, 2018, 2017 and 2016, respectively, which were reclassified out of accumulated other comprehensive loss during the period and are 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 marketable 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, 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)

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
December 31, 2017						
Corporate bonds	$109,238	$ (180)	$17,124	$ (102)	$126,362	$ (282)
	$109,238	$ (180)	$17,124	$ (102)	$126,362	$ (282)

As of December 31, 2018, marketable securities held by the Company which were in an unrealized loss position consisted of 102 investment grade security positions. The Company has the intent and ability to hold such securities until recovery and has determined that none of its investments were other-than-temporarily impaired as of December 31, 2018 or 2017.

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, 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

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	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total
December 31, 2017				
Cash equivalents:				
Money market mutual funds	$ —	$ 46,646	$ —	$ 46,646
Total cash equivalents	—	46,646	—	46,646
Marketable securities:				
Corporate bonds	—	129,738	—	129,738
Total marketable securities	—	129,738	—	129,738
Total cash equivalents and marketable securities	$ —	$ 176,384	$ —	$ 176,384

There were no transfers of financial instruments between levels of the fair value hierarchy during the years ended December 31, 2018 and 2017.

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, 2018 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.

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. As of December 31, 2018 and 2017, non-marketable equity securities had carrying values of $0.4 million and are included in other assets on the consolidated balance sheets. Since the acquisition of the securities, the Company has not identified any observable price changes or changes in circumstances that would have an adverse effect on the fair value of the securities as of December 31, 2018 and 2017. No remeasurements or impairment losses were recorded on non-marketable equity securities during the years ended December 31, 2018, 2017 and 2016.

5. Property and Equipment, Net

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

	December 31, 2018	December 31, 2017
Lab equipment	$ 14,417	$ 8,561
Computer equipment and software	2,002	1,481
Furniture and fixtures	1,915	1,384
Leasehold improvements	11,751	5,828
Construction-in-progress	5,854	—
Total property and equipment	35,939	17,254
Accumulated depreciation and amortization	(7,237)	(3,277)
Property and equipment, net	$ 28,702	$ 13,977

Construction-in-progress in the table above consists of certain costs incurred and reported by the Company's landlord at 9800 Medical Center Drive. Please refer to Note 6 for further information on the Company's lease agreements. Construction costs incurred by the Company for the building at 9800 Medical Center Drive were less than $0.1 million as of December 31, 2018.

During the years ended December 31, 2018, 2017 and 2016, the Company recorded depreciation expense of $4.0 million, $2.7 million and $0.5 million, respectively.

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6. Commitments and Contingencies

Lease Commitments

The Company recognizes rent expense on a straight-line basis over the term of its operating leases commencing on the date the Company takes possession of the leased property. Tenant improvement allowances that are considered to be lease incentives from the lessor are recorded as deferred rent and amortized as a reduction of rent expense over the term of the lease from the possession date.

9800 Medical Center Drive Lease

In November 2018, the Company entered into a lease for approximately 132,000 square feet of office and laboratory facilities in a new building to be constructed at 9800 Medical Center Drive in Rockville, Maryland (the 9800 Medical Center Drive Lease). Construction of the new building, which will be conducted by the landlord, is expected to be completed in 2020 and the lease will expire approximately 16 years from the delivery of the leased premises to the Company, subject to certain extension and termination options. Under the terms of the 9800 Medical Center Drive Lease, the Company will receive a $14.6 million tenant improvement allowance from the landlord to construct additional improvements to the leased premises. 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 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 $0.8 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. Accordingly, for accounting purposes only, the Company is deemed the owner of the leased premises during the construction period. Certain estimated construction costs incurred and reported by the landlord are recorded as property and equipment, with a corresponding financing lease obligation, on the consolidated balance sheets. The portion of the lease allocated to the land on which the building is located is treated for accounting purposes as an operating lease that commenced upon the execution of the 9800 Medical Center Drive Lease in November 2018. Imputed rent expense attributable to the land portion of the lease was not material for the year ended December 31, 2018.

Other Lease Commitments

In March 2015, the Company entered into a non-cancelable 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. Under the amended lease, the Company has received a $0.4 million tenant improvement allowance from the landlord which will be deferred and 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 a 7.5-year, non-cancelable 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. The Company has an option to extend the term of the lease for an additional five years. 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 received a $0.8 million tenant improvement allowance from the landlord which will be deferred and amortized on a straight-line basis as a reduction of rent expense over the term of lease.

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The Company leases additional office and laboratory facilities in Rockville, Maryland and New York, New York, as well as laboratory and other equipment, under non-cancelable operating leases with various expiration dates through 2021 and which may contain annual escalations of rental payments. As required by the Company's lease agreement for its office space in New York, New York, 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 of December 31, 2018, future minimum lease payments under 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		