APPLIED GENETIC TECHNOLOGIES CORP
Form 10-K
September 12, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the Fiscal Year Ended June 30, 2016

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number: 001-36370

APPLIED GENETIC TECHNOLOGIES CORPORATION

(Exact Name of Registrant as Specified in Its Charter)

Delaware	59-3553710
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

14193 NW 119th Terrace

Suite 10

Alachua, Florida 32615

(Address of Principal Executive Offices, Including Zip Code)

(386) 462-2204

(Registrant's Telephone Number, Including Area Code)

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

Title of class	Name of exchange on which registered
Common Stock, $.001 par value	NASDAQ Global Market

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

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

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 o No x

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 x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes x No o

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. x

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

Large accelerated filer o Accelerated filer x

Non-accelerated filer o Smaller reporting company o

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

The aggregate market value of the voting common shares held by non-affiliates of the registrant was approximately $83.4 million, computed by reference to the closing sale price of the common stock as reported by The NASDAQ Global Market on December 31, 2015, the last trading day of the registrant's most recently completed second fiscal quarter. The Company has no non-voting common shares.

As of August 31, 2016, a total of 18,053,284 shares of the registrant's common stock, $0.001 par value per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the registrant's Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission on or before December 19, 2016 are incorporated by reference in Part III of this Annual Report on Form 10-K.

APPLIED GENETIC TECHNOLOGIES CORPORATION

ANNUAL REPORT ON FORM 10-K

FOR FISCAL YEAR ENDED JUNE 30, 2016

TABLE OF CONTENTS

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections entitled “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contains forward-looking statements. These statements may relate to, but are not limited to, expectations of our future results of operations, business strategies and operations, financing plans, potential growth opportunities, potential market opportunities and the effects of competition, as well as assumptions relating to the foregoing. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. These risks and other factors include, but are not limited to, those listed under “Risk Factors.” In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “could,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “pre “potential,” “might,” “would,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. Actual events or results may differ materially.

There may be events in the future that we are not able to accurately predict or control and that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. Except as required by applicable law, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained in this Annual Report on Form 10-K after we file it, whether as a result of any new information, future events or otherwise. Before you invest in our common stock, you should be aware that the occurrence of any of the events described in the “Risk Factors” section and elsewhere in this Annual Report on Form 10-K could harm our business, prospects, operating results and financial condition. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

Except as otherwise indicated, all share and per share information referenced in this report has been adjusted to reflect the 1-for-35 reverse split with respect to our common stock effected on March 4, 2014.

As used herein, except as otherwise indicated by context, references to “we,” “us,” “our,” or the “Company” refer to Applied Genetic Technologies Corporation.

PART I

ITEM 1. BUSINESS

Overview

We are a clinical-stage biotechnology company using gene therapy based on adeno-associated virus, or AAV, to develop genetic therapies to treat patients with inherited diseases. Each treatment is precisely designed to address a specific genetic disorder. Our most advanced gene therapy programs are designed to produce treatments that will restore visual function in patients with rare blinding diseases. Genetic therapies are complex with interdependent components that must work in harmony. Fifteen years of gene therapy experience allows us to design and construct all critical gene therapy components and bring them together to develop potentially effective treatments for patients. We are committed to attracting and maintaining a team with a substantial breadth of clinical and scientific expertise who can foster an atmosphere of scientific growth and discovery.

Our strategy is to leverage the capabilities of our gene therapy platform to address diseases in ophthalmology where there is significant unmet medical need. We have concentrated initially on underserved orphan indications that are

small enough to allow for clinical trials on a manageable scale but have a sufficient prevalence by orphan disease standards to provide a substantial commercial opportunity that we believe we can serve using a small, targeted commercial infrastructure. The eye diseases we are targeting are well understood with highly predictive animal models and clearly defined clinical endpoints, characteristics that we believe will facilitate clinical development and regulatory approval of our product candidates. We believe our initial focus on these orphan eye diseases will provide us with an attractive business opportunity and position us to drive the advancement of gene therapy technology. We plan to leverage our experience in orphan ophthalmology to develop new treatments for eye diseases with larger patient populations, such as wet age-related macular degeneration, or wet AMD. We will also evaluate opportunities to extend the commercial application of our gene therapy platform in other underserved indications beyond ophthalmology and to that end we recently announced initiation of research efforts in otology to identify opportunities to use our platform to address genetic causes of hearing loss.

Our most advanced products consist of four ophthalmology development programs across three targets, X linked retinoschisis (XLRS), X-linked retinitis pigmentosa (XLRP), caused by mutations in the RPGR gene, and achromatopsia (ACHM) caused by mutations in either the CNGB3 gene or the CNGA3 gene. These three inherited orphan diseases of the eye are caused by mutations in single genes that significantly affect visual function and currently lack effective medical treatments.

- XLRS is characterized by abnormal splitting of the layers of the retina, resulting in poor visual function in young boys, which can progress to legal blindness in adult men. Additionally, approximately 40% of patients are at risk of retinal hemorrhage or detachment. We currently are enrolling patients in a Phase 1/2 clinical trial with our XLRS product candidate.
- ACHM is characterized by the absence of cone photoreceptor function, resulting in extremely poor visual acuity, light sensitivity, day blindness and complete loss of color discrimination. We currently are enrolling patients in a Phase 1/2 clinical trial for our ACHM B3 product candidate. We anticipate filing an IND for our second ACHM product candidate targeting the "A3" gene this year.
- XLRP is a disease characterized by progressive degeneration of the retina, which can lead to total blindness in adult men. We are currently conducting IND enabling preclinical studies for our XLRP product candidate. We expect to file an IND in 2017, and thereafter initiate a Phase 1/2 clinical trial in the United States. In July 2015, we entered into a broad collaboration and license agreement with Biogen MA, Inc., a wholly owned subsidiary of Biogen Inc., or Biogen, to develop gene-based therapies for multiple ophthalmic diseases. Our XLRS and XLRP product candidates are licensed to Biogen pursuant to this agreement together with options to three discovery stage programs.

We continue to move forward additional ophthalmology indications, such as AMD and blue cone monochromacy, or BCM, in early research studies. We also have active programs to identify novel capsids and promoters in order to advance our gene therapy platform as well as projects to continue advancing our proprietary manufacturing platform.

Our gene therapy platform is based on viral vectors that utilize a modified version of non-replicating AAV to deliver a functional copy of a gene to the patient's own cells through a variety of delivery methods, and we have obtained preliminary indications of safety and efficacy in clinical trials. These vectors deliver the functional genetic material to the nucleus of the cell, providing safe, sustained expression of the therapeutic protein to treat the disease without modifying the existing DNA of the patient.

We employ a highly targeted approach to selecting and designing our product candidates, choosing to develop therapies for indications having significant unmet medical need, clinical feasibility and commercial potential. We have a significant intellectual property portfolio and substantial gene therapy experience, which we believe will allow us to design and implement all critical gene therapy components and bring them together to develop potentially effective treatments for patients. These components include the capsid, promoter, gene cassette, formulation, manufacturing and physical delivery.

Our proprietary AAV vector manufacturing process is both reproducible and scalable with a favorable cost of goods. We have assembled an experienced team with a substantial breadth of clinical, scientific, and management expertise who can foster an atmosphere of scientific growth and discovery. Our team works with a group of scientific advisors, and has strong collaborative relationships with recognized leaders in the field of ophthalmology, otology and gene therapy.

Our AAV vectors can be used to introduce functional genes into many different cell types by a variety of delivery methods and can carry genes of up to 4,000 base pairs in length, a payload capacity sufficient to accommodate more than 90% of the individual genes in the human genome. We have developed a proprietary manufacturing process that we believe will enable our vectors to be manufactured reliably, and at high quality, on a commercial scale. Our gene therapy platform therefore has the potential to provide treatments for many other diseases outside of our current focus, including those with large dosing requirements or in larger markets. We expect to explore additional therapeutic areas selectively, either alone or through partnerships.

The chart below summarizes our current gene therapy programs:

Our initial focus on orphan ophthalmology

Many chronically debilitating diseases for which there are currently no effective treatments have patient populations too small to attract the interest of large commercial entities. We believe that such orphan diseases can provide us with an attractive business opportunity. We are concentrating initially on several underserved diseases that have a relatively high prevalence by orphan disease standards but are small enough to allow for clinical trials on a manageable scale and provide markets that we believe we can serve using a small, targeted commercial infrastructure.

We are focused on treatments that can restore visual function for patients with rare blinding eye diseases for which we believe there is a significant unmet medical need. The diseases we are targeting are also of interest to us due to a number of factors that, in combination, have enabled us to screen and more accurately predict the potential safety and efficacy of product candidates at an early stage of development:

- Well-understood disease mechanisms. Because sight is the most important sense to humans—many people report that they fear blindness even more than premature death—even very rare diseases that cause vision loss have been studied extensively and are well-understood down to the molecular mechanism of action.
- Monogenic diseases. We are initially pursuing eye diseases where the genetic abnormality is known and is caused by mutations in a single gene, known as monogenic diseases. We therefore know exactly what gene sequence to insert and which cell types to target for treatment, thus mitigating the uncertainty of disease biology.
- Highly predictive animal models. For many eye diseases there are highly predictive animal models in which the disease is caused by the same underlying genetic defect and has clinical outcomes that are similar to those in humans.
    - Local delivery of therapeutic agent. Direct delivery to the eye of a therapeutic agent, via methods already widely used in ophthalmology, allows us to use lower doses, with reduced risk of unintended effects.
- Short time to clinical data. In our XLRS and ACHM trials, once the appropriate dose is determined we expect to obtain meaningful clinical data from patients within six months after a one-time administration of the product candidate, which we believe will facilitate the clinical development of our product candidates.

Ophthalmology is also attractive to us as a clinical stage company because treatments for diseases affecting vision have clearly defined, objective clinical endpoints with validated measurement tools that are accepted by the United States Food and Drug Administration, or FDA. Other orphan drug companies have spent considerable time and resources working with the FDA to identify acceptable clinical endpoints and develop measurement tools in sometimes ill-defined diseases. In ophthalmology four accepted endpoints—visual acuity, visual fields, contrast sensitivity and color vision—are well understood and routinely measured by

clinicians. In addition, the FDA consistently applies these endpoints and provides guidance on how much improvement is required for clinical relevancy. We believe these clearly defined endpoints will help accelerate the process of clinical study and regulatory approval for our ophthalmic products.

Finally, through our internal research work and in collaboration with partners, we have obtained preliminary safety data in clinical trials with the two major delivery routes used in ophthalmology: intravitreal and subretinal injection. In clinical trials conducted with a previous partner, 19 patients with wet AMD were treated by intravitreal injection of an AAV vector, and in other trials conducted by us and others more than 75 patients with Leber congenital amaurosis type 2, or LCA2, have been treated with subretinal injections of AAV vectors. No reports of serious adverse events attributed to the vector used in either of those studies were noted, and promising indications of efficacy were demonstrated for LCA2 patients.

Otology

On May 9, 2016, we announced a new initiative in the area of otology in which we will use our capabilities to develop potential gene therapy products that can address genetic causes of hearing loss. Hearing loss is one of the most common human sensory deficits and it is estimated that nearly half of the cases are suspected to have a genetic origin. Of the inherited forms of hearing loss, more than 300 genetic causes have been defined with the specific gene identified for more than 70. Despite the impairment that can be caused by deafness, very little progress has been made in developing therapies that go beyond the temporary and partial solutions provided by hearing aids and cochlear implants. In multiple academic research studies, replacement of defective genes in animal models with normal copies has been shown to improve sound propagation in the auditory hair cells, making this a potentially promising application of AAV gene therapy. Additionally, the inner ear shares many of the characteristics that make ophthalmology attractive: it is anatomically well defined and is a small, well contained space where the target cells to be treated are easily identified. In addition, the clinical outcome measures for treatments for hearing loss are well defined. Developing product candidates for conditions having these characteristics is a natural complement to our ophthalmology portfolio strategy as we apply our core capabilities and expertise to a new disease field. As part of our efforts in otology, we have formed a scientific advisory board to help guide our target selection and will announce product candidates when we formally begin development plans.

Our strategy

Our objective is to become the world leader in developing and commercializing gene therapy treatments for patients with severe diseases, with a primary focus in ophthalmology, and thereby to provide a better life for patients with these diseases. Our strategy to accomplish this goal is to:

- Develop and commercialize drugs in orphan ophthalmology. Our lead product candidates are treatments for the severe orphan eye diseases XLRS, ACHM, and XLRP. Given the severity of these diseases and the current lack of treatment options, a one-time-treatment alternative that corrects the underlying genetic defect would provide superior long-term value for patients, their families and the healthcare system more broadly.
- Expand our position in ophthalmology.
- Continue our leadership position in orphan ophthalmology. We have developed significant experience in the orphan ophthalmology space through our work on XLRS, ACHM, XLRP and LCA2. We have strong relationships with key opinion leaders in the field and with leading patient advocacy groups. We have received grants aggregating $9.5 million from the Foundation Fighting Blindness, or FFB, the National Institutes of Health, or NIH, the National Eye Institute, or NEI, and the FDA. Our scientific advisory board is comprised of leaders in the fields of ophthalmology and genetics, including one of our scientific founders, William W. Hauswirth, Ph.D., the Rybaczki-Bullard Professor of Ophthalmology and Molecular Genetics at the University of Florida, College of Medicine. We believe this experience provides a foundation to efficiently identify and develop additional orphan ophthalmology indications.

- Expand our product offerings to AMD. We plan to develop new treatments for AMD by leveraging our experience developing products in orphan ophthalmology and our work with Genzyme on a first generation product. Advances have been made in understanding the disease etiology and the number of known potential targets has increased since the first gene therapy programs attempting to treat AMD were designed. We plan to use our resources and access to experts in this field to evaluate these new targets and identify potential product candidates that can be moved into the clinic.
- Seek opportunities for strategic partnerships and acquisitions in ophthalmology gene therapy. On July 1, 2015, we entered into a broad collaboration and license agreement with Biogen to develop gene-based therapies for the XLRS and XLRP programs and three discovery programs. We believe there may be additional opportunities for us to partner with companies and academic groups. We expect that our breadth of experience in research,

manufacturing, clinical and regulatory matters will help us to identify and execute in-licenses, co-development agreements, intellectual property acquisitions or manufacturing agreements that would further extend our leadership position in ophthalmology gene therapy.

- Extend our expertise in AAV vector design, delivery and manufacturing. We believe that our understanding of our target indications and our robust internal expertise in viral vector design including the identification of novel capsids and the optimization of genes and promoters, physical vector delivery, vector manufacturing, clinical trial design and clinical trial conduct are significant competitive advantages. We intend to continue to devote substantial resources to developing the science underlying successful AAV vector design and delivery, such as our external research collaborations with organizations such as 4D Molecular Therapeutics and University of Florida to identify next generation capsids and Synpromics to develop optimized promoters. We are also expanding our discovery capabilities to further enhance our ability to develop next generation products. To that end we have grown our research personnel from 25 employees as of June 30, 2015 to 39 at June 30, 2016 and we plan to continue our growth into 2017. We have also expanded our facilities to approximately 21,300 square feet of laboratory and office space this year from approximately 7,000 square feet, with plans to add an additional 3,000 square feet in 2017.
- Expand our manufacturing capabilities. Our new process development and pilot manufacturing facility is now operational, and as we advance further into clinical development we plan to further develop our internal manufacturing capabilities. We also plan to continue to decrease our dependence on a single contract manufacturer by qualifying and contracting with multiple backup contractors. We recently began the design phase for construction of a current good manufacturing practices, or cGMP, facility at our Florida headquarters in preparation for moving product candidates into later stages of development. We believe these investments will facilitate the more rapid advancement of our product candidates through regulatory approval while reducing risk, and will enhance the therapeutic and commercial potential of our gene therapy platform.
- Pursue orphan indications with high unmet medical need and greater probability of clinical, regulatory and commercial success. We will continue to focus on diseases for which the underlying genetic defect is well characterized and can be addressed by correcting or inserting a single gene, for which predictive animal models exist and for which clinical endpoints are objective and are accepted by the FDA. We believe that focusing on these types of indications will enable us to obtain data more rapidly and accelerate clinical studies and regulatory approval of our products. Given the relatively low prevalence of orphan diseases and the strong key opinion leader communities and patient advocacy groups around them, we also believe these markets can be served with a small, targeted commercial infrastructure.
- Evaluate opportunities to leverage our gene therapy platform to address indications outside of ophthalmology. We intend to develop and partner selectively to expand the scope of our pipeline and the utilization of our gene therapy platform. The adaptability of our platform also presents an opportunity for us to selectively form collaborative alliances to expand our capabilities and product offerings into a range of genetically defined diseases and potentially to accelerate the development and commercialization of gene therapy products more broadly. We have a collaboration with Biogen that provides us with significant resources to expand our product development activities as well as access to significant development and commercialization expertise. Also, we recently announced a new effort in otology for which we will use our platform capabilities to develop potential therapies to address genetic causes of hearing loss.

Gene therapy background

Genes enable production of proteins that perform a vast array of functions within all living organisms. Many diseases have a genetic aspect whereby a mutated gene is passed down from generation to generation. Mutated genes can cause production of abnormal proteins, or loss of production of a protein, which can cause disease.

Gene therapy involves the introduction of a functional copy of a gene into a patient’s own cells using a delivery system most commonly based on a viral vector to treat the genetic defect. Gene therapy has the potential to change the way these patients are treated, by correcting the underlying genetic defect that is the cause of their disease rather than offering treatments that only address symptoms. We believe that by correcting the underlying genetic defect, gene

therapy can provide transformative disease modifying effects—potentially with long-term durable clinical benefits based on a one-time therapeutic administration.

The promise of gene therapy has evolved over the last decade, with a growing body of clinical data that we believe has provided evidence of efficacy and safety in a variety of disease areas, improvements in vector design and manufacturing processes by us and others and the establishment of regulatory guidelines for the development and approval of gene therapy products. These advances have led to increased investment from the biopharmaceutical industry and supported the emergence of gene therapy as an important therapeutic modality for patients with significant unmet medical needs.

Our gene therapy platform

Our approach to gene therapy product development is conceptually straightforward. We design an AAV vector that will carry the functional gene necessary to express the desired protein, produce the vector using our proprietary production methods, and then deliver the product directly to the appropriate cells in a patient by a suitable physical delivery method. Although the concept of gene therapy is simple, the process of developing and manufacturing AAV vectors capable of delivering the genetic material safely into a patient's own cells is highly technical and demands significant expertise, experience and know-how.

Our gene therapy platform is built on our core competencies in three key areas:

- vector selection and design;
- vector manufacturing and formulation; and
- vector delivery.

Our vector selection and design process

AAV vectors. The success of a gene therapy platform is highly dependent on the vector selected. Our platform is based on the use of a modified version of the non-replicating adeno-associated virus to deliver the correct DNA directly to the nucleus of the cells affected by the disease. We believe that AAV vectors are particularly well suited for treating our target diseases and have advantages over other viral vectors, such as adenovirus, herpes virus and lentivirus. These advantages include:

Simplicity —AAV is a small, simple non-enveloped virus with only two native genes. This makes the virus straightforward to work with from a vector engineering standpoint.

Stability —AAV is extremely stable: it is resistant to degradation by shear, solvents and enzymes, facilitating purification and final formulation. AAV stability could also enable development of a freeze-dried formulation, should this become necessary for larger markets where shipping and distribution of the current frozen formulation would be challenging.

Sustained expression —Unlike vectors based on other viruses, our AAV vectors are capable of inserting the functional gene into the patient's cells as an extra-chromosomal episome, which is a stable, circular form of DNA in the nucleus of cells. Inserting the functional gene as an episome supports long-term production of the protein, leading to sustained therapeutic effect, without altering the patient's native DNA. Sustained expression is a powerful advantage of using AAV as a vector: a one-time therapeutic administration of a functional gene into a cell can potentially support protein production for the life of the cell, which, in the cell types we are currently focused on treating, may approximate the duration of the patient's lifetime.

Safety —We believe AAV vectors are the safest for use in human gene therapy. In contrast, clinical trials using other vectors, such as lentivirus, adenovirus and herpes virus, have reported serious adverse events. The safety advantages of AAV vectors include the following:

- AAV elicits a low immune response, reducing the risk of adverse inflammatory reactions. In contrast, trials with adenoviral vectors have reported severe inflammatory reactions.
- AAV vectors, while they provide sustained expression, do not alter the patient's native DNA, and safety is therefore improved over vectors that alter the patient's DNA. Trials using early versions of lentiviral vectors, which insert genes directly into, and thereby alter, the patients' DNA, resulted in several well-publicized adverse events, including reported cases of leukemia.

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AAV has never been linked to human disease, unlike most other viruses used as gene delivery vectors such as adenovirus, herpes virus and lentivirus.

- AAV vectors have no viral genes remaining, eliminating the possibility that any viral genes will cause an adverse event.

AAV vectors have been used in more than 100 human clinical trials, by us and others, with no serious adverse events traced to the use of AAV as the gene delivery vector. In our direct experience with human clinical trials for LCA2, alpha 1 antitrypsin deficiency, or AAT deficiency, and wet AMD, over 100 patients were treated using AAV vectors, with no serious adverse events attributed to the vector. In a Phase 2 trial of our AAT deficiency product candidate, patients were treated with doses more than 300-fold higher than those planned for use in any of our ophthalmic indications, with no serious adverse events reported.

Carrying capacity —AAV vectors have the capacity to carry therapeutic gene sequences up to 4,000 base pairs in length into a patient's cell. As more than 90% of human genes have coding sequences less than 3,000 base pairs in length, we expect to be able to pursue a wide variety of indications with our AAV vectors.

Vector design. After the selection of the vector type, there are many other critical factors to be considered when designing a gene therapy product. These include selecting the appropriate:

- therapeutic gene,
- promoter and related gene regulatory elements,
- AAV sequences needed to signal replication and packaging, and
- AAV capsid (the protein shell) in which these elements are packaged.

The first step in vector design is to identify the therapeutic protein that we want the patient's own cells to produce, and many times optimize the gene for efficient therapeutic protein expression in patient's own cells, and then insert that efficient gene into an AAV vector. Production of the protein requires a promoter, which is a genetic element that drives expression. Certain promoters function well only in certain cell types, whereas other promoters function well in almost any cell type. We make our selection by comparing different promoters in the specific type of cells that are affected in each disease target, ideally in an animal whose physiology is close to that of humans, to find the promoter that best enables production of therapeutic levels of protein in that cell type.

After the promoter and gene of interest are selected, we insert these elements between AAV viral sequences that are needed for replication and packaging of the vector into the AAV capsid. There are hundreds of variations of AAV capsids with different efficiencies in their ability to bind to and enter varying cell types. We select the capsid for a specific product candidate after comparing different capsids in the type of cells that are affected by the targeted disease.

One of our key capabilities is our depth of understanding of the complex interplay between the clinical disease, the cells in the patient's body that need treatment, the selection of a capsid and a promoter, the design of the gene construct and the physical administration method. We have spent years conducting research on the best combinations of these elements with the aim of developing safe and effective gene therapy treatments.

Vector manufacturing: our H.A.V.E. method

We have developed a proprietary, high-yield vector manufacturing process using scalable technologies for herpes-assisted vector expansion, which we refer to as our H.A.V.E. manufacturing method. While the H.A.V.E. manufacturing method uses the herpes virus as a helper in the first step of a four-step AAV vector manufacturing process, there is no herpes virus in the final product. Our H.A.V.E. manufacturing method addresses problems of low productivity and low efficacy that have historically plagued efforts to manufacture AAV vectors and enables us to produce vectors with improved potency, efficiency and safety over processes previously used by us and others. It also enables us to produce a more purified and concentrated end product, as evidenced by an approximately 25- to 30-fold reduction in non-infectious viral contaminants as compared to vectors used in previous clinical trials.

Our manufacturing process has been reviewed by both the FDA and the European Medicines Agency, or EMA, and has been authorized for production of product candidates for use in clinical trials in the United States and Europe. Our manufacturing process is also reproducible and scalable. It has been transferred successfully to Genzyme and to SAFC (a part of Millipore Sigma), our contract manufacturing organization, where it is used in manufacturing clinical materials pursuant to the FDA's cGMP requirements.

7

While SAFC continues to be our primary contract manufacturer, our new process development facility is now operational and we are conducting equipment evaluation runs with multiple vendors to support development of commercial processes for our product candidates, if approved. Additionally, we are vetting multiple new cGMP contract manufacturers to ensure sufficient capacity for all programs as they advance in the clinic and to account for any unforeseeable circumstances. Further we have begun design work on an internal cGMP facility at our Florida headquarters.

We own or have licensed 26 issued patents and 6 pending patent applications covering our manufacturing technology. We believe that our core competency and intellectual property estate in vector manufacturing differentiate us competitively and provide a key element of our gene therapy platform.

Vector delivery

Our gene therapy platform allows for vector delivery by a variety of methods, and we select the method that is best suited for the disease we are targeting. The method used depends on the type of cells we are targeting for treatment.

In ophthalmology, the product candidate can best be delivered to cells in the eye by either intravitreal or subretinal injection.

Intravitreal injection into the vitreous humor, which is the clear gel that fills the space between the lens and the retina of the eye, is best for delivering the product candidate to the retinal neurons in the inner retina (the portion of the retina closest to the lens), to photoreceptors located in the fovea (the very center of the macula, which is the central part of the retina that is required for fine visual acuity), and other cells in the lateral portions of the eye. This routine procedure can be carried out in an ophthalmologist’s office.

Subretinal injection between the photoreceptors in the outer retina and the retinal pigment epithelium just below the retina are best for delivering the product candidate to the outer retina, farthest from the lens, where the AAV vector can readily enter photoreceptor cells and retinal pigment epithelium cells. This is a short, outpatient surgical procedure that is frequently performed by retinal surgeons.

We expect to use intravitreal injection as the method of delivery for our XLRS product candidate and subretinal injection as the method of delivery for our ACHM and XLRP product candidates. Other exploratory methods of delivering vector to anatomically defined sites are under evaluation.

Like the eye, the inner ear sensory organ – the organ of Corti – is bathed by fluid-filled spaces, enabling accessible vector administration. Surgical techniques used to introduce AAV include microinjection into the cochlear via an apical cochleostomy or through the round window membrane. These methods of administration of our product candidates are well established for the safe and effective delivery of other drugs and protein products. AAV vectors can be delivered by these and other methods to a wide array of other cells, such as heart muscle cells in certain cardiac diseases or directly into the brain in certain neurologic diseases.

Our approach can potentially arrest, correct or treat a disease with a one-time therapeutic administration, as many of the cells to which the product candidate is delivered will survive for the life of the patient and treatment of those cells thereby has the potential to deliver life-long effects. For example, cells in the retina, important in XLRS and ACHM, mature shortly after birth and in the absence of disease exist unchanged for the life of the patient. Once treated with our gene therapy product candidates, these cells have the potential to express the therapeutic protein for the remaining life of the cell. This approach potentially provides significant value to patients, families, providers and payors.

Our product programs

Our lead programs address XLRS, ACHM, and XLRP, which are orphan diseases of the eye that are caused by mutations in single genes, significantly affect visual function starting at birth and currently lack effective medical treatments.

We initially developed our gene therapy platform and obtained clinical evidence of its safety and efficacy in proof-of-concept programs involving two other eye diseases: LCA2 and wet AMD. We obtained clinical evidence of safety and tolerability with both programs as well as encouraging signs of biologic activity. We chose to not continue the development of the LCA2 product for a number of reasons, but most importantly because we believed the disease characteristics and market opportunity for our current lead programs were more attractive.

Our lead programs

X-linked retinoschisis

XLRS is an inherited retinal disease, meaning that children are born with the defective gene that causes poor visual function that significantly affects daily living activities. XLRS is specifically caused by mutations in the RS1 gene, which is located on the X chromosome and encodes the retinoschisin, or RS1, protein. Retinoschisin is expressed and secreted primarily from photoreceptor cells and binds strongly and specifically to the surface of photoreceptor and bipolar cells in the retina. Mutated forms of retinoschisin are unable to bind properly, resulting in schisis, or splitting of the layers of the retina, primarily in the macula. The disease begins early in childhood, and affected boys typically have best-corrected visual acuity of 20/60 to 20/120 at initial diagnosis. Complications such as retinal hemorrhage or retinal detachment occur in up to 40% of patients, especially in older patients. According to Molecular Genetics of Inherited Eye Diseases (1988), the incidence rate for XLRS is between one in 5,000 and one in 20,000 males. Using an incidence rate of 1 in 11,500 and assuming half the population is male, we estimate that there are about 13,000 persons in the United States and about 22,000 persons in Europe with XLRS, or 35,000 persons in the United States and Europe combined.

The diagnosis of XLRS is made based on clinical findings and results of imaging studies and Electro Retino Gram (ERG). Clinical findings include reduced visual acuity and a characteristic spoke-wheel appearance of the macula when viewed by an ophthalmoscope, which is the instrument commonly used by ophthalmologists and optometrists to view the retina. Images obtained by optical coherence tomography, or OCT, a method of viewing layers of the eye somewhat like a sonogram, show spaces between the layers of the retina within the macula and fovea in most school-age boys with XLRS. These spaces mean that electrical signals cannot move from the photoreceptors to other

retinal neurons and on to the brain, resulting in poor vision. When this is measured by ERG testing it can be detected by an abnormal ERG response.

The figure below shows an OCT image from a normal individual (top) and from a patient with XLRS (bottom). The black spaces indicated by the arrows in the bottom portion of the figure demonstrate splitting of the layers of the retina leaving spaces that interfere with the movement of electrical signals.

There is currently no approved treatment for XLRS. Management of disease manifestations includes low vision aids such as large-print textbooks, preferential seating in the front of the classroom and use of handouts with high contrast. Surgery may be required to address complications of vitreous hemorrhage or full-thickness retinal detachment. Anecdotal reports suggest that topical carbonic anhydrase inhibitors may provide some reduction in the degree of schisis detected by OCT and improvement in visual acuity in some but not all patients, but the absence of controlled clinical trials makes interpretation of these reports difficult. In addition, treatment with carbonic anhydrase inhibitors does not address the fundamental genetic defect in persons affected by XLRS. Neither carbonic anhydrase inhibitors nor any other medicinal products have been approved by regulatory agencies for treatment of XLRS.

Our XLRS product candidate

Our gene therapy approach involves using an AAV vector to insert a functional copy of the RS1 gene into the patient's retinal cells, thereby inducing those cells to produce the normal retinoschisin protein. Our XLRS product candidate contains the RS1 gene and a promoter that has been shown to work well in primate retinal cells, and is packaged in an AAV capsid that is able to efficiently enter cells in the inner layers of the retina after intravitreal injection.

The mechanism by which the XLRS product candidate is believed to improve visual function is described below. After the vector containing a functional copy of the RS1 gene enters a retinal cell, the gene is processed by normal biochemical processes into a stable DNA episome in the nucleus of the cell. This stable form of the gene allows production of the normal retinoschisin protein which is then secreted from the retinal cells and binds to the surfaces of photoreceptor and bipolar cells in the retina, which may correct the abnormal splitting of the layers of the retina. Upon light stimulation of the photoreceptor cells, the presence of the retinoschisin allows normal transmission of electrical signals from the photoreceptor cells to the bipolar cells and then to other retinal neurons that transmit the signals to the visual cortex in the brain. Production of normal retinoschisin continues as long as the episome persists in the cell, which may be for many years or even life-long, thereby providing long-term potential benefit after a one-time therapeutic administration.

Preclinical proof of concept for our XLRS product candidate

In mouse models of XLRS, our gene therapy approach restores to normal the abnormal ERG response that is characteristic of XLRS. Mouse models of XLRS have been developed by deactivating, or knocking out, the RS1 gene in mice. These "knockout" mice have clinical features similar to humans with XLRS, including reduced visual acuity, schisis cavities detected by OCT, and a markedly abnormal ERG response.

The figure below shows staining for retinoschisin (top row) and for nuclei in retinal cells (bottom row) in a normal mouse (left), a RS1 knockout mouse in the absence of treatment (middle) and a RS1 knockout mouse treated with an AAV-RS1 vector (right). The knockout mouse retina has no expression of retinoschisin and has splitting and disorganization of the layers of the retina, indicated by the arrowheads in the middle panel of the nuclear staining. After treatment, RS1 staining is present in a normal fashion and the nuclear staining shows restoration of the organization of the cell layers in the retina (right).

Based on data from Min et al. Molecular Therapy (2005)

Treatment by injection of an AAV vector expressing either mouse or human RS1 in these knockout mice improved visual function as measured by increased ERG b-wave responses.

The figure below shows improved ERG responses in RS1 knockout mice at various times after treatment with an AAV-RS1 vector compared to ERG responses in untreated control RS1 knockout mice. The figure shows a progressive decrease in the ERG response in the untreated mice but a slower decrease and eventual increase in the ERG response in the treated mice.

Based on data from Min et al. Molecular Therapy (2005)

We have concluded that intravitreal injection is the preferred route of administration for an AAV-RS1 vector. We therefore evaluated intravitreal injection of an AAV vector expressing a marker protein packaged in several different AAV capsids in monkeys and demonstrated that a vector packaged in an engineered capsid was able to target expression to the macula, which is the primary area in which retinoschisis occurs.

The figure below shows expression of a marker protein (white areas) in the macula, fovea and nerve fibers of a monkey retina after intravitreal injection of a vector contained in the engineered capsid. We believe that intravitreal injection of a vector containing the RS1 gene in the same engineered capsid would show expression of retinoschisin in the same areas.

Based on AGTC animal study data

Planned clinical development of our XLRS product candidate

We are currently enrolling patients in a Phase 1/2 clinical trial the primary endpoint of which is safety. Secondary endpoints include efficacy analyses. The current clinical protocol, illustrated below, anticipates enrollment of up to 27 patients.

As of August 2016, we have enrolled a total of eight patients – six of whom are in the lowest dose level and two are in the middle dose level. While this number is lower than we had hoped to report on at this point in the study we have identified a path forward to complete the trial expeditiously.

Safety data to date has shown that our XLRS product candidate has been generally well tolerated. We did observe mild to moderate ocular inflammation in the majority of patients, which resolved either without treatment or after treatment with topical or oral corticosteroids. Since the primary endpoint of the study is safety, we amended the protocol to provide for standard prophylactic corticosteroids versus the original protocol that allowed for treatment with corticosteroids only after inflammation was observed.

Enrollment has been slower than we anticipated in the study for a number of reasons which are summarized here and further explained in the following paragraphs. The reasons for the slow enrollment include delays due to patients not meeting one or more study eligibility criteria, a protocol amendment, as mentioned above, to allow use of prophylactic corticosteroids that required institutional review board approvals at each site, and the necessity to re-test the study agent for a process component. We believe we have resolved these areas in order to meet our future enrollment plans.

The Phase 1/2 clinical trial is currently being conducted at six clinical sites that specialize in inherited retinal diseases, an increase from the three originally planned sites in order to address the need to identify more patients that meet the eligibility criteria. These sites include: the Casey Eye Institute in Portland, Oregon, the Retina Foundation of the Southwest in Dallas, Texas, the Kellogg Eye Center in Ann Arbor, Michigan, the Massachusetts Eye and Ear Infirmary in Boston, Massachusetts, the Baylor College of Medicine in Houston, Texas and the University of California San Francisco in San Francisco, California. We have also signed a contract with a seventh site and are in the process of evaluating additional sites that can help to accelerate screening and enrollment. With the assistance from patient advocacy groups, academic centers, our investigators and our collaboration partner Biogen, we have completed screening on over 100 patients, eight of whom are enrolled and approximately 20 of whom meet the eligibility requirements for the expansion group which will provide additional safety data at the maximal tolerated dose. We continue our patient outreach and currently have multiple new patients in the screening process.

We are measuring a wide range of secondary endpoints that might provide early indications of potential efficacy and will help us design a subsequent trial. We have not observed any significant improvements in secondary endpoints in the six patients treated at the lowest dose level. As we are still in the process of completing the dose escalation phase of the trial, we plan to report results on these groups once we have enough data to draw meaningful conclusions from the results. As a result, we do not expect to report further data on the XLRS study this year.

We have also completed enrollment in a natural history study in persons affected by XLRS and results from the study will be presented in appropriate scientific meetings and publications in the future.

Completion of the Phase 1/2 clinical trial and the natural history study will guide us in finalizing the design of a pivotal Phase 3 clinical trial. In the planned pivotal Phase 3 trial, we would expect to enroll 40 - 75 patients who will be evaluated for changes in visual function over a 12-month period. If successful, we believe the results of this second trial could support submission of a Biologics License Application, or BLA, to the FDA in the United States and a Marketing Authorization Application, or MAA, to the EMA in Europe for our XLRS product candidate.

As a part of our collaboration, Biogen has obtained worldwide commercialization rights for the XLRS program. We will be responsible for the clinical development program through product approval. Biogen will support the clinical development costs, subject to certain conditions, following the first-in-human study. We have an option to share development costs and profits after the initial clinical trial data are available, and an option to co-promote the second

of two products (XLRS and XLRP) to be approved in the United States.

Congenital achromatopsia (ACHM)

ACHM is an inherited retinal disease, meaning that children are born with the defective gene that causes poor visual function which significantly affects daily activities. ACHM is present from birth and throughout life and is characterized by the lack of cone photoreceptor function. Cone photoreceptors which are concentrated in the macula and the fovea, respond to moderate or bright intensity light and mediate fine visual acuity. Individuals with ACHM have markedly reduced visual acuity, photophobia or light sensitivity, and complete loss of color discrimination. Their only functioning photoreceptors are rod photoreceptors, which respond to low intensity light conditions and mediate night vision but cannot achieve fine visual acuity. Best-corrected visual acuity in persons affected by ACHM, even under subdued light conditions, is usually about 20/200, a level at which people are considered legally blind. They also experience extreme light sensitivity resulting in even worse visual acuity under normal daylight conditions, or day blindness.

ACHM can be caused by mutations in any of at least five genes that are required for normal cone photoreceptor function. The most common causes are mutations in the CNGB3 gene (about half of all cases) or CNGA3 gene (about one-fourth of all cases). These genes encode the CNGB3 and CNGA3 proteins, which combine to form a channel in the photoreceptor membrane that is required for phototransduction, the process whereby a light signal is converted to an electrical signal that is then transmitted to the brain. According to Retinal Dystrophies and Degenerations (1988), the incidence rate for ACHM is approximately one in 30,000 people, and we therefore estimate that there are about 10,000 people in the United States and about 17,000 people in Europe with ACHM. Of these, about half, or a total of 13,500 in the United States and Europe combined, have the form of the disease caused by mutations in the CNGB3 gene and approximately 6,800 people have the form of the disease caused by mutations in the CNGA3 gene.

There is currently no approved treatment for ACHM. Symptoms are managed by the use of dark lenses to reduce discomfort from ambient light, and low vision aids such as high-powered magnifiers for reading. Children with ACHM are provided preferential seating in the front of classrooms to allow maximum benefit from their magnifying devices.

Our ACHM product candidates

Our gene therapy approach to treatment of ACHM involves using an AAV vector to insert a functional copy of the CNGB3 or CNGA3 gene into the patient's photoreceptor cells. Together these two genes account for 75% of the ACHM patient population. Our ACHM product candidates contain either the CNGB3 or the CNGA3 gene and a proprietary promoter, PR1.7, that has been shown in preclinical studies to drive efficient gene expression in primate cone photoreceptors and restores cone photoreceptor function in dog, mouse and sheep models of ACHM. We have identified an AAV capsid that works well for subretinal delivery and are evaluating additional AAV capsids to identify those that work well for intravitreal delivery that could be used in follow-on products.

The mechanism by which the ACHM CNGB3 or A3 product candidate is believed to improve visual function is described below. After the vector containing a functional CNGB3 A3 gene enters a photoreceptor cell, the gene is processed by normal biochemical processes into a stable DNA episome in the nucleus of the cell. The stable form of the gene allows production of the normal CNGB3 or A3 protein, which combines with proteins already being produced in the cell, to form a channel in the photoreceptor membrane that is required for phototransduction. Restoration of phototransduction enables cone photoreceptors to convert light entering the eye into an electrical signal that is transmitted to other retinal neurons and then to the visual cortex in the brain. Production of normal CNGB3 or A3 protein continues as long as the episome persists in the cell, which may be for many years or potentially life-long, thereby providing long-term potential benefit after a one-time therapeutic administration.

Preclinical proof of concept for our ACHM product candidates

In mouse, dog and sheep models of ACHM, our product candidates were able to restore photoreceptor function, improve visual acuity and mitigate photophobia and day blindness.

ACHM occurs in two breeds of dogs, Alaskan malamutes and German shorthaired pointers, due to mutations in the CNGB3 gene that either produce an abnormal protein or completely prevent production of the protein. Both breeds have clinical characteristics similar to human ACHM patients, with day blindness and absence of retinal cone function as measured by ERG. Treatment by subretinal injection of an AAV vector expressing human CNGB3 restored cone function in dogs with either mutation. Cone-specific ERG responses were undetectable in these dogs before treatment but were clearly detected after treatment. Day blindness was demonstrated before treatment by testing the ability of the dogs to navigate a maze under progressively brighter conditions. Before treatment, it took the ACHM dogs progressively longer to navigate the maze as the ambient light increased from dim light to normal room lighting and even longer with normal outdoor daytime lighting. After treatment, the day blindness was substantially eliminated,

and the treated ACHM dogs were able to navigate the maze under bright light conditions at almost the same speed as normal dogs.

The figure below shows the average time taken to navigate a maze as the ambient light intensity was increased for three groups of dogs: normal dogs, dogs with ACHM that were untreated and dogs with ACHM that were treated with our ACHM product candidate. The figure shows that under low light conductions (0.2 lux, equivalent to the light conditions on a moonlit night), when vision is normally mediated only by rod photoreceptors, all three groups navigated the maze rapidly. As the light intensity was progressively increased (to 646 lux, equivalent to the light conditions in a business office), and vision became mediated by cone photoreceptors, the untreated ACHM dogs took progressively longer to navigate the maze, as they collided with walls in the maze and had to advance by trial and error. In contrast, as the light intensity was progressively increased, the time taken to navigate the maze did not change for normal dogs and increased only slightly for the treated ACHM dogs.

Based on Komaromy et al. Human Molecular Genetics (2010)

Untreated ACHM dogs also demonstrated photophobia and day blindness when outdoors in daylight, which severely limited their ability to interact with people and objects in their environment. After treatment there was a dramatic improvement in this important clinical manifestation of ACHM. The restored function persisted for more than 2.5 years (the longest duration tested).

In addition, a mouse model of ACHM was developed by knocking out the CNGB3 gene in mice. These knockout mice have markedly impaired cone photoreceptor function, as measured by ERG and visual acuity testing. Treatment by subretinal injection of an AAV vector expressing human CNGB3 in the knockout mice improved cone-specific ERG responses to nearly normal levels and improved visual acuity, as measured by their ability to follow a rotating pattern of vertical stripes of varying thickness.

There is also a sheep model of ACHM caused by mutations in the CNGA3 gene. These sheep have clinical characteristics similar to human ACHM patients, with day blindness and absence of retinal cone function as measured by ERG. In collaboration with scientists at three academic centers in Israel (The Volcani Center, the Koret School of Veterinary Medicine and the Hadassah-Hebrew University Medical Center), we conducted a preclinical study evaluating the safety and efficacy of our product candidate for CNGA3-related ACHM using the sheep model, which uses the same promoter and capsid used in our CNGB3 product candidate, administered by subretinal injection. Cone-specific ERG responses, which were undetectable in these sheep before treatment, were clearly detected after treatment. Day blindness was demonstrated before treatment by testing the ability of the sheep to navigate a maze under bright light conditions. After treatment, the day blindness was substantially eliminated, and the treated sheep were able to navigate the maze under bright light conditions, as illustrated in the figure below. At both the higher and lower doses tested, the maze transit time was similar, and clearly improved over the pre-dose performance.

These results agree closely with a previously published proof-of-concept study, in which the performance of AAV treated animals approached that of normal (unaffected) animals. See table below.

Based on data from Banin et al. (2015) Molecular Therapy; 23 9, 1423–1433

16

Planned clinical development of our CNGB3-related ACHM product candidate

We are currently enrolling patients in a Phase 1/2 clinical trial in which the primary endpoint is safety. Secondary endpoints include efficacy analysis. The current clinical protocol, illustrated below, anticipates enrollment of up to a total of 24 ACHM CNGB3 patients.

The Phase 1/2 clinical trial is being conducted at four clinical sites that specialize in inherited retinal diseases: the Casey Eye Institute in Portland, Oregon, the Pangere Center for Inherited Retinal Diseases in Chicago, Illinois, the Bascom Palmer Eye Institute in Miami, Florida, and Vitreo Retinal Associates in Gainesville, Florida. An additional site is performing advanced optical testing on every patient. As of August 2016, two patients are currently enrolled in the lowest dose group, which is a lower number of patients than we had hoped to report on at this point in the study.

Vendor errors in testing of the study agent for a process component resulted in a delay to the initiation of enrollment in this trial.

We have dosed two patients and the future enrollment schedule will depend on the preliminary data from these patients. As a first in man study, our internal and external teams are following the first patients very carefully over time, to meet our primary objective of patient safety before proceeding with further study enrollment involving a larger number of patients. We will release data when we have sufficient data to draw meaningful conclusions from the results.

We have completed enrollment in a natural history study in persons affected by ACHM caused by CNGB3 mutations and results from the study will be presented in appropriate scientific meetings and publications.

Completion of the Phase 1/2 clinical study and the natural history study will guide us in finalizing the design of a pivotal Phase 3 clinical trial. In the planned pivotal Phase 3 trial, we expect that between 40 and 75 patients will be enrolled and evaluated for changes in visual function over a 12-month period following treatment. If successful, we believe the results of this pivotal Phase 3 trial could support our submission of a BLA to the FDA and of an MAA to the EMA for our ACHM-B3 product candidate.

Planned clinical development of our CNGA3-related ACHM product candidate

We expect to submit the IND for our ACHM CNGA3 product candidate by the end of 2016. Once the IND has been cleared by the FDA, we anticipate enrolling 24 ACHM CNGA3 patients in a Phase 1/2 clinical trial with a design similar to the design of the ACHM-CNGB3 study described in the figure above.

We have also initiated an international natural history study in patients with CNGA3-related ACHM, at the Bascom Palmer Eye Institute in Miami, Florida, and the Hadassah-Hebrew University Medical Center in Jerusalem, Israel.

X-linked retinitis pigmentosa

Retinitis pigmentosa is an inherited retinal dystrophy with progressive loss of vision, meaning children are born with defective genes that cause poor visual function that significantly affects daily activities and worsens over time. XLRP is commonly first observed in boys and young men who notice problems with vision under low light conditions, or night blindness, followed by a restriction of peripheral visual fields, or tunnel vision, leading to poor central vision and eventually to total blindness.

The incidence rate for retinitis pigmentosa is about one in 4,000 people, according to Retinitis Pigmentosa (1988), and we estimate that there are about 75,000 people in the United States and 125,000 people in Europe with retinitis pigmentosa, or 200,000 people in the United States and Europe combined. According to a paper by Dr. Marianne Haim published in Acta Ophthalmologica (1992), about 10% of cases of retinitis pigmentosa are XLRP, from which we therefore estimate that there are about 20,000 persons with XLRP in the United States and Europe combined.

Preclinical studies in a dog model of XLRP caused by mutations in the RPGR gene demonstrated a reduction in the rate of disease progression in eyes that received a subretinal injection of an AAV vector expressing the correct form of the gene. A comparative dose range finding study of our XLRP product candidate in dogs demonstrated expression of the RPGR protein in photoreceptors and improvement in structural and functional parameters associated with disease progression in this model. IND-enabling good laboratory practices, or GLP, toxicology studies are underway in two relevant disease models — the dog model discussed above and also in an RPGR knockout mouse model. After completion of these studies, we expect to submit an IND to the FDA in 2017.

We are conducting a natural history study in patients with XLRP caused by RPGR mutations. This study will document the progression of the disease in the absence of treatment and provide important information about the best methods for measuring visual function and other parameters in these patients, which will guide us in the design of subsequent clinical trials in which our product candidate will be tested for safety and efficacy. The study is being conducted at the Scheie Eye Institute in Philadelphia, Pennsylvania.

As a part of our collaboration, Biogen obtained worldwide commercialization rights for our XLRP program. We will lead the clinical development program through the completion of first-in-human trials. Biogen will support the clinical development costs, subject to certain conditions, following the IND-enabling studies. We have an option to share development costs and profits after the initial clinical trial data are available, and an option to co-promote the second of two products (XLRS and XLRP) to be approved in the United States.

Other opportunities in ophthalmology

We believe our current gene therapy platform will enable us to develop and test new AAV vectors that carry gene sequences for other inherited diseases in ophthalmology, and that by leveraging our work on our four lead programs we can reduce the need for early research work. In this way, we anticipate being able to move products efficiently through preclinical studies and into clinical development. We also believe that there are large-market ophthalmology diseases where AAV vectors may provide benefit, such as wet AMD.

Wet AMD

AMD is a retinal disease that affects older adults and results in a loss of vision in the center of the visual field (the macula). It is a major cause of blindness and visual impairment and occurs in neovascular (“wet”) or non-neovascular (“dry”) forms. There are an estimated 3.2 million persons with wet AMD in the United States and Europe combined. Wet AMD is characterized by the abnormal growth of blood vessels in the retina stimulated by a protein called vascular endothelial growth factor, or VEGF, and is currently treated with intravitreal injections of anti-VEGF

agents delivered every one to two months, for an indefinite period. An effective gene therapy product has the potential to improve on the approximately 35% success rate for existing therapies by targeting other critical factors, and to reduce the burdensome injection frequency for patients and physicians.

Based on our proof-of-concept studies, we believe that gene therapy offers a potential long-term solution to treat wet AMD with a single injection. Additionally, as in the case of “cocktail” treatment paradigms in oncology, there is a strong rationale for combination therapy to become the standard of care in wet AMD. For instance, we are aware that others are conducting Phase 3 trials of an anti-platelet-derived growth factor, or PDGF, agent in combination with anti-VEGF agents for wet AMD. We believe that, while the predictability of targeting VEGF itself would mitigate development risk, the most compelling gene therapy approach would offer not only sustained expression but also pathway synergy with existing anti-VEGF options. We have defined our preferred target profile, are proceeding with a comprehensive analysis of possible targets, and are conducting preclinical efficacy studies in order to select candidate targets for clinical evaluation.

Once a candidate target is identified, the development pathway for wet AMD therapies has been well-established. Given our experience gained from previous efforts, including our prior relationship with Genzyme, our already-established manufacturing infrastructure, our deep clinical capabilities and our well defined regulatory path, we expect to be able to file an IND for a wet AMD product candidate and execute a clinical trial efficiently.

Other autosomal recessive retinal diseases

It is estimated that approximately 290 genes causing inherited retinal disease have been identified, of which 186 are autosomal recessive, or X-linked, and therefore most amenable to treatment by gene replacement therapy. Among the 42 most common autosomal recessive forms of retinitis pigmentosa, LCA and cone or cone-rod dystrophy, 38 have gene coding regions of less than 3,760 nucleotides and can therefore be readily accommodated within our AAV vectors. We are continuing to evaluate indications having these characteristics to select those most appropriate for addition to our longer-term product development pipeline. As an example, in January 2016 we announced a research effort in BCM, a rare genetic disease of the retina that almost exclusively affects males. It is a hereditary condition linked to the X chromosome that manifests with a partial dysfunction of the cones of the retina. BCM can result in reduced visual acuity, impaired color vision, photosensitivity, myopia and infantile-onset nystagmus. These manifestations are similar to those in ACHM caused by mutations in the CNGB3 or CNGA3 gene.

Manufacturing

Until recently, there has been a lack of manufacturing infrastructure to enable the production of gene therapies in a reliable and reproducible manner at a commercially viable scale. The historical challenges for gene therapy manufacturing relate to the difficulty of developing constructs that provide the necessary helper functions, and in having systems that provide adequate yield, scalability and potency. We have made significant investments in developing improved manufacturing processes, which include the following:

- We have developed proprietary AAV vector manufacturing processes and techniques that produce a more purified and concentrated product candidate, as evidenced by the approximately 25- to 30-fold reduction in non-infectious viral contaminants as compared to vectors used in many previous clinical trials.
- We do not need a specially cloned and isolated cell line for each of our disease targets; we instead use specially engineered replication-incompetent herpes simplex helpers, or HSV helpers, which are stable and straightforward to clone.
- We have developed over 30 assays to accurately characterize our process and the HSV and AAV vectors we produce.
- We have developed a purification system applicable to multiple AAV capsids.
- We are investing in the development of mid- to large-scale manufacturing processes to enable the manufacture of our product candidates at commercial scale.

We believe these improvements and our continued investment in our manufacturing platform will enable us to develop best-in-class, next generation gene therapy products.

Our viral vector production platform for AAV-based gene therapeutics, which we call the herpes-assisted vector expansion, or H.A.V.E. method, offers significant benefits in comparison with the methods used by others to manufacture AAV vectors, as summarized in the following table.

AAV production method	Straightforward cloning	High efficiency	High yield	Scalable

Transfection	Yes	No	No	No
Baculovirus	No	No	Yes	Yes
Adenovirus	No	Yes	Yes	Yes
Our H.A.V.E. method	Yes	Yes	Yes	Yes

The four key steps involved in our proprietary H.A.V.E. manufacturing method are as follows:

- First, the therapeutic gene and the appropriate AAV capsid genes are inserted into individual HSV helpers, and these helpers are individually grown in a complementing cell line called V27. The complementing cell line is required to provide critical functions that allow the replication-incompetent HSV helpers to grow; the same cell line is used to produce HSV helpers for all disease targets. This step occurs in disposable culture vessels of increasing size, up to and

including disposable stirred tank bioreactors. The HSV helpers are harvested, minimally processed and concentrated to prepare them for use in producing our AAV vectors. These HSV helpers can be stored frozen for years before use.

- Next, the two HSV helpers are used together to infect a cell line called sBHK, allowing for packaging of the therapeutic gene into the AAV capsid and to produce our AAV vectors. The sBHK cell line does not provide the critical functions that would allow for growth of the HSV helpers, which provides an added layer of safety. The same sBHK cell line is used to produce AAV vectors for all disease targets. This step occurs in disposable culture vessels of increasing size depending on the amount of AAV vector that is required. The AAV vector is recovered by using a detergent solution to break open the sBHK cells and release the AAV vectors. This step also destroys any residual HSV helpers that were used to infect the sBHK cells.
    - The third step is to purify the harvested AAV vector using two chromatography columns. The exact method used to column-purify our AAV vectors varies depending on the AAV capsid used in the product candidate; we have developed purification methods for multiple AAV capsids. We have shown in formal clearance studies that the combination of detergent treatment and two chromatography columns can remove up to 10^{14} (100 trillion) units of HSV. This step also helps to eliminate any remaining parts, such as proteins or DNA, of the HSV helpers and sBHK production cells.
- The final step is to formulate, filter and fill the AAV vector in appropriate containers for use in animal or human studies. This filled AAV vector drug product can be stored frozen for many years before use.

H.A.V.E. Production of our AAV Vectors for Gene Therapy

The H.A.V.E. method is inherently flexible, allowing the manufacture of a wide range of AAV vectors without the need to modify the manufacturing steps used to produce the HSV helpers or AAV vectors. We have already demonstrated our manufacturing knowledge through multiple successful production batches of both HSV helpers and AAV vectors at SAFC, our contract manufacturing organization, under current good manufacturing practices, or GMP.

Research is already underway to meet our future manufacturing needs. Our new process development and pilot manufacturing facility is now operational and we will continue to decrease our dependence on a single contract manufacturer by qualifying and contracting with multiple new contractors and by further developing our internal manufacturing capabilities. We recently began the design phase of construction for a cGMP facility at our Florida headquarters in preparation for moving products forward into later stages of development. We believe these investments will facilitate the more rapid advancement of our products through regulatory approval and enhance the therapeutic and commercial potential of our gene therapy platform.

Strategic collaborations and acquisitions

We have formed strategic alliances where both parties contribute expertise to enable the discovery and development of potential gene therapy product candidates. To access the substantial funding and other resources required to develop and commercialize gene therapy products, we intend to seek additional opportunities to form strategic alliances with collaborators who can augment our industry-leading gene therapy expertise.

On July 1, 2015, we entered into a broad collaboration and license agreement with Biogen to develop gene-based therapies for multiple ophthalmic diseases. Biogen made an upfront payment to us in the amount of $124.0 million, which included a $30.0 million equity investment and certain prepaid research and development expenditures. Biogen will be granted a license to the XLRS and XLRP programs and the option to license discovery programs for two additional ophthalmic indications and one non-ophthalmic indication at the time of clinical candidate selection. In February 2016, we announced Biogen's selection of adrenoleukodystrophy, or ALD, as the non-ophthalmic indication of the three discovery programs. Under the collaboration, we are eligible to receive upfront and milestone payments exceeding $1 billion. This includes up to $472.5 million collectively for the two lead programs, which also will carry royalties in the high single digit to mid-teen percentages of annual net sales. In addition, Biogen may make payments up to $592.5 million across the discovery programs, along with royalties in the mid-single digits to low teen percentages of annual net sales for the discovery programs. In October 2015, Biogen paid us an additional $5.0 million upon achievement of the first enrollment milestone for XLRS.

Biogen will also receive an exclusive license to use our proprietary manufacturing technology platform to make AAV vectors for up to six genes, three of which are at our discretion, in exchange for payment of milestones and royalties.

We have also entered into an agreement with SAFC, which also is our current contract manufacturing organization, for cGMP manufacture of clinical grade material for third parties. This arrangement allows us to approach other gene therapy companies that might benefit from our manufacturing and vector design capabilities. Under such an arrangement, we could potentially license our manufacturing technology and receive upfront payments, milestones and royalties. SAFC would do the manufacturing of commercial grade material.

We also plan to continue to in-license additional intellectual property to support our current programs, to establish new development programs and to support our manufacturing technology. Additionally, we will seek to partner with other commercial gene therapy companies and academic institutions to leverage our expertise in vector design, research, manufacturing and the regulatory process. The goal of these collaborations would be to forge strategic partnerships around technologies and programs that would fit with our current and future development pipeline. In general, we would seek new intellectual property, development programs in rare diseases, pipeline products where the regulatory pathway is understood, partners with strong scientific, clinical and management expertise, and programs that have synergy with our current knowledge base and product pipeline that would add to our industry leadership. We would also be looking at programs where the disease being treated has a large enough patient population that there would be adequate financial returns for the investment of resources.

Our relationship with the University of Florida

All of our scientific founders spent part of their careers at the University of Florida, or UF, and three are still UF faculty members. Since our inception we have licensed significant technology from and funded research at multiple labs at UF. Pursuant to four agreements, we have licensed three U.S. patents and multiple pending applications

covering inventions made at UF. UF has multiple capabilities in genetic cloning, gene therapy manufacturing, animal model development and facilities for both small and large animal testing, and in certain instances we have benefited from the ability to conduct important research at UF without having to expand in-house facilities and personnel. We interact frequently with the Powell Gene Therapy Center at UF and have an excellent working relationship with the UF Office of Technology Licensing.

In May 2013, we and UF were jointly awarded an $8.3 million dollar grant from the NEI to support development of our ACHM CNGB3 product candidate, with Dr. William Hauswirth, one of our scientific founders and Professor and holder of the Rybaczki-Bullard Chair in the Department of Ophthalmology at UF, as principal investigator. As a sub-awardee, we expected to receive approximately $3.8 million over five years under this grant. As of June 30, 2016, we had received payments in the aggregate amount of $1.9 million under this grant.

Our relationships with patient advocacy groups and academic centers

We have long believed that when developing products to treat orphan indications it is important to form strong relationships with patient advocacy groups, and we have done this successfully with both the Foundation Fighting Blindness, or FFB, and the Alpha-1 Foundation. Both organizations are well known for their advocacy of patients' interests in obtaining diagnosis, developing treatments and providing for reimbursement. Both actively support research into treatment, and we have been awarded three research grants totaling $1.6 million from the FFB and one grant of $0.3 million from the Alpha-1 Foundation. More importantly, both organizations have been instrumental in assisting us in forming ties with disease experts, recruiting patients into clinical trials and helping us to understand the needs, wants and concerns of patients. We also have relationships with other advocacy organizations such as Achroma Corp and the BCM Family Foundation.

We also have formed strong relationships with key academic centers across the United States that have core competencies in gene therapy, orphan ophthalmology and AAT deficiency. These centers conduct sponsored research, act as advisors and collaborate with us on grant proposals. Since our inception, we have been awarded a variety of grant funding, either independently or with our collaborators. This funding has provided peer-reviewed scientific validation of our programs and has facilitated critical early stage research for our lead product candidates.

Intellectual property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties and seeking patent term extensions where available. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy that may be important for the development of our business. In addition to IP and trade secrets, we also will rely on regulatory protection afforded through orphan drug designations, data exclusivity and market exclusivity for our products, when possible.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

We have developed or in-licensed numerous patents and patent applications and possess substantial know-how and trade secrets relating to the development and commercialization of gene therapy products. Our proprietary intellectual property, including patent and non-patent intellectual property, is generally directed to, for example, certain genes and promoters, methods of transferring genetic material into cells, processes to manufacture our AAV-based product candidates and other proprietary technologies and processes related to our lead product candidates.

As of August 19, 2016, our patent portfolio included approximately 62 patents and patent applications that we own and approximately 73 patents and patent applications that we have licensed. More specifically, we own five U.S. patents, seven pending U.S. applications, 32 foreign patents and 18 foreign patent applications. We have licensed 22

U.S. patents, four pending U.S. applications, 35 foreign patents and 12 pending foreign patent applications. Of the patents and patent applications that we own or license, 32 cover methods to manufacture AAV vectors, the longest lived and most significant of which is expected to expire in 2025. Ten of the patent applications that we own are directed to small cone promoters and uses thereof. A patent issuing from this group could have an expiration date in 2034.

Our objective is to continue to expand our portfolio of patents and patent applications in order to protect our gene therapy product candidates and AAV manufacturing process. Our owned and licensed patent portfolio includes patents and patent applications directed to our XLRS, ACHM, XLRP and AAT deficiency programs, as well as our foundational AAV production platform. See also "—License agreements."

In addition to the above, we have established expertise and development capabilities focused in the areas of preclinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, regulatory affairs and clinical trial design and implementation. We believe that our focus and expertise will help us develop products based on our proprietary intellectual property and to expand our intellectual property.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. The issued patents that we own and license are expected to expire on various dates from 2016 to 2029.

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent per approved drug may be extended. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a new drug application, or NDA, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. 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 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. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

License agreements

We have rights to use and exploit multiple issued and pending patents under licenses from other entities. We consider the commercial terms of these licenses, which provide for modest milestone and royalty payments, and their provisions regarding diligence, insurance, indemnification and other similar matters, to be reasonable and customary for our industry.

Information about our principal licenses is set forth below.

University of Florida

We currently have four license agreements with the University of Florida Research Foundation, or UFRF, an affiliate of UF, of which the principal licenses are as follows:

- A license from UFRF signed in September 2001 relates to the AAV construct containing the AAT gene and the method to treat AAT deficiency using this construct. We have an exclusive license in all fields of use.

Under the terms of this license, we made cash and stock-based up-front payments to UFRF and are required to make payments ranging from the mid-five figures to the low-six figures based upon development, regulatory and commercial milestones for any products covered by the in-licensed intellectual property. Assuming that we meet each of the specified development, regulatory and commercial milestones not more than once for each product, which we expect will be the case, the maximum aggregate milestone payments payable under this license with respect to any individual product that we commercialize will be $0.3 million. We will also be required to pay a royalty on net sales of products covered by the in-licensed intellectual property in the mid-single digits. The royalty is subject to reduction for any third-party payments required to be made, with a minimum floor in the low single digits. We have the right to sublicense our rights under this agreement, and we will be required to pay a percentage of such license income in the low-double digits. We are required to make annual maintenance payments in the low four figures under this license, which payments are creditable against royalty payments on a year-by-year basis.

This license will terminate upon the expiration of all of the patents subject to the license. Additionally, UFRF may terminate this license upon certain breaches by us of the terms of the license and we may terminate the license at any time by submitting written notice to UFRF.

The longest-lived patent covered by this license is expected to expire in 2019.

- A joint license from UFRF and Johns Hopkins University, or JHU, signed in October 2003 relates to a particular HSV construct and various compositions thereof. We have an exclusive license in all fields of use.

Under the terms of this license, we made cash and stock-based up-front payments to UFRF and JHU and are required to make payments ranging from the mid-five figures to the low-six figures based upon development, regulatory and commercial milestones for any products covered by the in-licensed intellectual property. Assuming that we meet each of the specified development, regulatory and commercial milestones not more than once for each product, which we expect will be the case, the maximum aggregate milestone payments payable under this license with respect to any individual product that we commercialize will be $0.5 million. We will also be required to pay a royalty on net sales of products covered by the in-licensed intellectual property in the low-single digits. We have the right to sublicense our rights under this agreement, and we will be required to pay a percentage of such license income in the low-double digits. We are required to make annual maintenance payments in the low four figures under this license, which payments are creditable against royalty payments on a year-by-year basis.

This license will terminate upon the earlier to occur of the expiration of all of the patents subject to the license and the date on which royalty payments, once commenced, cease for more than three calendar quarters. Additionally, UFRF and JHU may terminate this license upon certain breaches by us of the terms of the license and we may terminate the license at any time by submitting written notice to UFRF.

The longest-lived patent covered by this license is expected to expire in 2022.

- Two licenses from UFRF, signed in September and November 2012, respectively, relate to the use of engineered AAV capsids. We have an exclusive license to the patents covered by the November 2012 license in the fields of ACHM, XLRS and XLRP and a semi-exclusive license in all other fields of orphan ophthalmology. We have a non-exclusive license in all fields of use with respect to the patents covered by the September 2012 license. Currently these patents are most useful for ACHM, XLRS and XLRP but could be important for treating a wide variety of diseases as the mutant capsids have been shown to be able to enter cells more effectively than standard AAV capsids.

Under the terms of these licenses, we made cash up-front payments to UFRF and are required to make payments ranging from the mid-five figures to the low-six figures based upon development, regulatory and commercial milestones for any products covered by the in-licensed intellectual property. Assuming that we meet each of the specified development, regulatory and commercial milestones not more than once for each product, which we expect will be the case, the maximum aggregate milestone payments payable under these licenses with respect to any individual product that we commercialize will be $0.6 million. We will also be required to pay a royalty on net sales of products covered by the in-licensed intellectual property in the low-single digits. We have the right to sublicense our rights under these agreements, and we will be required to pay a percentage of such license income in the mid-single digits. We are required to make annual maintenance payments in the mid four figures under these licenses, which payments are creditable against royalty payments on a year-by-year basis.

These licenses will continue until the expiration of all of the patents subject to the licenses, provided or, if later, a date specified in the license. Additionally, UFRF may terminate this license upon certain breaches by us of the terms of the licenses and we may terminate the licenses at any time by submitting written notice to UFRF.

The longest-lived patent covered by these licenses is expected to expire in 2029. There are also patent applications pending under these licenses.

University of Alabama at Birmingham

A license agreement from the UAB Research Foundation affiliated with The University of Alabama at Birmingham signed in 2006, relates to one U.S. patent with claims covering the use of HSV helpers to produce AAV vectors. The patent is expected to expire in 2025. Effective in July 2015, we modified the license from co-exclusive to exclusive.

Under the terms of this license, we made a cash up-front payment to the UAB Research Foundation, and we will be required to make payments ranging from the mid-five figures to the low-six figures based upon development and regulatory milestones for any products covered by the in-licensed intellectual property. Assuming that we meet each of these development and regulatory milestones not more than once for each product, which we expect will be the case, the maximum aggregate milestone payments payable under this license with respect to any individual product that we commercialize will be $0.5 million. We will also be required to pay a royalty on net sales of products covered by the in-licensed intellectual property in the low-single digits. We have the right to

sublicense our rights under this agreement, and we will be required to pay a percentage of such license income in the mid-single digits. We are required to make annual maintenance payments in the mid-four figures under this license, which payments are creditable against royalty payments on a year-by-year basis.

This license will terminate upon the expiration of all of the patents subject to the license. Additionally, the UAB Research Foundation may terminate this license upon certain breaches by us of the terms of the license and we may terminate the license at any time by submitting written notice to the UAB Research Foundation.

Collaboration with 4D Molecular Therapeutics

In April 2015, we signed an agreement with 4D Molecular Therapeutics (“4DMT”) to conduct research on optimized next generation capsids to target specific target cell populations within the human retina using 4DMT’s Directed Evolution AAV vector discovery platform. We have an option to enter into a licensing agreement if the confirmatory studies are successful.

Collaboration with Synpromics Limited

In December 2015, we entered into an agreement with Synpromics to utilize Synpromics' proprietary technology to develop and optimize synthetic promoters. In the event that results from the research are promising, we have options to license promoters that result from the collaboration efforts.

Over the past year we have progressed our collaborations with 4DMT and Synpromics to identify novel potent cell-specific capsids and promoters.

Competition

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products, and any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our proprietary technology estate 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, specialty pharmaceutical and biotechnology companies, as well as from academic institutions and governmental agencies and public and private research institutions that may develop potentially competitive products or technologies. To the extent that we develop product candidates for indications with larger patient populations, such as wet AMD, we expect to experience particularly intense competition from larger and better funded pharmaceutical companies. Any product candidate for wet AMD that we may develop will compete with established drugs such as Genentech’s Lucentis and Avastin, Regeneron’s Eylea, and new drug candidates being developed by others, including Genzyme, that are currently in clinical trials, as well as other treatment modalities such as photodynamic therapy.

Currently there are no approved products for any of our lead orphan ophthalmology indications of XLRS, ACHM and XLRP. We believe the key competitive factors that will affect the success of our product candidates, if approved, are likely to be their 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.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those 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. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position or a period of market exclusivity in the case of “orphan indications” before we are able to enter the market.

Government regulation

Biological products, including gene therapy products, are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or 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. Before clinical testing of biological products may begin, we must submit an IND which must go into effect, and each clinical trial protocol for a gene therapy product candidate is reviewed by the FDA and, in some instances, the NIH, through its

Recombinant DNA Advisory Committee, or RAC. FDA approval of a BLA also must be obtained before marketing of biological products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. CBER works closely with the NIH and its RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical and societal issues related to proposed and ongoing gene therapy protocols. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also 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, social and legal concerns about gene therapy, genetic testing and genetic research have led to the enactment of legislation such as the Genetic Information Nondiscrimination Act of 2008 and 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.

Recent developments in regulation of gene therapy

Although the FDA has not yet approved any human gene therapy product for sale, it has provided guidance for the development of gene therapy products. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies, or OCTGT, within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee, or CTGTAC, to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical guidelines, chemistry, manufacturing and control, or CMC, guidelines and other guidelines, all of which are intended to facilitate industry's development of gene therapy products. While no gene therapy products have received FDA approval to date, we believe that several gene therapy products will be submitted to the FDA for approval over the next several years.

In 2012, the EMA approved a gene therapy product called Glybera, which is the first gene therapy product approved by regulatory authorities anywhere in the Western world. Most recently, Strimvelis became the second gene therapy product approved by the EMA.

United States biological products development process

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

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLP, requirements 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 trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices, or GCP, requirements and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological

product candidate for its intended use;

- submission to the FDA of a Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product candidate is produced to assess compliance with GMP requirements, to assure that the facilities, methods and controls are adequate to preserve the biological product candidate's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval, or licensure, of the BLA prior to any commercial marketing or sale of the product candidate in the United States.

Before testing any biological product candidate, including a gene therapy product candidate, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP requirements.

When a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, along with the submission of an IND to the FDA, the protocol and related documentation is submitted to and the trial is registered with the NIH Office of Science Policy, or OSP, pursuant to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA, however many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The oversight bodies at the initial clinical site(s) (Institutional Review Board (IRB) and Institutional Biosafety Committee (IBC)) are responsible for recommending whether or not the clinical study requires public review by the RAC, a federal advisory committee, which discusses protocols that raise novel or particularly important scientific, safety or ethical considerations. This recommendation is included with the protocol and related documentation submitted to the OSP as part of the trial registration process. The OSP may agree or disagree with that recommendation. Should the oversight bodies recommend public RAC review and the OSP concur, the protocol will then be reviewed at one of the NIH RAC's quarterly meetings for which information must be submitted at least eight weeks in advance. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

The clinical trial 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 trial 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 trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, and the trial oversight bodies and the OSP decide that full public review of the protocol is warranted, initiation of the protocol will be delayed until after completion of the RAC review process. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trials.

Clinical trials 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 trial sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials 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 trial subject or his or her legal representative and must monitor the clinical trial until completed. Clinical trials also must be reviewed by an institutional biosafety committee, or 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.

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

Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some product candidates for severe or life-threatening diseases, especially when the product candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

Phase 2. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for product approval and labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. Depending on the type of product and mechanism of action, the FDA may recommend that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire, of trial subjects.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected suspected adverse reactions, any findings from other trials, 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 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 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial 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 trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product candidate 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 trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene transfer trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials. Over the last several years the FDA has issued helpful guidance on development of gene therapy products and shown a willingness to work closely with developers, especially with those working in orphan disease areas.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the biological product candidate as well as finalize a process for manufacturing the product candidate in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with the 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.

United States review and approval processes

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product candidate. The BLA must include results of product development, laboratory and animal studies, human trials, information on the manufacture and composition of the product candidate, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the

biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product candidate 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.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule for fiscal year 2017, which becomes effective October 1, 2016, the user fee for an application requiring clinical data, such as a BLA, is $2,038,100. PDUFA also imposes an annual product fee for biologics ($97,750) and an annual establishment fee ($512,200) on facilities used to manufacture prescription biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for product candidates designated as orphan drugs, unless the product candidate also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the 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 candidate is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product candidate is being manufactured in accordance with GMP regulations to assure and preserve the product candidate's identity, safety, strength, quality, potency and purity. 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, or REMS, is necessary to assure the safe use of the biological product candidate. A REMS may be imposed to ensure safe use of the drug, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. 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 candidate is manufactured. The FDA will not approve the product candidate unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product candidate within required specifications. Additionally, before approving a BLA, the FDA may inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure GMP 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 trials 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 trials. 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 candidate 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 candidate. 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 trials, sometimes referred to as Phase 4 clinical trials, 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 the PDUFA is to review 90% of standard BLAs in 10 months and 90% of priority BLAs in six months, whereupon a review decision is to be made. 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 within the last three months before the PDUFA goal date.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product candidate intended to treat a rare disease or condition, which is generally 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 candidate. Orphan product designation must be requested before submitting an NDA or BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product candidate that has orphan designation subsequently receives the first FDA approval 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 does not have 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 has similar, but not identical, benefits.

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 that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate 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 candidate at any time during the clinical development of the product candidate. Unique to a Fast Track product candidate, 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 candidate 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 priority review and accelerated approval. Any product candidate 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 disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product candidate designated for priority review in an effort to facilitate the review, and aims to review such applications within six months as opposed to ten months for standard review. Additionally, a product candidate 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 trials establishing that the product candidate 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 or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biological product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Lastly, under the provisions of the new Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or

life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval and receive the same benefits as drugs with Fast Track designation. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process.

Post-approval requirements

Maintaining 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 GMP requirements. 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 GMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products include reporting of GMP deviations that may affect the identity, potency, purity and overall safety of a distributed 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 may also be subject to official lot release. In this case, 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 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"), 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 GMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain GMP 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, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

United States 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 United States 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 or more of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

A biological product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued “Written Request” for such a study.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or Affordable Care Act, 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 trial or trials. 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 twelve years of exclusivity from the time of first licensure of the reference product. On April 10, 2013, President Obama released his proposed budget for fiscal year 2014 and proposed to cut this twelve-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity for brand biologics due to minor changes in product formulations, a practice often referred to as “evergreening.” 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.

Pharmaceutical Coverage, Pricing and Reimbursement

Sales of our products, when and if approved for marketing, will depend, in part, on the extent to which our products will be covered by third-party payors, such as federal, state, and foreign government health care programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor not to cover our product candidates could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Given the potential for long term durable therapeutic benefit from the single administration of a gene therapy product, the question of appropriate pricing and method of payment, including annuity payments and “pay for performance” schemes, is currently an active discussion and, depending on outcome, could affect the use of our products and our financial performance.

Other Healthcare Laws

Although we currently do not have any products on the market, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations, many of which may become more applicable to us if our product candidates are approved and we begin commercialization. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Employees

As of June 30, 2016, we had 53 full-time employees, 34 of whom have Ph.D., M.D. or other post-graduate degrees. Of these full-time employees, 39 are engaged in research and development activities and 14 are engaged in finance, legal, human resources, facilities and general management.

All of our personnel are co-employees of AGTC and a professional human resource service organization, TriNet HR Corporation, or TriNet. Under our agreement with TriNet, TriNet is a co-employer of our personnel, and is responsible for administering all payroll functions, including tax withholding, and providing health insurance and other benefits for these individuals. We reimburse TriNet for these costs and pay TriNet an administrative fee for its services. We are responsible for, and control, all aspects of the hiring, retention, compensation, management and supervision of our personnel. We consider the terms of our contract with TriNet to be reasonable and customary and believe this arrangement provides substantial benefit to us, in the form of lower costs for employee benefits and a reduced administrative burden on us.

We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

Corporate information

We were incorporated in Florida in January 1999 and reincorporated in Delaware in October 2003. On April 1, 2014, we completed our initial public offering of our common stock, which is traded on The NASDAQ Global Market under the symbol "AGTC." Our principal executive offices are located at 14193 NW 119th Terrace, Suite 10, Alachua, Florida 32615, and our telephone number is (386) 462-2204. Our corporate website address is www.agtc.com. Information contained on or accessible through our website is not a part of this annual report.

We use "AGTC" and the double helix logo as trademarks in the United States and other countries. As of June 30, 2016, these trademarks have been registered in the United States, European Union and Japan.

This annual report contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this annual report, including logos, artwork, and other visual displays, may appear without the or ™ symbols, but such references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any such companies.

Implications of being an emerging growth company

As a company with less than $1 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal controls over financial reporting.

We may take advantage of these exemptions for up to five years from the date of our initial public offering of common stock or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenue, we have more than $700 million in market value of our stock held by non-affiliates or we issue more than $1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available exemptions.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

33

Item 1A. Risk Factors

You should carefully consider the risks and uncertainties described below, together with the information included elsewhere in this Annual Report on Form 10-K and other documents we file with the SEC. The risks and uncertainties described below are those that we have identified as material, but are not the only risks and uncertainties facing us. Our business is also subject to general risks and uncertainties that affect many other companies, such as overall U.S. and non-U.S. economic and industry conditions including a global economic slowdown, geopolitical events, changes in laws or accounting rules, fluctuations in interest and exchange rates, terrorism, international conflicts, major health concerns, natural disasters or other disruptions of expected economic and business conditions. Additional risks and uncertainties not currently known to us or that we currently believe are immaterial also may impair our business operations and liquidity.

Risks related to our financial condition and capital requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a clinical-stage biotechnology company, and we have not yet generated revenues from product sales. We have incurred losses from operations in each year since our inception in 1999, and net losses of $1.4 million, $24.3 million, and $15.9 million for each of the fiscal years ended June 30, 2016, 2015 and 2014, respectively. As of our most recent fiscal year ended June 30, 2016, we had an accumulated deficit of $90.0 million. Our prior losses, combined with expected future losses, have had and may continue to have an adverse effect on our stockholders' equity and working capital.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and, to a lesser extent, through research grants from third parties or milestone payments from a collaborator. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations or additional grants. We anticipate that it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend upon the size of any markets in which our product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for our product candidates in those markets.

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

- continue our research and preclinical and clinical development of our product candidates;
- expand the scope of our current clinical trials for our product candidates;
- initiate additional preclinical studies, clinical trials or other studies for our product candidates;
- further develop our gene therapy platform, including the process for design, delivery and manufacturing of our vectors for our product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone or other payments under any in-license agreements;

- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;

- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Our ability to generate revenue from product sales is highly uncertain and we may never achieve or sustain profitability, which could depress the market price of our common stock, and could cause you to lose part or all of your investment.

All of our revenue generated to date has come from research grants from third parties or license fees or milestone payments from collaborations. Our ability to generate substantial revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners such as Biogen, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. We do not anticipate generating revenues from product sales for at least the next several years, if ever. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if any of our product candidates, if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenues from product sales depends heavily on our success in:

- completing research and preclinical and clinical development of our product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining adequate coverage and reimbursement from third-party payors for our product candidates;
- obtaining market acceptance of our product candidates and gene therapy as a viable treatment option;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- identifying and validating new gene therapy product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; 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, particularly to the extent that we seek to commercialize any product for an indication, such as wet AMD, that has a patient population significantly larger than those addressed by our current lead product candidates. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory agencies, domestic or foreign, to perform clinical trials 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 failure to become and remain profitable would depress the market price of our

common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

In order to obtain regulatory approval for and commercialize our product candidates, we will need to raise additional funding in the future, which may not be available on acceptable terms, or at all. Failure to obtain necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

Other than our product candidates for the treatment of XLRS and ACHM CNGB3, all of our lead programs in orphan ophthalmology and otology are currently in preclinical development. Developing gene therapy products is expensive, and we expect our research and development expenses to increase substantially as we advance our current product candidates in clinical trials and as we undertake preclinical studies of new product candidates.

Our operations have consumed substantial amounts of cash since inception. As of June 30, 2016, our cash and cash equivalents and investments amounted to $172.7 million. Our research and development expenses were $38.9 million, $16.5 million and $8.5 million for the fiscal years ended June 30, 2016, 2015 and 2014, respectively. We believe that our existing cash and cash equivalents at June 30, 2016 will be sufficient to enable us to advance planned preclinical studies and clinical trials for our lead product candidates for at least the next two years. In order to complete the process of obtaining regulatory approval for our lead product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our lead product candidates, if approved, we will require substantial additional funding. Also, our current operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches.

Any such fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, financing may not be available to us in the future in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, and we may be required to relinquish or license on unfavorable terms rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, financial condition, results of operations and prospects and cause the price of our common stock to decline.

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

Our cash balances and investment portfolio are subject to various risks, any of which could adversely impact our financial position.

As of June 30, 2016, we had cash and cash equivalents and investments in the aggregate amount of $172.7 million, which represents approximately 96% of our total assets. These investments are subject to general credit, liquidity,

market, political, sovereign and interest rate risks, which may be exacerbated by unusual events that affect global financial markets. A material part of our investment portfolio consists of money market accounts and certificates of deposits. If global credit and equity markets experience prolonged periods of decline, our investment portfolio may be adversely impacted and we could determine that our investments may experience an other-than-temporary decline in fair value, requiring impairment charges that could adversely affect our financial results. A failure of any of the financial institutions in which our deposits exceed FDIC limits could also have an adverse impact on our financial position.

Risks related to the discovery and development of our product candidates

All of our product candidates are in preclinical or clinical development. Clinical drug development is expensive, time consuming and uncertain, and we may ultimately not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities, which regulations differ from country to country. Our product candidates are in various stages of development and are subject to the risks of failure typical of drug development. The development and approval process is expensive and can take many years to complete, and its outcome is inherently uncertain. We have not submitted an application for or received marketing approval for any of our product candidates. We have limited experience in conducting and managing the later stage clinical trials necessary to obtain regulatory approvals, including approval by the FDA. To receive approval, we must, among other things, demonstrate with substantial evidence from clinical trials that the product candidate is both safe and effective for each indication for which approval is sought, and failure can occur in any stage of development. Satisfaction of the approval requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the pharmaceutical product. We cannot predict if or when we might receive regulatory approvals for any of our product candidates currently under development.

The FDA and foreign regulatory authorities also have substantial discretion in the drug approval process. The number and types of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions, and there may be varying interpretations of data obtained from preclinical studies or clinical trials, either of which may cause delays or limitations in the approval or the decision not to approve an application. Regulatory agencies can delay, limit or deny approval of a product candidate for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the patients recruited for a particular clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the results may not confirm the positive results from earlier preclinical studies or clinical trials;
- we may be unable to demonstrate that a product candidate’s clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of FDA or comparable foreign regulatory authorities to support the submission of a biologics license application, or BLA, or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- regulatory agencies might not approve or might require changes to our manufacturing processes or facilities; or
- regulatory agencies may change their approval policies or adopt new regulations in a manner rendering our clinical data insufficient for approval.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position

and adversely impact our stock price. Furthermore, any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. These limitations may limit the size of the market for the product.

We are not permitted to market our product candidates in the United States or in other countries until we receive approval of a BLA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Obtaining approval of a BLA can be a lengthy, expensive and uncertain process. If we fail to obtain FDA approval to market our product candidates, we will be unable to sell our product candidates in the United States, which will significantly impair our ability to generate any revenues. In

addition, failure to comply with FDA and non-U.S. regulatory requirements may, either before or after product approval, if any, subject our company to administrative or judicially imposed sanctions, including:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production;
- imposition of restrictions on operations, including costly new manufacturing requirements; and
- refusal to approve pending BLAs or supplements to approved BLAs.

Even if we do receive regulatory approval to market a product candidate, any such approval may be subject to limitations on the indicated uses for which we may market the product. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or our collaborators to commence product sales. Any delay in obtaining, or an inability to obtain, applicable regulatory approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability.

Our gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only two such products have been approved in Europe.

We have concentrated our product research and development efforts on our gene therapy platform, and our future success depends on the successful development of this approach. There can be no assurance that any development problems we experience in the future related to our gene therapy platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience unanticipated problems or delays in expanding our manufacturing capacity or transferring our manufacturing process to commercial partners, which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA, the EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on clinical hold

even if the RAC has provided a favorable review of the drug. Also, before a clinical trial can begin at an NIH-funded institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee, or IBC, have to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these 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 our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected for orphan ophthalmology product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

Success in animal studies or early clinical trials may not be indicative of results obtained in later trials.

Trial designs and results from animal studies or previous clinical trials are not necessarily predictive of our future clinical trial designs or results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may also fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in animal studies or having successfully advanced through initial clinical trials. There can be no assurance that the success we achieved in the animal studies for our lead product candidates will result in success in our clinical trials of those product candidates.

There is a high failure rate for drugs and biological products proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which 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.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates as well as completion of required follow-up periods. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. For example, trials using early versions of lentiviral vectors, which integrate with, and thereby alter, the host cell’s DNA, have led to several well-publicized adverse events, including reported cases of leukemia. If there are delays in accumulating the required number of clinical events in trials for our product candidates where clinical events are a primary endpoint, there may be delays in completing the trial. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with the required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. For example, enrolling eligible patients in novel orphan drug trials can be challenging and we have encountered slower-than-expected enrollment in our phase 1/2 clinical trial for our XLRS product candidate as a result of patients not meeting one or more study eligibility criteria. Our clinical trials have and may continue to be delayed by the necessity to re-test the study agent and delays related to a protocol amendment that required approval by institutional review boards at the clinical sites. Challenges such as these in enrolling a sufficient number of patients to conduct our clinical trials as planned, may cause us to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business. We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates

In particular, each of the conditions for which we plan to evaluate our product candidates are rare genetic disorders with limited patient pools from which to draw for clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants.

Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;

- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- our ability to monitor patients adequately during and after treatment.

We plan to seek initial marketing approval for our product candidates in the United States and the European Economic Area, or EEA. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, the EMA or other foreign regulatory authorities. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;
- different standards for conducting clinical trials;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

We may encounter substantial delays in our 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 such product candidates in humans. Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing.

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

- delays in raising, or inability to raise, sufficient capital to fund the planned clinical trials;
- inability to generate sufficient preclinical, toxicology, or other data to support the initiation of human clinical trials;
- delays in reaching a consensus with regulatory agencies on trial design;
- identifying, recruiting and training suitable clinical investigators;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in obtaining required IRB approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays due to changing standard of care for the diseases we are targeting;
- adding new clinical trial sites;
- imposition of a clinical hold by regulatory agencies, after review of an IND application or equivalent application or an inspection of our clinical trial operations or trial sites;
- failure by our CROs, other third parties or us to adhere to clinical trial requirements;
- loss of product due to shipping delays or delays in customs in connection with delivery to foreign countries for use in clinical trials;
- failure to perform in accordance with the FDA's good clinical practices, or GCP requirements or applicable regulatory guidelines in other countries;

- delays in the manufacture, testing, release, import or export for use of sufficient quantities of our product candidates for use in clinical trials by our vendors, such as the vendor testing errors recently experienced in our ongoing clinical trials;
- failure by us or our vendors to manufacture our product candidate in accordance with the FDA's good manufacturing practice, or GMP, requirements or applicable regulatory guidelines in other countries;
- delays by us or our contract vendors in the testing, validation and delivery of our product candidates to the clinical trial sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
    - clinical trial sites deviating from trial protocol or clinical trial sites or patients dropping out of a trial;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- the costs of clinical trials of our product candidates may be greater than we anticipate; or
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs.

Further, a clinical trial may be suspended or terminated by us, our collaborators, the IRBs, in the institutions in which such trials are being conducted, the Data Safety Monitoring Board, or DSMB, for such trial, or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In appropriate circumstances, we may also elect to temporarily suspend an ongoing clinical trial to further study unexpected results, even if those results would not require us to formally suspend the trial under the applicable regulatory requirements or clinical protocols. Such temporary suspension could include further testing of trial materials and the need to review subject responses to ensure safety. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Any inability to successfully complete 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 or our third-party collaborators make manufacturing or formulation changes to product candidates, we or they may need to conduct additional trial to bridge the modified product candidates to earlier versions. Clinical trial delays could also 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 and results of operations.

If the results of our clinical trials are inconclusive or if there are safety concerns or 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 with the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;

- have regulatory authorities withdraw 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.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and impair our ability to commercialize our product candidates.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any potential marketing approval.

As with many pharmaceutical and biological products, treatment with our product candidates may produce undesirable side effects or adverse reactions or events. These adverse events may occur despite our belief that our AAV vectors have an improved safety profile over prior such treatments.

Known adverse side effects that could occur with treatment with AAV vectors include an immunologic reaction to the capsid protein or gene at early time points after administration. In previous clinical trials involving AAV viral vectors for gene therapy, some subjects experienced serious adverse events, including the development of T-cell response due to immune response against the vector capsid proteins. If our vectors demonstrate a similar effect, or other adverse events, we may be required to halt or delay further clinical development of our product candidates. In addition, theoretical adverse side effects of AAV vectors include replication and spread of the virus to other parts of the body and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, also known as cancer, which could potentially enhance the risk of malignant transformation. Potential procedure-related events, including inflammation or injury to the eye, are similar to those associated with standard ophthalmic intervention procedures. There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. If any such adverse events occur, our clinical trials could be suspended or terminated and the FDA, the EMA or other foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial. 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 will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

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

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

We may be unable to obtain orphan product designation or exclusivity for some of our product candidates. If our competitors are able to obtain orphan product exclusivity for their products that are the same 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 Europe, 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 generally defined as having a patient population of fewer than

200,000 individuals diagnosed annually 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, the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union Community. Additionally, 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 biological product. Our product candidates for the treatment of LCA2, XLRS, ACHM (in the form caused by mutations in the CNGB3 and CNGA3 genes) and AAT deficiency have been granted orphan drug designations by the FDA, and our product candidates for the treatment of XLRS, ACHM (in the form caused by mutations in the CNGB3 and CNGA3 genes), XLRP (in the form caused by mutations in the RPGR gene) and AAT deficiency have been granted orphan medicinal product designation by the European Commission. We may request orphan drug designation for our other product candidates in the future but there can be no assurances that the FDA will grant any of our product candidates such designation. Additionally, the designation by the FDA of any of our product candidates as an orphan drug does not guarantee that the FDA will accelerate regulatory review of or ultimately approve that product candidate.

Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and 10 years in Europe. The European exclusivity period 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 lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

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 can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

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

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested, may not approve the price we intend to charge for our product candidate, may impose significant limitations in the form of narrow indications, warnings, precautions or contra-indications with respect to conditions of use or may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory agencies 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.

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

Even if we obtain regulatory approval in a jurisdiction for our product candidates, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

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

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain product or otherwise require the withdrawal of product from the market;
- refuse to permit the import or export of products; or
- refuse to allow us to enter into supply contracts, including government contracts.

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

In addition, the FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

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 adversely affect 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 must also 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 greater 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 the EMA for approval in the EEA, but obtaining such approval is a lengthy and expensive process and the EMA has its own procedures for

approval of product candidates. Even if a product candidate is approved, the FDA or the EMA, 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 clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the EEA also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval of a product candidate in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, 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 will be adversely affected.

Risks related to our reliance on third parties

We expect to rely on third parties to conduct aspects of our product manufacturing and protocol development, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, and monitoring and management of our ongoing and planned preclinical and clinical programs. We have expanded our internal capabilities to include a full scale pilot facility to facilitate continued improvement in our manufacturing process. We are also in the design phase for a cGMP facility at our Florida headquarters to support later stage clinical development. We currently rely, and expect to continue to rely, to a significant degree, on third parties for the production of our clinical trial materials. In such cases, we expect to control only certain aspects of their activities.

Under certain circumstances, these third parties may be entitled to terminate their engagements with us or we may seek to terminate our engagement with them. Because of the complexities inherent in gene therapy manufacturing, we expect that any engagement by us of a new third party manufacturer for our product candidates would take a substantial amount of time to establish. Accordingly, if we need to enter into alternative arrangements, it could delay our product development activities. We are currently negotiating with and conducting pilot work at three alternative third-party manufacturers to expand our capacity and mitigate risk. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study and trial protocols. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study and trial plans and protocols, or if there are disagreements between us and these third parties, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND submissions and approval of our product candidates. In some such cases we may need to locate an appropriate replacement third-party relationship, which may not be readily available or on acceptable terms, which would cause additional delay with respect to the approval of our product candidates and would thereby have a material adverse effect on our business, financial condition, results of operations and prospects.

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

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- delays in the production of our product candidates associated with transitioning to a new third-party manufacturer;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

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

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

All parties involved in the preparation of therapeutics for clinical trial or commercial sale, including our existing contract manufacturer for our product candidates, SAFC, are subject to extensive regulation. Components of a finished therapeutic product

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

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party manufacturers. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or our third-party manufacturers 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 third parties with whom we contract could materially harm our business.

As described above in "Business," we have encountered delays in clinical trial material availability as a result of difficulties in proper testing. If we or any of our third-party manufacturers or testing contractors fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate, or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition and results of operations to be materially harmed.

Additionally, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply of our products. While we are currently working to establish a relationship with alternative third-party manufacturers, we do not currently have a backup manufacturer of our product candidate supply for clinical trials or commercial sale. Because of the complexities inherent in our gene therapy manufacturing, we expect that there will be a significant period of time following our engagement of an alternative third-party manufacturer before that manufacturer will be in a position to provide an adequate supply of our product candidates for our clinical trials. In addition, any alternative manufacturer will also need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

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

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

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

We and our CROs are required to comply with the FDA's and other regulatory authorities' GCP, GMP and good laboratory practice, or GLP, requirements for conducting, recording and reporting the results of our preclinical studies and clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these requirements through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCP requirements, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCP requirements, which may render the data generated in those trials unreliable. In addition, our future clinical trials will require a sufficient number of

test subjects to evaluate the safety and effectiveness of our product candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

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

Switching or adding CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, prospects, financial condition and results of operations.

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

Collaborations with third parties, such as our collaboration with Biogen, may be important to our business. If these collaborations are not successful, our business could be adversely affected.

We have a collaboration with Biogen to develop, seek regulatory approval for and commercialize gene therapy products to treat XLRS and XLRP. The collaboration agreement also provides for discovery programs targeting three indications whereby we will conduct discovery, research and development activities for those additional drug candidates through the stage of clinical candidate designation, after which, Biogen may exercise an option to continue to develop, seek regulatory approval for and commercialize the designated clinical candidate. In addition, under our manufacturing agreement with Biogen, we granted Biogen an exclusive license to use our proprietary technology platform outside of the collaboration to make AAV vectors for up to three available genes and three additional genes that we may approve in our discretion. An unsuccessful outcome in pending and future clinical trials for which Biogen is responsible could be harmful to the public perception and prospects of our gene therapy platform.

Our license relationships with Biogen and any future collaboration we enter into in the future, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- exclusivity rights we negotiate with our collaborators may be unenforceable in certain jurisdictions;
- 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 collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators may decide not to continue the development of collaboration products and could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

- take-over or step-in rights granted to a collaborator with respect to one or more of our product candidates, may cause us to have limited control over future development activities and/or realize diminished economic or other benefits upon the ultimate commercialization of that product candidate;
- a collaborator with marketing, distribution and commercialization 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;
- if we fail to obtain orphan product designation for a partnered product, we may realize diminished economic benefit upon the ultimate commercialization of that product candidate;
- restrictions and commitments contained in collaborations may have the effect of preventing us from independently undertaking development and other efforts that may appear to be attractive to us;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, might cause delays or termination of the research, development or commercialization of such product candidates, might lead to additional responsibilities for us with respect to such product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- 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;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborations may be terminated at the convenience of the collaborator or for a material breach by either party, and, if a collaboration is terminated, we could be required to make payments to the collaborator or have our potential payments under the collaboration reduced; and
- in the event of the termination of a collaboration, we could be required to raise additional capital to pursue further development or commercialization of the product candidates returned to us by our former collaborator.

If our collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our gene therapy platform and product candidates could be delayed and we may need additional resources to develop product candidates and gene therapy platform. As a result of these or other factors, we may not receive the benefits that we expect from our collaborations.

In the event Biogen terminates the collaboration for a material breach by us, we will be restricted from competing with Biogen for two years in the terminated programs with Biogen having the right, in lieu of termination, to elect to maintain the license from us and reduce the royalties and milestones in a manner specified in the agreement.

Additionally, subject to its contractual obligations to us, if one of our collaborators is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected. Under a previous collaboration agreement, Genzyme has options, which expire in 2017, to license a previous version of our manufacturing technology as it existed at the time of the license for specified genes implicated in lysosomal storage diseases.

We may in the future determine to collaborate with other pharmaceutical and biotechnology companies for development and potential commercialization of product candidates other than those covered by our collaboration with Biogen. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and the

negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement with any such new party will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Moreover, we may not be successful in our efforts to establish 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 and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. If we license product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and

company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction.

If we are unable to reach agreements with suitable 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 or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake 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 or bring them to market or continue to develop our gene therapy platform and our business may be materially and adversely affected.

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 to manufacture our viral vectors and our product candidates, and because we collaborate with various organizations and academic institutions on the advancement of our gene therapy platform, 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, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees 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, such as trade secrets.

Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor’s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks related to commercialization of our product candidates

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

We currently have no sales and marketing organization and have no experience selling and marketing our product candidates. 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 sales force or the establishment of a contract sales force to market any products we may develop will be expensive and time-consuming, particularly to the extent that we seek to commercialize any product for an indication, such as wet AMD, that has a patient population significantly larger than those addressed by our current lead product candidates, 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 with other entities to utilize their mature marketing and distribution capabilities, but we may be unable to enter into marketing agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We will be competing with many companies that currently have extensive and well-funded 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.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are more advanced or effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products, and any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our proprietary technology estate 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, specialty pharmaceutical and biotechnology companies, as well as from academic institutions and governmental agencies and public and private research institutions that may develop potentially competitive products or technologies.

Currently there are no approved products for any of our lead orphan ophthalmology indications of XLRS, ACHM and XLRP. We believe the key competitive factors that will affect the success of our product candidates, if approved, are likely to be their 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.

We believe there are a number of companies that are working on AAV-based gene therapy technology and that there are companies developing gene therapies in the field of orphan ophthalmology, on which we are currently focused, which have programs that are at the clinical and pre-clinical stages. Other companies could also potentially seek to enter this field.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. To the extent that we develop product candidates for indications with larger patient populations, such as wet AMD, we expect to experience particularly intense competition from larger and better funded pharmaceutical companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

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 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 governmental 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 costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon a number of 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 approval for a product from governmental and private payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. 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 is available only to 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 high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental 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 other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Currently, no gene therapy products have been approved for coverage and reimbursement by the Centers for Medicare & Medicaid Services, or CMS, the agency responsible for administering the Medicare program, and it is difficult to predict what CMS 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 new products. Moreover, reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. 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 United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental 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. 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. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with no gene therapy product approved to date in the United States and only two gene therapy products approved to date in Europe. 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 specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, trials using early versions of lentiviral vectors, which integrate with, and thereby alter, the host cell’s DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize lentiviral vectors, our product candidates use a viral

delivery system. Adverse events in our clinical trials or the clinical trials of other gene therapy companies, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or PPACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses 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, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded

prescription drugs, and subjects additional drugs to lower pricing under the 340B drug pricing program by adding new entities to the program.

In addition, other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect on April 1, 2013. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Ethical, social and legal concerns about gene therapy and genetic research could result in additional regulations restricting or prohibiting the products and processes we may use. Even with the requisite approvals from the FDA in the United States and other government bodies internationally, the commercial success of our product candidates will depend in part on the medical community's, patients', and third-party payors' acceptance of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party 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, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the clinical indications for which the product candidate is approved;
- the safety of product candidates seen in a broader patient group, including its use outside the approved indications;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the cost of treatment relative to alternative treatments;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of the product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors. If any of our product candidates is approved but fails to achieve market acceptance among physicians, patients, or health care payors, we will not be able to generate significant revenues from such product, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

52

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any of our product candidates are approved for commercialization, we may enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- 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;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- 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, typhoons, floods and fires.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

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

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates based on our gene therapy platform. Although certain of our product candidates are currently in clinical or preclinical development, we may fail to identify other potential product candidates for clinical development for a number of reasons. For example, our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate, which would have a material adverse effect on 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.

Risks related to our business operations

We incur significant increased costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently

implemented by the Securities and Exchange Commission, or SEC, and The NASDAQ Global Market impose various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas. Recent legislation permits us, as a smaller "emerging growth company," to implement many of these requirements over a longer period and up to five years from the end of the fiscal year in which our initial public offering closed,

which was April 1, 2014. We are taking advantage of the flexibility accorded to us by this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We may not be successful in complying with these obligations, and compliance with these obligations could be time-consuming and expensive. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services.

We have identified material weaknesses in our internal control over financial reporting, and if we are unable to maintain effective internal control over financial reporting, investors could lose confidence in our financial statements and our company which could have a material adverse effect on our business and our stock price.

Our management previously determined that as of June 30, 2015 and 2014, we had material weaknesses in our internal control over financial reporting, which related to the design and operation of our closing and financial reporting processes and our accounting for debt, equity and convertible instruments. Management has determined that as of June 30, 2016, the material weakness in our internal control over financial reporting related to the design and operation of our closing and financial reporting processes still existed. These material weaknesses in our internal control over financial reporting are primarily due to the fact that we did not have the appropriate resources with the appropriate level of experience and technical expertise to oversee our closing and financial reporting processes and to address the accounting and financial reporting requirements related to our issuances of convertible notes, preferred stock warrants, stock options, preferred stock and preferred stock purchase rights.

If we fail to fully remediate material weaknesses or fail to maintain effective internal controls in the future, it could result in a material misstatement of our financial statements, which could cause investors to lose confidence in our financial statements and our company or cause our stock price to decline. Our independent registered public accounting firm has not assessed the effectiveness of our internal control over financial reporting and, under the JOBS Act, will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an emerging growth company, which may increase the risk that weaknesses or deficiencies in our internal control over financial reporting go undetected.

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 activities, and, in the longer term, build a sales force and commercial 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 possible 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 products 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.

We may enter into or seek to enter into business partnerships, combinations and/or acquisitions which may be difficult to integrate, disrupt our business, divert management attention or dilute stockholder value.

A key element of our strategy is to enter into business partnerships, combinations and/or acquisitions. We have limited experience in making acquisitions, which are typically accompanied by a number of risks, including:

- the difficulty of integrating the operations and personnel of the acquired companies;
- the potential disruption of our ongoing business and distraction of management;
- potential unknown liabilities and expenses;
- the failure to achieve the expected benefits of the combination or acquisition;

- the maintenance of acceptable standards, controls, procedures and policies; and
- the impairment of relationships with employees as a result of any integration of new management and other personnel.

If we are not successful in completing acquisitions that we may pursue in the future, we would be required to reevaluate our business strategy and we may have incurred substantial expenses and devoted significant management time and resources in seeking to complete the acquisitions. In addition, we could use substantial portions of our available cash as all or a portion of the purchase price, or we could issue additional securities as consideration for these acquisitions, which could cause our stockholders to suffer significant dilution.

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 our executive officers, the loss of whose services may adversely impact the achievement of our objectives. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives and scientific personnel in our industry, which is likely to continue. As a result, competition for skilled personnel 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 for individuals with similar skill sets. In addition, failure to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

In order to induce valuable employees to remain at AGTC, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, prospects, financial condition or results of operations. We do not maintain “key man” insurance policies on the lives of these individuals or any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They may also provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we can offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can discover, develop and commercialize product candidates will be limited.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities.

We are exposed to the risk that our employees, CROs, principal investigators, consultants and commercial partners may engage in fraudulent conduct or other illegal activity or may fail to disclosure unauthorized activities to us. Misconduct by these parties could include intentional, reckless and/or negligent failures to comply with:

- the laws and regulations of the FDA and non-U.S. regulators, including those laws requiring the reporting of true, complete and accurate information to such regulatory bodies;
- manufacturing standards we have established;
- healthcare fraud and abuse laws and regulations in the United States and similar foreign laws; or
- laws requiring the accurate reporting of financial information or data or the disclosure of 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 may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to

all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental 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, including the imposition of significant fines or other sanctions.

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.

Our operations may be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws. If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, many of these laws will become more directly applicable to our operations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, the federal civil and criminal False Claims Acts and Physician Payments Sunshine Act and regulations. These laws may 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 may affect our ability to operate 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;
- 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 payers that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or 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, or 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 requires 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;
- the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, and its implementing regulations, which may impact, among other things, reimbursement rates by federal health care programs and commercial insurers;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts

on our marketed drugs, when and if approved; participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, when and if approved, increased infrastructure costs and potentially limit our ability to offer certain marketplace discounts; and

- state 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 industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict certain 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 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.

In addition, any sale of our products or product candidates, if commercialized outside of the United States, may also subject us to foreign laws governing prescription drug marketing and fraud and abuse, including laws similar to the U.S. healthcare laws mentioned above. 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. In addition, recent health care reform legislation has strengthened these laws. For example, the PPACA, among other things, amends the intent requirements of the federal Anti-Kickback Statute and the criminal statute governing healthcare fraud. A person or entity can now be found guilty of violating the Anti-Kickback Statute and the federal criminal healthcare fraud statute without actual knowledge of the statute or specific intent to violate it. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental 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, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If the use of our product candidates harms patients, we could be subject to costly and damaging product liability claims.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. For example, we may be sued if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs due to related litigation;
- distraction of management’s attention from our primary business;
- substantial monetary awards to trial participants, patients or other claimants;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. While we believe our product liability insurance coverage is sufficient in light of our current clinical programs. The amount of the product liability coverage that we carry varies from time to time, depending on a number of factors, the most significant of

which are the nature and scope of the clinical trials in which we are engaged and the number of patients being treated with our product candidates in these trials. This amount may increase or decrease in the future. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability and any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the commercial sale of our products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which

we have no coverage. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, manufacture and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. Although we believe that our procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We rely on our relationship with a professional employer organization for our human relations function and as a co-employer of our personnel, and if that party failed to perform its responsibilities under that relationship, our relations with our employees could be damaged and we could incur liabilities that could have a material adverse effect on our business.

All of our personnel, including our executive officers, are co-employees of AGTC and a professional employer organization, TriNet HR Corporation, or TriNet. Under the terms of our arrangement, TriNet is the formal employer of all of our personnel, and is responsible for administering all payroll, including tax withholding, and providing health insurance and other benefits for these individuals. We reimburse TriNet for these costs, and pay TriNet an administrative fee for its services. If TriNet fails to comply with applicable laws, or its obligations under this arrangement, our relationship with our employees could be damaged. We could, under certain circumstances, be held liable for a failure by TriNet to appropriately pay, or withhold and remit required taxes from payments to, our employees. In such a case, our potential liability could be significant and could have a material adverse effect on our business.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Substantially all of our operations are conducted from our headquarters located near Gainesville, Florida. Hurricanes or other natural disasters could severely disrupt our operations, damage our research facilities or destroy stored research materials that could be difficult to replace, and otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. In addition, despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors and consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our

operations, it could result in a material disruption of our development programs and our business operations. 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 our operations or the operations of our third-party contract manufacturer, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. For example, the loss of clinical trial data from our clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If our security measures, disaster recovery and business continuity plans are not adequate in the event of such a breach, serious disaster or similar event, we could incur substantial expenses and the further development and commercialization of our product candidates could be delayed, which could have a material adverse effect on our business.

Interruptions in the supply of product or inventory loss may adversely affect our operating results and financial condition.

Our product candidates are manufactured using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes, as well as strict company and government standards for the manufacture and storage of our products, subjects us to production risks. While product batches released for use in clinical trials or for commercialization undergo sample testing, some defects may only be identified following product release. In

addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. Most of our product candidates must be stored and transported at temperatures within a certain range. If these environmental conditions deviate, our product candidates' remaining shelf-lives could be impaired or their efficacy and safety could become adversely affected, making them no longer suitable for use. The occurrence or suspected occurrence of production and distribution difficulties can lead to lost inventories, and in some cases product recalls, with consequential reputational damage and the risk of product liability. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and delays of new product launches. Any interruption in the supply of finished products or the loss thereof could hinder our ability to timely distribute our products and satisfy customer demand. Any unforeseen failure in the storage of the product or loss in supply could delay our clinical trials and, if our product candidates are approved, result in a loss of our market share and negatively affect our revenues and operations.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

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 resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or 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.

Our ability to use our net operating loss carryforwards may be subject to limitation.

Under Section 382 of the Internal Revenue Code of 1986, as amended, substantial changes in our ownership may limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such annual limitation may significantly reduce the utilization of our net operating loss carryforwards before they expire. We believe it is likely that transactions that have occurred in the past and other transactions that may occur in the future, could trigger an ownership change pursuant to Section 382, which could limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income, if any.

Cyber attacks or other breaches of network or other information technology security could have an adverse effect on our business.

Cyber attacks or other breaches of network or information technology security may cause equipment failures or disruptions to our operations. While, to date, we have not been subject to cyber attacks or other cyber incidents which, individually or in the aggregate, have been material to our operations or financial condition, the preventative actions we take to prevent or detect the risk of cyber incidents and protect our information technology and networks may be insufficient to prevent or detect a major cyber attack in the future. If we fail to prevent the theft of valuable information such as financial data, sensitive information about the us, our patients or our intellectual property, or if we fail to protect the privacy of patient and employee confidential data against breaches of network or information technology security, it would result in damage to our reputation, which could adversely impact the confidence of our partners, investors and employees. Any of these occurrences could result in a material adverse effect on our results of

operations and financial condition.

Risks related to our intellectual property

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

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 technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable

aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. 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 issued patents that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Third parties may initiate legal proceedings alleging claims of intellectual property infringement, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement

lawsuits, interferences, oppositions and inter partes reexamination proceedings before the United States Patent and Trademark Office and corresponding foreign patent offices. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed

during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, methods for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available 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 access to the same technologies licensed to us.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to gene therapy product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have rights to the intellectual property to develop our gene therapy product candidates. Because a key element of our business strategy is to pursue in-licensing and intellectual property acquisitions for additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify on terms that we find acceptable, or at all. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with United States and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame 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.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

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.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. We are a party to intellectual property license agreements with the University of Florida Research Foundation, an affiliate of the University of Florida, Johns Hopkins University and the UAB Research Foundation, an affiliate of The University of Alabama at Birmingham, each of which is important to our business, 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, milestone payment, royalty and other obligations on us. If we 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.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. It is possible that we may fail to obtain any of these 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 develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates,

which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our 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 cases, patent prosecution of our licensed technology is controlled solely by the licensor. 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. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. 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 intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the 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 become involved in lawsuits to protect or enforce our patents or other intellectual property or the patents or other intellectual property of our licensors, which could be expensive, time-consuming and ultimately unsuccessful.

Competitors may infringe our patents or other intellectual property or the patents or other intellectual property of our licensors. In response, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us, alleging that we infringe their patents. Additionally, if the party against whom we bring a claim of infringement has a relationship with one or more of our collaborators, licensors or other strategic counterparties, our relationship with that counterparty may be harmed. Similarly, because our intellectual property is potentially useful for the treatment of serious diseases, any third party infringers may be viewed sympathetically by the public and our assertion of an infringement claim against them may hurt our reputation. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those

rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Issued patents covering our product candidates or methods of manufacturing could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, or methods of manufacturing our product candidates, the defendant could counterclaim that the patent covering

our product candidate or method is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the United States Patent and Trademark Office, or made a misleading statement, during prosecution. Third parties may also 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, and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation of or amendment to our patents in such a way that they no longer cover our product candidates or manufacturing methods. 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 we and the patent examiner 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 or methods of manufacturing our products. Such a loss of patent protection could have a material adverse impact on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ individuals who 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 independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. 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, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. While it is our policy to require our employees and contractors who may be involved in the 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 develops intellectual property that we regard as our own. We could be subject to ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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 have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the United States Patent and Trademark Office and various governmental patent agencies outside of the United States

in several stages over the lifetime of the patents and/or applications. We rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The United States Patent and Trademark Office and various non-U.S. governmental patent agencies require compliance with a number of 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 in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which 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 have a material adverse effect on our business.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and therefore obtaining and enforcing biotechnology patents is costly, time-consuming and inherently uncertain.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent and Trademark Office recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts, and the United States Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We have not yet sought FDA approval of names for any of our product candidates and failure to secure such approvals could adversely affect our business.

Any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our 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.

Risks related to ownership of our common stock

An active trading market for our common stock may not be sustained.

Although we have listed our common stock on The NASDAQ Global Market, an active trading market for our common stock may not be sustained. In the absence of an active trading market for our common stock, you may not be able to resell shares of our common stock at or above the price you paid, or at all.

The market price for our common stock may be volatile, which could contribute to the loss of your investment.

Fluctuations in the price of our common stock could contribute to the loss of all or part of your investment. If an active market for our common stock develops and continues, the trading price of our common stock is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of the factors listed below could have a material adverse effect on your investment in our common stock. In such circumstances the trading price of our common stock may not recover and may experience a further decline.

Factors affecting the trading price of our common stock may include:

- our failure to develop and commercialize our product candidates;
- actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;
- changes in the market's expectations about our operating results;
- adverse results or delays in preclinical studies or clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval for any of our product candidates;
- success of competitive products;
- adverse developments concerning our collaborations and our manufacturers;
- inability to obtain adequate product supply for any product candidate for clinical trials or commercial sale or inability to do so at acceptable prices;
- the termination of a collaboration or the inability to establish additional collaborations;
- unanticipated serious safety concerns related to the use of any of our product candidates;
- our ability to effectively manage our growth;
- the size and growth, if any, of the orphan ophthalmology and other targeted markets;
- our operating results failing to meet the expectation of securities analysts or investors in a particular period or failure of securities analysts to publish reports about us or our business;
- changes in financial estimates and recommendations by securities analysts concerning our company, the gene therapy market, or the biotechnology and pharmaceutical industries in general;
- operating and stock price performance of other companies that investors deem comparable to us;
- overall performance of the equity markets;

- announcements by us or our competitors of acquisitions, new product candidates or programs, significant contracts, commercial relationships or capital commitments;

- our ability to successfully market our product candidates;
- changes in laws and regulations affecting our business, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our product candidates and gene therapy platform;
- commencement of, or involvement in, litigation involving our company, our general industry, or both;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of shares of our common stock available for public sale;
- additions or departures of key scientific or management personnel;
- any major change in our board or management;
- changes in accounting practices;
- ineffectiveness of our internal control over financial reporting;
- sales of substantial amounts of common stock by our directors, executive officers or significant stockholders or the perception that such sales could occur; and
- general economic and political conditions such as recessions, interest rates, fuel prices, international currency fluctuations and acts of war or terrorism.

Broad market and industry factors may materially harm the market price of our common stock irrespective of our operating performance. The stock market in general, and The NASDAQ Global Market and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of ours, may not be predictable. A loss of investor confidence in the market for technology or software stocks or the stocks of other companies which investors perceive to be similar to us, the opportunities in the digital simulation market or the stock market in general, could depress our stock price regardless of our business, prospects, financial conditions or results of operations.

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

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us, our business, our markets and our competitors. We do not control these analysts. As a newly public company, we have only limited coverage by securities analysts. If securities analysts do not continue to cover our common stock, the lack of research coverage may adversely affect the market price of our common stock. Furthermore, if one or more of the analysts who do cover us downgrade our stock or if those analysts issue other unfavorable commentary about us or our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fails to regularly publish reports on us, we could lose visibility in the market and interest in our stock could decrease, which in turn could cause our stock price or trading volume to decline and may also impair our ability to expand our business with existing customers and attract new customers.

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

We are an “emerging growth company,” as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years from the end of the fiscal year in which our initial public offering closed, which was April 1, 2014. However, circumstances could cause us to lose that

status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any December 31 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following June 30 or, if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a

“smaller reporting company” which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities, potential acquisitions, in-licenses, or collaborations and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock.

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

We have never declared or paid any cash dividends on our common stock. We currently intend to retain any future earnings to fund our future growth and do not expect to declare or pay any dividend on shares of our common stock in the foreseeable future. As a result, you may only receive a return on your investment in our common stock if the market price of our common stock appreciates and you sell your shares at a price above your cost.

We could be subject to securities class action litigation.

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

Anti-takeover provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions in Delaware law, might discourage, delay or prevent a change of control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Our certificate of incorporation, bylaws and Delaware law contain provisions that could have the effect of rendering more difficult or discouraging an acquisition deemed undesirable by our board of directors, even if doing so would

benefit our stockholders or remove our current management. Our corporate governance documents include provisions:

- providing for three classes of directors with the term of office of one class expiring each year, commonly referred to as a staggered board;
- authorizing blank check preferred stock, which could be issued with voting, liquidation, dividend and other rights superior to our common stock;
- limiting the liability of, and providing indemnification to, our directors and officers;
- eliminating the ability of our stockholders to call and bring business before special meetings and to take action by written consent in lieu of a meeting;
- requiring advance notice of stockholder proposals for business to be conducted at meetings of our stockholders and for nominations of candidates for election to our board of directors;

- controlling the procedures for the conduct and scheduling of board and stockholder meetings;
- limiting the determination of the number of directors on our board and the filling of vacancies or newly created seats on the board to our board of directors then in office; and
- providing that directors may be removed by stockholders only for cause.

These provisions, alone or together, could delay hostile takeovers and changes in control or changes in our management.

As a Delaware corporation, we are also subject to provisions of Delaware law, including Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Alachua, Florida

Our corporate headquarters are located in Alachua, Florida. In January 2016, we moved into a new combined-use facility consisting of approximately 21,000 square feet of laboratory and office space. The initial lease term for this facility is 10 years and we have options to extend the term of the lease for three additional five-year periods. Our prior leased facilities encompassed approximately 7,000 square feet of office and laboratory space. Operating leases associated with the prior facilities expired in December 2015.

Cambridge, Massachusetts

In August 2015, we entered into a two-year lease to occupy approximately 3,000 square feet of office and laboratory space in Cambridge, Massachusetts. This second facility primarily focuses on business development, pharmacology, and basic research and development.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any pending legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

68

PART II

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

Market Information

Our common stock has been listed on The NASDAQ Global Market under the symbol "AGTC" since March 27, 2014. Prior to that date, there was no public market for our common stock. The following table sets forth, for the periods indicated, the high and low intraday sales prices of our common stock as reported by The NASDAQ Global Market:

	2016		2015	
	High	Low	High	Low
First fiscal quarter	$20.10	$12.43	$25.46	$14.70
Second fiscal quarter	$21.43	$12.04	$28.24	$16.20
Third fiscal quarter	$20.13	$12.12	$25.42	$19.26
Fourth fiscal quarter	$19.86	$12.76	$22.99	$14.40

As of August 31, 2016, a total of 18,053,284 shares of our common stock were outstanding and we had 30 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, to finance the growth and development of our business. We do not expect to pay any cash dividends on our common stock in the foreseeable future.

Securities Authorized For Issuance Under Equity Compensation Plans

For information regarding securities authorized for issuance under our equity compensation plans, see Part III, Item 12, "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters."

Comparative Stock Performance

The following stock performance graph compares the cumulative total return to stockholders for our common stock for the period commencing March 27, 2014 (the date on which our common stock commenced trading on The NASDAQ Global Market) and ended June 30, 2016 against the cumulative total return of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The calculation of total cumulative returns assumes a $100 investment in our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index, and assumes reinvestment of all dividends, if any. The historical information set forth below is not necessarily indicative of future performance.

	3/14	6/14	6/15	6/16
Applied Genetic Technologies Corporation	100.00	156.50	103.93	95.73
NASDAQ Composite Index	100.00	104.95	119.24	116.43
NASDAQ Biotechnology Index	100.00	109.47	148.57	106.23

ITEM 6: SELECTED FINANCIAL DATA

The following selected financial data should be read in conjunction with our financial statements and related notes in Part II, Item 8 of this Annual Report on Form 10-K and with our "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of this Annual Report on Form 10-K.

Our selected statement of operations data for the fiscal years ended June 30, 2016, 2015 and 2014 and our selected balance sheet data as of June 30, 2016 and 2015 are derived from our audited financial statements included elsewhere in this report. Our historical results are not necessarily indicative of results to be expected for any future period. The selected financial data in this section are not intended to replace our financial statements and the related notes.

Selected Financial Data

	Fiscal Year Ended June 30,				
	2016	2015	2014	2013	2012
	(in thousands except per share data)				
Statement of Operations Data:					
Revenue:					
Collaboration Revenue	$46,751	$—	$—	$—	$—
Grant revenue	610	1,682	917	439	718
Sponsored research and other revenue	-	672	212	503	364
Total revenue	47,361	2,354	1,129	942	1,082
Operating expenses:					
Research and development	38,864	18,118	8,503	3,133	2,354
General and administrative	10,586	8,768	5,182	1,403	787
Total operating expenses	49,450	26,886	13,685	4,536	3,141
Loss from operations	(2,089)	(24,532)	(12,556)	(3,594)	(2,059)
Other income (expense):					
Investment income, net	711	216	42	10	—
Interest expense	—	—	—	(191)	(69)
Fair value adjustments to warrant liabilities (1)	—	—	(441)	(8)	204
Fair value adjustments to Series B purchase rights (1)	—	—	(2,904)	(1,207)	—
Other	(3)	(2)	(49)	—	—
Total other (expense) income, net	708	214	(3,352)	(1,396)	135
Net loss	$(1,381)	$(24,318)	$(15,908)	$(4,990)	$(1,924)
Net loss per share, basic and diluted (2)	$(0.08)	$(1.50)	$(4.46)	$(45.78)	$(17.65)
Weighted-average shares outstanding, basic and diluted (2)	17,810	16,253	3,568	109	109

	As of June 30,				
	2016	2015	2014	2013	2012
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents	$28,868	$39,187	$8,623	$8,893	$774
Short and long-term investments	$143,847	$46,083	$64,450	$14,000	$—
Total assets	$180,797	$90,174	$77,407	$25,490	$2,824
Current liabilities	$54,743	$4,642	$2,534	$3,460	$1,494
Convertible preferred stock	$—	$—	$—	$58,103	$32,524

Total stockholders' equity (deficit)	$109,288	$85,532	$74,873	$(36,183)	$(31,290)

(1) See Note 13 of Notes to Financial Statements appearing elsewhere in this annual report on Form 10-K for a description of the fair value adjustments to our warrant liabilities and Series B purchase rights.
(2) See Note 2 of Notes to Financial Statements appearing elsewhere in this annual report on Form 10-K for a description of the method used to calculate basic and diluted net loss per share.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the financial statements and notes included in Part IV, Item 15 of this Annual Report on Form 10-K. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, including but not limited to those set forth in "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

We are a clinical-stage biotechnology company using gene therapy based on adeno-associated virus, or AAV, to develop genetic therapies to treat patients with inherited diseases. Each treatment is precisely designed to address a specific genetic disorder. Our most advanced gene therapy programs are designed to produce treatments that will restore visual function in patients with rare blinding diseases. Genetic therapies are complex with interdependent components that must work in harmony. Fifteen years of gene therapy experience allows us to design and construct all critical gene therapy components and bring them together to potentially develop effective treatments for patients. We are committed to attracting and maintaining a team with a substantial breadth of clinical and scientific expertise who can foster an atmosphere of scientific growth and discovery.

In July 2015, we entered into a collaboration agreement with Biogen, which we refer to as the collaboration agreement, pursuant to which we and Biogen will collaborate to develop, seek regulatory approval for and commercialize gene therapy products to treat XLRS, XLRP, and discovery programs targeting three indications based on our adeno-associated virus vector technologies. The collaboration agreement became effective in August 2015. In February 2016, we announced Biogen's selection of ALD as the non-ophthalmic indication of the three discovery programs.

We have granted Biogen for the XLRS and XLRP programs, and upon the exercise of the option for the applicable discovery program, an exclusive, royalty-bearing license, with the right to grant sublicenses, to use adeno-associated virus vector technology and other technology controlled by us for the licensed products or discovery programs developed under the collaboration agreement. We and Biogen have also granted each other worldwide licenses, with the right to grant sublicenses, of our respective interests in other intellectual property developed under the collaboration outside the licensed products or discovery programs.

Under the collaboration agreement, we received a non-refundable upfront payment of $94.0 million and a milestone payment of $5.0 million during the fiscal year ended June 30, 2016. As a result of the upfront and milestone payments made by Biogen, we became liable to our various research partner institutions for sub-license and milestone payments, which led us to record an expense for collaboration-related license fees of $12.0 million. In addition, during the year ended June 30, 2016 we recorded other revenue of $585,000 under the collaboration agreement, which was primarily comprised of reimbursable costs for post-funding development activities that we conducted.

We are also eligible to receive payments of up to $467.5 million based on the successful achievement of future milestones under the two lead programs and up to $592.5 million based on the exercise of the option for and the successful achievement of future milestones under the three discovery programs. Biogen will pay revenue-based royalties for each licensed product at tiered rates ranging from high single digit to mid-teen percentages of annual net sales of the XLRS or XLRP products and at rates ranging from mid-single digit to low-teen percentages of annual net sales for the discovery products. Due to the uncertainty surrounding the achievement of the future milestones, such payments were not considered fixed or determinable at the inception of the collaboration agreement and accordingly,

will not be recognized as revenue unless and until they become earned. We achieved the first milestone under the XLRS program in late August 2015, which triggered a milestone payment from Biogen of $5.0 million and the recording of milestone revenue. We are not able to reasonably predict if and when any of the remaining milestones will be achieved.

Biogen will also receive an exclusive license to use our proprietary manufacturing technology platform to make AAV vectors for up to six genes, three of which are at our discretion, in exchange for payment of milestones and royalties.

In addition to the collaboration agreement, on July 1, 2015, we also entered into an equity agreement with Biogen. Under the terms of the equity agreement, Biogen purchased 1,453,957 shares of our common stock, at a purchase price equal to $20.63 per share, for an aggregate cash purchase price of $30.0 million. We received these cash proceeds from Biogen in August 2015. The shares issued to Biogen constitute restricted securities that may not be resold by Biogen other than in a transaction registered under the Securities Act of 1933, as amended, or pursuant to an exemption from such registration requirement.

Since our inception in 1999, we have devoted substantially all of our resources to development efforts relating to our proof-of-concept programs in ophthalmology and alpha-1 antitrypsin deficiency, or AAT deficiency, an inherited orphan lung disease, including activities to manufacture product in compliance with good manufacturing practices, preparing to conduct and conducting clinical trials of our product candidates, providing general and administrative support for these operations and protecting our intellectual property. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations primarily through the private placement of preferred stock, common stock, convertible notes and

warrants to purchase preferred stock and through our public offerings consummated in April 2014 and July/August 2014. We have also been the recipient, either independently or with our collaborators, of grant funding administered through federal, state, and local governments and agencies, including the United States Food and Drug Administration, or FDA, and by patient advocacy groups such as the Foundation Fighting Blindness, or FFB, and the Alpha-1 Foundation.

We have incurred losses from operations in each year since inception. Our net losses were $1.4 million, $24.3 million, and $15.9 million for each of the fiscal years ended June 30, 2016, 2015 and 2014, respectively. Substantially all our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant operating expenses for at least the next several years and anticipate that such expenses will increase substantially in connection with our ongoing activities, as we:

- conduct preclinical studies and clinical trials for our XLRS, ACHM and XLRP product candidates;
- continue our research and development efforts, including exploration through early preclinical studies of potential applications of our gene therapy platform in other indications in orphan ophthalmology and in wet AMD;
- manufacture clinical trial materials and develop larger-scale manufacturing capabilities;
- seek regulatory approval for our product candidates;
- further develop our gene therapy platform;
- add personnel to support our collaboration, product development and commercialization efforts; and
- continue to operate as a public company.

As of June 30, 2016, we had cash and cash equivalents and investments totaling $172.7 million.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years and which we believe is subject to significant uncertainty. We believe that our existing cash and cash equivalents and investments at June 30, 2016, will be sufficient to enable us to advance planned preclinical studies and clinical trials for our lead product candidates for at least the next two years. In order to complete the process of obtaining regulatory approval for our lead product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our lead product candidates, if approved, we will require substantial additional funding. Also, our current operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our products.

Other Collaborations

Synpromics Limited

In December 2015, we entered into an agreement with Synpromics Limited (“Synpromics”) to utilize Synpromics' proprietary technology to develop and optimize synthetic promoters. In the event that results from the research are promising, we have options to license promoters that result from the collaboration efforts.

4D Molecular Therapeutics

In April 2015, we signed an agreement with 4D Molecular Therapeutics (“4DMT”) to conduct research on optimized next generation capsids to target specific target cell populations within the human retina using 4DMT’s Directed Evolution AAV vector discovery platform. If promising capsids result from the research, we have an option to enter into a licensing agreement.

Financial operations overview

Revenue

Our ability to generate product revenue and become profitable depends upon our ability to successfully commercialize products. To date, we have not generated any revenues from the sales of products. During the fiscal year ended June 30, 2016, we recognized $46.8 million of revenue from our collaboration with Biogen. In the fiscal years ended June 30, 2015 and 2014, all our revenues were

derived from grants and sponsored research arrangements. Revenues from grants and sponsored research arrangements are recognized when there is reasonable assurance that they will be received and we have complied with the terms of the grant or the sponsored research arrangement.

Research and development expenses

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

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense;
- expenses incurred under agreements with academic research centers, contract research organizations, or CROs, and investigative sites that conduct our clinical trials;
- license fees;
- the cost of acquiring, developing, and manufacturing clinical trial materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;
- the timing and level of activity as determined by us or jointly with our partners;
- the level of funding received from our partners;
- whether or not we elect to cost share with our partners;
- the countries in which trials are conducted;
- future clinical trial results;
- uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies or elected as best practice by us;
- increased cost and delay associated with manufacturing or testing issues, including ongoing quality assurance, qualifying new vendors and developing in-house capabilities;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in or execution of any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

As of June 30, 2016, we had a total of 39 research and development personnel. From inception through June 30, 2016, we have incurred approximately $110.3 million in research and development expenses. We expect our research

and development expenses to increase for the foreseeable future as we continue the development of our XLRS, ACHM and XLRP product candidates and explore potential applications of our gene therapy platform in other indications.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including share-based compensation and travel expenses for our employees in executive, operational, finance and human resource functions. Other general and administrative expenses include facility-related costs and professional fees for directors, accounting and audit costs primarily associated with operating as a publicly-listed company, and legal services and expenses associated with our general operations and obtaining and maintaining patents.

We anticipate that our general and administrative expenses will continue to increase in the future as we hire additional employees to support our continued research and development efforts, collaboration arrangements, and the potential commercialization of our product candidates. Additionally, if and when we believe a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Other income (expense), net

Other income and expense consists primarily of interest earned on cash and cash equivalents and our held-to-maturity investments. In 2014 and before, other income and expense also included interest expense charged on previously-held debt and re-measurement gains and losses associated with the change in the fair value of liabilities associated with our prior Series B purchase rights and preferred stock warrants. We previously used the Black-Scholes option pricing model to estimate the fair value of liabilities associated with these Series B purchase rights and preferred stock warrants.

Critical accounting policies and estimates

The following discussion of critical accounting policies identifies the accounting policies that require application of management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain and may change in subsequent periods. It is not intended to be a comprehensive list of all of our significant accounting policies, which are more fully described in Note 2 of the notes to the financial statements appearing elsewhere in this annual report on Form 10-K. In many cases, the accounting treatment of a particular transaction is specifically dictated by generally accepted accounting principles, with no need for management's judgment in their application. There are also areas in which the selection of an available alternative policy would not produce a materially different result.

Revenue recognition

We have generated revenue primarily through collaboration agreements, sponsored research arrangements with nonprofit organizations for the development and commercialization of product candidates and revenues from federal research and development grant programs. We recognize revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

We evaluate the terms of sponsored research agreement grants and federal grants to assess our obligations and if our obligations are satisfied by the passage of time, revenue is recognized on a straight-line basis. In situations where the performance of our obligations has been satisfied when the grant is received, revenue is recognized upon receipt of the grant. Certain grants contain refund provisions. We review those refund provisions to determine the likelihood of repayment. If the likelihood of repayment of the grant is determined to be remote, the grant is recognized as revenue. If the probability of repayment is determined to be more than remote, we record the grant as a deferred revenue

liability, until such time that the grant requirements have been satisfied.

Collaboration revenue

As described above, on July 1, 2015, we entered into a collaboration agreement with Biogen. The terms of this agreement and other potential collaboration or commercialization agreements we may enter into generally contain multiple elements, or deliverables, which may include, among others, (i) licenses, or options to obtain licenses, to our technology, and (ii) research and development activities to be performed on behalf of the collaborative partner. Payments made under such arrangements typically include one or more of the following: non-refundable, up-front license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Multiple element arrangements are analyzed to determine whether the deliverables within the agreement can be separated or whether they must be accounted for as a single unit of accounting. Deliverables under an agreement are required to be accounted for as separate units of accounting provided that (i) a delivered item has value to the customer on a stand-alone basis; and (ii) if the agreement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is

considered probable and substantially in the control of the vendor. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

We determine the estimated selling price for deliverables within each agreement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE nor TPE are available. Determining the best estimate of selling price for a deliverable requires significant judgment. We use BESP to estimate the selling price related to licenses to our proprietary technology, since we often do not have VSOE or TPE of selling price for these deliverables. In those circumstances where we utilize BESP to determine the estimated selling price of a license to our proprietary technology, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating our best estimate of selling price, we evaluate whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration among multiple deliverables.

If the delivered element does not have stand-alone value or if the fair value of any of the undelivered elements cannot be determined, the arrangement is then accounted for as a single unit of accounting, and we recognize the consideration received under the arrangement as revenue on a straight-line basis over our estimated period of performance. Our anticipated periods of performance, typically the terms of our research and development obligations, are subject to estimates by management and may change over the course of the collaboration agreement. Such changes could have a material impact on the amount of revenue we record in future periods.

Milestone revenue

We apply the milestone method of accounting to recognize revenue from milestone payments when earned, as evidenced by written acknowledgement from the collaborator or other persuasive evidence that the milestone has been achieved and the payment is non-refundable, provided that the milestone event is substantive. A milestone event is defined as an event (i) that can only be achieved based in whole or in part on either our performance or on the occurrence of a specific outcome resulting from our performance; (ii) for which there is substantive uncertainty at the inception of the arrangement that the event will be achieved; and (iii) that would result in additional payments being due to us. Events for which the occurrence is either contingent solely upon the passage of time or the result of a counterparty’s performance are not considered to be milestone events. A milestone event is substantive if all of the following conditions are met: (i) the consideration is commensurate with either our performance to achieve the milestone, or the enhancement of the value to the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone; (ii) the consideration relates solely to past performance; and (iii) the consideration is reasonable relative to all the deliverables and payment terms (including other potential milestone consideration) within the arrangement.

We assess whether a milestone is substantive at the inception of the arrangement. If a milestone is deemed substantive and the milestone payment is nonrefundable, we recognize revenue upon the successful accomplishment of that milestone. Where a milestone is deemed non-substantive, we account for that milestone payment in accordance with the multiple element arrangements guidance and recognize revenue consistent with the related units of accounting for the arrangement over the related performance period.

During the fiscal year ended June 30, 2016, we recorded $5.0 million of milestone revenue after having achieved a patient enrollment-based milestone under our collaboration arrangement with Biogen.

Deferred revenue

Amounts received by us prior to satisfying the above revenue recognition criteria are recorded as deferred revenue on the balance sheet. Amounts not expected to be recognized within 12 months of the balance sheet date are classified as non-current deferred revenue.

Research and development expenses

Research and development costs include costs incurred in identifying, developing and testing product candidates and generally comprise compensation and related benefits and non-cash share-based compensation to research related employees; laboratory costs; animal and laboratory maintenance and supplies; rent; utilities; clinical and pre-clinical expenses; and payments for sponsored research, scientific and regulatory consulting fees and testing.

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones

are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. The significant estimates in our accrued research and development expenses are related to expenses incurred with respect to academic research centers, CROs, and other vendors in connection with research and development activities for which we have not yet been invoiced.

There may be instances in which our service providers require advance payments at the inception of a contract or in which payments made to these vendors will exceed the level of services provided, resulting in a prepayment of the research and development expense. Such prepayments are charged to research and development expense as and when the service is provided or when a specific milestone outlined in the contract is reached.

Share-based compensation

We account for share-based awards issued to employees in accordance with Accounting Standard Codification ("ASC") Topic 718, Compensation—Stock Compensation ("ASC 718") generally recognize share-based compensation expense on a straight-line basis over the periods during which the employees and non-employee directors are required to provide service in exchange for the award. In addition, we issue stock options and restricted shares of common stock to non-employees in exchange for consulting services and account for these in accordance with the provisions of ASC Subtopic 505-50, Equity-Based Payments to Non-employees ("ASC 505-50"). Under ASC 505-50, share-based awards to non-employees are subject to periodic fair value re-measurement over their vesting terms.

For purposes of calculating stock-based compensation, we estimate the fair value of stock options using a Black-Scholes option-pricing model. The determination of the fair value of share-based payment awards utilizing the Black-Scholes model is affected by our stock price and a number of assumptions, including expected volatility, expected life, risk-free interest rate and expected dividends. The expected volatility is primarily based on the historical volatility of peer company data while the expected life of the stock options is based on historical and other economic data trended into the future. The risk-free interest rate assumption is based on observed interest rates appropriate for the expected terms of our stock options. The dividend yield assumption is based on our history and expectation of no dividend payouts. If factors change and we employ different assumptions, stock-based compensation expense may differ significantly from what we have recorded in the past. If there is a difference between the assumptions used in determining stock-based compensation expense and the actual factors which become known over time, specifically with respect to anticipated forfeitures, we may change the input factors used in determining stock-based compensation costs for future grants. These changes, if any, may materially impact our results of operations in the period such changes are made.

Recent Accounting Pronouncements

In February 2016, the FASB issued Accounting Standards Update ("ASU") No. 2016-02, Leases (Topic 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet for those leases previously classified as operating leases under GAAP. The standard requires, in most instances, a lessee to recognize on its balance sheet a liability to make lease payments (the lease liability) and also a right-of-use asset representing its right to use the underlying asset for the lease term. The amendments are effective for fiscal years beginning after December 15, 2018, including interim periods within those periods, using a modified retrospective approach and early adoption is permitted. We are currently in the process of evaluating the impact of adoption of this standard on our financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Improvements to Employee Share-Based Payment Accounting, which amends ASC Topic 718, Compensation – Stock Compensation. The amendments simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, forfeitures, and classification on the statement of cash flows. The amendments are effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years and early adoption is permitted. We are currently in the process of evaluating the impact of adoption of this standard on our financial statements.

In November 2015, the FASB issued ASU No. 2015-17, Balance Sheet Classification of Deferred Taxes, requiring all deferred tax assets and liabilities, and any related valuation allowance, to be classified as noncurrent on the balance sheet. The classification change for all deferred taxes as noncurrent simplifies entities' processes as it eliminates the need to separately identify the net current and net noncurrent deferred tax asset or liability in each jurisdiction and allocate valuation allowances. We adopted the accounting standard with effect from the beginning of our third fiscal quarter ending March 31, 2016. The adoption of this standard did not have a material impact on our financial

statements.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. The amendments require management to perform interim and annual assessments of an entity's ability to continue as a going concern and provide guidance on determining when and how to disclose going concern uncertainties in the financial statements. The standard applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. We adopted the accounting standard with effect from the beginning of our third fiscal quarter ending March 31, 2016. The adoption of this standard did not have a material impact on our financial statements.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers. The guidance requires companies to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration to which the company expects to be entitled in exchange for those goods or services. It also requires enhanced disclosures about revenue, provides guidance for transactions that were not previously addressed comprehensively, and improves guidance for multiple-element arrangements. The guidance applies to any entity that either enters into contracts with customers to transfer goods or services or enters into contracts for the transfer of nonfinancial assets unless those contracts are within the scope of other standards. In July 2015, the FASB delayed the effective date of this guidance by one year. The guidance is now effective for public companies for annual periods beginning after December 15, 2017 as well as interim periods within those annual periods using either the full retrospective approach or modified retrospective approach. We are currently evaluating the impacts of the new guidance on our financial statements.

Emerging growth company status

The JOBS Act permits an “emerging growth company” such as ours to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have chosen to “opt out” of this provision and, as a result, we will comply with new or revised accounting standards as required when they are adopted. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

Results of operations

Comparison of the fiscal years ended June 30, 2016 and 2015

Revenue

	Fiscal year ended June 30, 2016	2015	Increase (Decrease)	% Increase (Decrease)
	(dollars in thousands)			
Collaboration revenue	$46,751	$—	$ 46,751	n/m
Grant revenue	610	1,682	(1,072)	(64)%
Sponsored research and other revenue	—	672	(672)	n/m
Total revenue	$47,361	$2,354	$ 45,007	n/m

Total revenue for fiscal year 2016 was $47.4 million compared to $2.4 million generated during fiscal year 2015. The increase was driven by revenue generated from our collaboration with Biogen, primarily comprised of the amortization of upfront fees and $5.0 million of milestone revenue earned during the fiscal year following achievement of a patient enrollment-based milestone under the terms of the collaboration agreement. Grant revenue generated during fiscal year 2016 decreased compared to 2015 due largely to reduced research and development activities under grant-funded projects. Other revenue recorded in 2015 related primarily to sponsored research revenue earned from a patient advocacy group and income that was generated from a right of reference agreement entered into with a strategic partner during that period.

Research and development expense

	Fiscal Year Ended June 30, 2016	2015	Increase (Decrease)	% Increase (Decrease)
	(dollars in thousands)			
Collaboration costs	$12,034	$—	$ 12,034	n/m
Outside program costs	11,965	10,800	1,165	11 %
Employee-related costs	5,631	2,923	2,708	93 %
Licenses, milestones and related fees	4,402	1,590	2,812	177 %
Share-based compensation	2,147	908	1,239	136 %
Other	2,685	1,897	788	42 %
Total research and development expense	$38,864	$18,118	$ 20,746	115 %

Research and development expense for fiscal year 2016 increased by $20.7 million to $38.9 million compared to fiscal year 2015, driven largely by $12.0 million of incremental costs associated with our collaboration arrangement with Biogen. Also contributing to the higher research and development expense were increased license and milestone fees from new collaboration arrangements with external partners and from our achievement of certain clinical development

and regulatory milestones which triggered additional milestone payments to some of our research partner institutions. In addition, employee-related and share-based compensation costs also increased year-over-year due primarily to the hiring of additional employees to support this increased level of research and development activity and the impact of new share-based incentives awarded during the year.

General and administrative expense

	Fiscal Year Ended June 30,		Increase (Decrease)	% Increase (Decrease)
	2016	2015		
	(dollars in thousands)			
Employee-related costs	$2,827	$2,231	$ 596	27 %
Share-based compensation	2,860	1,912	948	50 %
Legal and professional fees	1,144	1,909	(765)	(40)%
Other	3,755	2,716	1,039	38 %
Total general and administrative expense	$10,586	$8,768	$ 1,818	21 %

General and administrative expense for fiscal year 2016 increased by $1.8 million to $10.6 million compared to fiscal year 2015. The increase was primarily driven by the hiring of additional employees which resulted in higher share-based compensation and other employee-related costs. Other administrative expenses were also higher compared to 2015 due primarily to our ongoing expansion and the increasing costs of operating as a publicly-traded company. The impact of these incremental costs was partially offset by decreased legal and professional fees.

Other income (expense), net

For fiscal year 2016, other income (expense), net, which was primarily comprised of investment income, increased to $708,000 from $214,000 generated in 2015 due largely to comparatively higher cash and investment balances.

Comparison of the fiscal years ended June 30, 2015 and 2014

Revenue

	Fiscal year ended June 30, 2015	2014	Increase (Decrease)	% Increase (Decrease)	
	(dollars in thousands)				
Grant revenue	$1,682	$917	$ 765	83	%
Sponsored research	572	212	360	170	%
Other	100	0	100	100	%
Total revenue	$2,354	$1,129	$ 1,225	109	%

Total revenue for fiscal year 2015 increased by $1.2 million to $2.4 million compared to fiscal year 2014. The year-over-year increase was primarily driven by higher grant revenue resulting from increased research and development activities on grant-funded projects. In addition, sponsored research revenue was higher in 2015 compared to prior year largely as a result of the approval of our Investigational New Drug Application for XLRS that was filed with the FDA in March 2015, triggering milestone payments from a patient advocacy group. Other revenue was generated from a right of reference agreement that was entered into with a strategic partner during the first quarter of fiscal year 2015.

Research and development expense

	Fiscal Year Ended June 30, 2015	2014	Increase (Decrease)	% Increase (Decrease)	
	(dollars in thousands)				
Outside program costs	$10,800	$5,287	$ 5,513	104	%
Employee-related costs	2,923	1,504	1,419	94	%
Licenses, milestones and related fees	1,590	435	1,155	n/m	
Share-based compensation	908	77	831	n/m	
Other	1,897	1,635	262	16	%
Total research and development expense	$18,118	$8,938	$ 9,180	103	%

Research and development expense for fiscal year 2015 increased by $9.2 million to $18.1 million compared to fiscal year 2014. Outside program costs were higher due to increased research and development activity primarily relating to our XLRS, XLRP, ACHM and other product candidates. The increase in employee-related and share-based compensation costs was attributable to the hiring of additional employees to support the higher level of research and

development activity and to comparatively higher fair values of awards issued under our share-based compensation plans. The increase in licenses and related fees was largely the result of the collaboration agreement entered into with 4D Molecular Therapeutics.

General and administrative expense

	Fiscal Year Ended June 30,		Increase (Decrease)	% Increase (Decrease)	
	2015	2014			
	(dollars in thousands)				
Employee-related costs	$2,231	$1,665	$ 566	34	%
Share-based compensation	1,912	748	1,164	156	%
Legal and professional fees	1,909	844	1,065	126	%
Other	2,716	1,490	1,226	82	%
Total general and administrative expense	$8,768	$4,747	$ 4,021	85	%

General and administrative expense for fiscal year 2015 increased by $4.0 million to $8.8 million compared to fiscal year 2014. The increase in employee-related and share-based compensation costs was attributable to the hiring of additional employees and to comparatively higher fair values of awards issued under our share-based compensation plans. The increase in legal and professional fees was largely the result of the collaboration agreement entered into with Biogen while the increase in other administrative expenses was primarily due to higher insurance, accounting and other expenses associated with operating as a publicly-traded company.

Other income (expense), net

For fiscal year 2015, other income (expense), net of $214,000 was primarily comprised of investment income compared to an expense of $3.4 million in fiscal year 2014. The $3.4 million of expense recorded in 2014 was primarily attributable to fair value adjustments that were associated with our former Series B purchase rights and warrant liabilities, extinguished in connection with our initial public offering in April 2014.

Liquidity and capital resources

We have incurred cumulative losses and negative cash flows from operations since our inception in 1999, and as of June 30, 2016, we had an accumulated deficit of $90.0 million. It will be several years, if ever, before we have a product candidate ready for commercialization. We expect that our research and development and general and administrative expenses will continue to increase and as a result, we anticipate that we will require additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

During fiscal year 2016, we received a non-refundable upfront cash payment of $94.0 million under our collaboration arrangement with Biogen. Contemporaneous with this collaboration arrangement, we also entered into an equity agreement with Biogen under which we received an additional $30.0 million in cash in exchange for 1,453,957 shares of common stock that we issued to Biogen at a purchase price of $20.63 per share. Cash in excess of immediate requirements is invested in accordance with our investment policy which primarily seeks to maintain adequate liquidity and preserve capital by generally limiting investments to certificates of deposit and investment-grade debt securities that mature within 24 months. As of June 30, 2016, we had cash and cash equivalents and investments of $172.7 million.

As of June 30, 2016, our cash and cash equivalents were held in bank accounts and money market funds, while our short and long-term investments consisted of certificates of deposit and corporate and government bonds, none of which mature more than 24 months after the balance sheet date, consistent with our investment policy that seeks to maintain adequate liquidity and preserve capital.

Cash flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Fiscal Year Ended June 30,		
	2016	2015	2014
	(in thousands)		
Net cash provided by (used in):			
Operating activities	$70,991	$(19,485)	$(11,928)
Investing activities	(100,804)	17,892	(50,826)
Financing activities	19,494	32,157	62,484
Net (decrease) increase in cash and cash equivalents	$(10,319)	$30,564	$(270)

Operating activities. For fiscal year 2016, net cash provided by operating activities was primarily associated with the upfront cash proceeds of $104.8 million received in connection with the entry into our collaboration with Biogen, which included an allocation of $10.8 million from the equity agreement, and a milestone payment from Biogen of $5.0 million. These proceeds were partially offset by the impact of our net loss, including the amortization of deferred revenue and payments to certain research partner institutions in the aggregate amount of $12.0 million for sub-license, milestone and other costs which were all associated with the Biogen collaboration, and changes during the period in our working capital accounts. Net cash used in operating activities was $19.5 million and $11.9 million during the fiscal years ended 2015 and 2014, respectively, and primarily resulted from our net losses and changes in our working capital accounts.

Investing activities. Net cash used in investing activities for fiscal year 2016 consisted primarily of cash outflows of $208.2 million related to the purchase of investments and $2.6 million related to the purchase of property and equipment and the acquisition of intellectual property, including leasehold improvements at our new facility in Alachua, Florida. These cash outflows were partially offset by $110.0 million of proceeds from the maturity of investments. Net cash provided by investing activities during fiscal year 2015 of $17.9 million was primarily comprised of proceeds totaling $121.1 million from the maturity of investments, partially offset by cash outflows of $102.9 million related to the purchase of investments and $323,000 related to the acquisition and maintenance of intellectual property and purchase of property and equipment. For fiscal year 2014, net cash used in investing activities was $50.8 million and consisted primarily of the purchase of $80.0 million of investments and payments totaling $376,000 associated with the acquisition and maintenance of our intellectual property and purchase of property and equipment. These cash outflows were partially offset by $29.5 million of proceeds realized upon the maturity of short-term investments.

Financing activities. Net cash provided by financing activities was $19.5 million during fiscal year 2016 and consisted of $19.2 million of cash received in connection with our sale of shares of common stock to Biogen pursuant to the equity agreement executed on July 1, 2015 and $283,000 of cash received in connection with the exercise of stock options. Net cash provided by financing activities during fiscal year 2015 was $32.2 million, of which $32.0 million was related to the follow on public offering that we completed during our first quarter ended September 30, 2014 and $148,000 consisted of cash received in connection with the exercise of stock options. Net cash provided by financing activities during fiscal year 2014 was $62.5 million and consisted primarily of $51.6 million of net proceeds from the sale of common stock in our initial public offering, $10.7 million of proceeds from the issuance of our Series B-3 preferred stock and Series B purchase rights, and $194,000 of cash received from the exercise of stock options.

Operating capital requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are subject to all of the risks incident in the development of new gene therapy products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

We believe that our existing cash and cash equivalents and investments at June 30, 2016 will be sufficient to enable us to advance planned preclinical studies and clinical trials for our lead product candidates for at least the next two years. In order to complete the process of obtaining regulatory approval for our lead product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our lead product candidates, if approved, we will require substantial additional funding.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the timing and costs our planned clinical trials for our XLRS and ACHM product candidates;
- the timing and costs of our planned preclinical studies of our XLRP product candidate;
- the timing and level of activity as determined by us or jointly with our partners;
- the level of funding received from our partners;
- whether or not we elect to cost share with our partners;
- the initiation, progress, timing, costs and results of preclinical studies relating to potential applications of our gene therapy platform in other indications;

- our success in scaling our HAVE manufacturing method and expanding our manufacturing capabilities;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- subject to receipt of marketing approval, revenue received from commercial sales of our product candidates;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

Contractual obligations and commitments

The following table summarizes our contractual obligations at June 30, 2016:

In thousands	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Operating lease obligations (1)	$5,421	$804	$1,120	$1,076	$2,421
Purchase obligations (2)	2,072	163	343	270	1,296
Total	$7,493	$967	$1,463	$1,346	$3,717

(1) Our current leased facilities encompass approximately 21,000 square feet of laboratory and office space in Alachua, Florida under a lease arrangement that will expire in December 31, 2025. In addition, we occupy approximately 3,000 square feet of office and laboratory space in Cambridge, Massachusetts under a lease arrangement that is set to expire in August 2017. Obligations at June 30, 2016 under noncancelable operating leases relate to both of these leasing arrangements.

(2) Consists of minimum annual royalties and maintenance fees under license agreements with third parties. In addition to these minimum annual payments, we may be required to make future payments related to milestones or royalties on future sales of specified products. These contingent payments generally become due and payable only upon achievement of specified developmental, regulatory or commercial milestones. The amount and timing of any of such payments are not known due to the uncertainty surrounding the successful research, development and commercialization of the products and, as such, have not been included in the above table.

Contingent contractual obligations

We also have obligations arising under our license agreements to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones (such as the start of a clinical trial, filing of a Biologics License Application, or BLA, approval by the FDA or product launch). We have not included these obligations on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed nor determinable. These obligations include:

- Under each of our various licenses with the University of Florida Research Foundation, or UFRF, covering the AAV construct containing the AAT gene and the method to treat AAT deficiency using this construct, a small cone cell specific promoter, and the use of engineered capsids and under our joint license with UFRF and Johns Hopkins University covering a particular HSV construct and various compositions thereof, we will be required to make

payments based upon development, regulatory and commercial milestones for any products covered by the in-licensed intellectual property. We will also be required to pay a royalty on net sales of products covered by the in-licensed intellectual property. We have the right to sublicense our rights under this agreement, and we will be required to pay a percentage of such license income. We are required to make annual maintenance payments under these licenses, which payments are creditable against royalty payments on a year-by-year basis.

- Under our license agreement with the UAB Research Foundation pursuant to which we license a patent covering the use of HSV helpers to produce AAV vectors, we will be required to make payments based upon development and regulatory milestones for any products covered by the in-licensed intellectual property. We will also be required to pay a royalty on net sales of products covered by the in-licensed intellectual property. We have the right to sublicense our rights under this

agreement, and we will be required to pay a percentage of such license income. We are required to make annual maintenance payments under this license, which payments are creditable against royalty payments on a year-by-year basis.

If any of our product candidates that utilize technology licensed under these agreements reached commercialization, we will be obligated to make royalty payments ranging from 0.5% to 4.0% of our net sales of the applicable product. We are responsible for a portion of the costs related to the preparation, filing, issuance, prosecution and maintenance of the patents covered by the license agreements. In fiscal years 2016, 2015 and 2014, we paid annual royalty and milestone payments in the aggregate amounts of $963,000, $122,000 and $87,000, respectively.

We enter into contracts in the normal course of business with contract research organizations for preclinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Off-balance sheet arrangements

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

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity

Our financial instruments at June 30, 2016 consisted primarily of cash and cash equivalents and short-term and long-term investments totaling $172.7 million. These financial instruments are exposed to the impact of interest rate changes which may result in fluctuations to our interest income. Due to the nature of our investments in money market funds, certificates of deposits, and debt instruments of corporations and U.S. government agencies, all of which generally mature within a two-year period of their purchase date, the estimated fair values of these financial instruments approximate their carrying amounts at June 30, 2016.

We maintain our investment portfolio in accordance with our investment policy. The primary objectives of this investment policy are to maintain adequate liquidity, preserve capital and to meet our operating needs. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Our investments are also subject to interest rate risk and may decrease in value if market interest rates increase. However, due to the conservative nature of our investments and relatively short investment periods, we believe interest rate risk is mitigated and an immediate 10% increase in interest rates would not have a material effect on the fair market value of our portfolio. We do not own derivative financial instruments. Accordingly, we do not believe that there is any material market risk exposure with respect to derivative or other financial instruments.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA
APPLIED GENETIC TECHNOLOGIES CORPORATION

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Applied Genetic Technologies Corporation

We have audited the accompanying balance sheets of Applied Genetic Technologies Corporation (the Company) as of June 30, 2016 and 2015, and the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended June 30, 2016. Our audits also included the financial statement schedule of the Company listed in Item 15(a). These financial statements and financial statement schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Applied Genetic Technologies Corporation as of June 30, 2016 and 2015, and the results of its operations and its cash flows for each of the three years in the period ended June 30, 2016, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly in all material respects the information set forth therein.

/s/ RSM US LLP

Raleigh, North Carolina

September 12, 2016

APPLIED GENETIC TECHNOLOGIES CORPORATION

BALANCE SHEETS

In thousands, except per share data	At June 30, 2016	2015
ASSETS		
Current assets:		
Cash and cash equivalents	$28,868	$39,187
Investments	69,664	22,454
Grants receivable	954	883
Prepaid and other current assets	3,089	1,608
Total current assets	102,575	64,132
Investments	74,183	23,629
Property and equipment, net	2,627	478
Intangible assets, net	1,321	1,448
Grants receivable	—	480
Other assets	91	7
Total assets	$180,797	$90,174
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$1,331	$1,191
Accrued and other liabilities	6,514	3,451
Deferred revenue	46,898	—
Total current liabilities	54,743	4,642
Deferred revenue, net of current portion	16,766	
Total liabilities	71,509	4,642
Stockholders' equity:		
Common stock, par value $.001 per share, 150,000 shares authorized; 18,053 and 16,491 shares issued;18,048 and 16,476 shares outstanding at June 30, 2016 and June 30, 2015, respectively	18	16
Additional paid-in capital	199,303	174,168
Accumulated deficit	(90,033)	(88,652)
Total stockholders' equity	109,288	85,532
Total liabilities and stockholders' equity	$180,797	$90,174

The accompanying notes are an integral part of the financial statements.

88

APPLIED GENETIC TECHNOLOGIES CORPORATION

STATEMENTS OF OPERATIONS

	For the fiscal years ended June 30,		
In thousands, except per share amounts	2016	2015	2014
Revenue:			
Collaboration revenue	$ 46,751	$ —	$ —
Grant revenue	610	1,682	917
Sponsored research and other revenue	—	672	212
Total revenue	47,361	2,354	1,129
Operating expenses:			
Research and development	38,864	18,118	8,503
General and administrative	10,586	8,768	5,182
Total operating expenses	49,450	26,886	13,685
Loss from operations	(2,089)	(24,532)	(12,556)
Other income (expense):			
Investment income, net	711	216	42
Fair value adjustments to warrant liabilities	—	—	(441)
Fair value adjustments to Series B purchase rights	—	—	(2,904)
Other expense	(3)	(2)	(49)
Total other income (expense), net	708	214	(3,352)
Net loss	$ (1,381)	$ (24,318)	$ (15,908)
Net loss per share, basic and diluted	$ (0.08)	$ (1.50)	$ (4.46)
Weighted average shares outstanding, basic and diluted	17,810	16,253	3,568

The accompanying notes are an integral part of the financial statements.

APPLIED GENETIC TECHNOLOGIES CORPORATION

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

In thousands	Common Stock Outstanding Shares	Amount	Additional Paid-in Capital	Accumulated Deficit	Total
Balance, June 30, 2013	109	$ —	$ 12,243	$ (48,426)	$ (36,183)
Issuance of common stock, net of issuance costs	4,853	5	51,796	—	51,801
Reclassification of warrants to purchase stock to additional paid-in capital	—	—	551	—	551
Conversion of convertible preferred stock to common stock	9,120	9	73,778	—	73,787
Share-based compensation expense	—	—	825	—	825
Net loss	—	—	—	(15,908)	(15,908)
Balance, June 30, 2014	$ 14,082	$ 14	$ 139,193	$ (64,334)	$ 74,873
Issuance of common stock, net of issuance costs	2,300	2	32,007	—	32,009
Share-based compensation expense	—	—	2,820	—	2,820
Shares issued under employee plans	94	—	148	—	148
Exercise of warrants	15	—	—	—	—
Net loss	—	—	—	(24,318)	(24,318)
Balance, June 30, 2015	$ 16,491	$ 16	$ 174,168	$ (88,652)	$ 85,532
Issuance of common stock, net of issuance costs	1,494	2	19,805	—	19,807
Share-based compensation expense	—	—	5,007	—	5,007
Shares issued under employee plans	59	—	283	—	283
Exercise of warrants	9	—	40	—	40
Net loss	—	—	—	(1,381)	(1,381)
Balance, June 30, 2016	18,053	$ 18	$ 199,303	$ (90,033)	$ 109,288

The accompanying notes are an integral part of the financial statements.

APPLIED GENETIC TECHNOLOGIES CORPORATION

STATEMENTS OF CASH FLOWS

In thousands	For the fiscal years ended June 30, 2016	2015	2014
Cash flows from operating activities			
Net loss	$(1,381)	$(24,318)	$(15,908)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	5,007	2,820	825
Share-based collaboration expense	636	—	—
Depreciation and amortization	567	376	334
Fair value adjustments to warrant liabilities	—	—	441
Fair value adjustments to Series B purchase rights	—	—	2,904
Changes in operating assets and liabilities:			
Decrease (increase) in grants receivable	409	(876)	(343)
(Increase) decrease in prepaid and other assets	(1,114)	419	(1,351)
Increase in accounts payable	140	228	156
Increase (decrease) in deferred revenues	63,664	—	(212)
Increase in accrued and other liabilities	3,063	1,866	1,226
Net cash provided by (used in) operating activities	70,991	(19,485)	(11,928)
Cash flows from investing activities			
Purchase of property and equipment	(2,471)	(225)	(158)
Purchase of and capitalized costs related to intangible assets	(121)	(98)	(218)
Maturity of investments	109,968	121,079	29,500
Purchase of investments	(208,180)	(102,864)	(79,950)
Net cash (used in) provided by investing activities	(100,804)	17,892	(50,826)
Cash flows from financing activities			
Proceeds from issuance of common stock, net of issuance costs	19,211	32,009	51,607
Proceeds from exercise of common stock options	283	148	194
Proceeds from issuance of preferred stock and Series B purchase rights, net of issuance costs	—	—	10,683
Proceeds from exercise of convertible preferred stock warrants	—	—	1
Payment of bank term notes and capital lease	—	—	(1)
Net cash provided by financing activities	19,494	32,157	62,484
Net (decrease) increase in cash and cash equivalents	(10,319)	30,564	(270)
Cash and cash equivalents, beginning of period	39,187	8,623	8,893
Cash and cash equivalents, end of period	$28,868	$39,187	$8,623
Supplemental disclosure of non-cash financing activities			
Conversion of convertible preferred stock to common stock	$—	$—	$73,787
Conversion of Series B purchase rights to Series B-3 convertible preferred stock	$—	$—	$5,000
Conversion of preferred stock warrants to common stock warrants	$—	$—	$551

The accompanying notes are an integral part of the financial statements.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

(1) Organization and Operations:

Applied Genetic Technologies Corporation (the "Company" or "AGTC") was incorporated as a Florida corporation on January 19, 1999 and reincorporated as a Delaware corporation on October 24, 2003. The Company is a clinical-stage biotechnology company primarily developing gene therapy products designed to transform the lives of patients with severe inherited orphan diseases in ophthalmology. On April 1, 2014, AGTC completed its initial public offering ("IPO") and now trades on NASDAQ under the ticker symbol AGTC.

On July 30, 2014, the Company completed a follow on public offering in which it sold 2,000,000 shares of common stock at a public offering price of $15.00 per share. On August 1, 2014, the Company sold an additional 300,000 shares of common stock at a public offering price of $15.00 per share pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the follow on offering. The aggregate net proceeds received by the Company from the follow on offering, including exercise of the overallotment option, amounted to $32.0 million, net of underwriting discounts and commissions and other offering expenses.

The Company has devoted substantially all of its efforts to research and development, including clinical trials. The Company has not completed the development of any products. The Company has generated revenue from collaboration agreements, sponsored research payments and grants, but has not generated product revenue to date and is subject to a number of risks similar to those of other early stage companies in the biotechnology industry, including dependence on key individuals, the difficulties inherent in the development of commercially viable products, the need to obtain additional capital necessary to fund the development of its products, development by the Company or its competitors of technological innovations, risks of failure of clinical studies, protection of proprietary technology, compliance with government regulations and ability to transition to large-scale production of products. As of June 30, 2016, the Company had an accumulated deficit of $90.0 million and expects to continue incurring losses for the foreseeable future. The Company has financed its operations to date primarily through sales of common stock, private placements of its convertible preferred stock, collaborations, bank debt, convertible debt financings, grant funding and cash receipts for sponsored research. At June 30, 2016, the Company had cash and cash equivalents and investments of $172.7 million.

(2) Summary of Significant Accounting Policies:

Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP") and, in the opinion of management, include all adjustments necessary for a fair presentation of the Company's financial position, results of operations, and cash flows for each period presented.

Certain amounts reported previously have been reclassified to conform to the current year presentation, with no effect on stockholders' equity or net loss as previously presented.

Segment Reporting

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 in making decisions regarding resource allocation and assessing performance. To date, we have viewed our operations and managed our business as one segment.

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and cash equivalents

Cash consists of funds held in bank accounts. Cash equivalents consist of short-term, highly liquid investments with original maturities of 90 days or less at the time of purchase and generally include money market accounts.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

Investments

The Company's investments consist of certificates of deposit and debt securities classified as held-to-maturity. Management determines the appropriate classification of debt securities at the time of purchase and reevaluates such designation as of each balance sheet. Debt securities are classified as held-to-maturity when the Company has the positive intent and ability to hold the securities to maturity. Held-to-maturity securities are stated at amortized cost, adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in investment income. Interest on securities classified as held-to-maturity is included in investment income.

The Company uses the specific identification method to determine the cost basis of securities sold.

Investments are considered to be impaired when a decline in fair value is judged to be other-than-temporary. The Company evaluates an investment for impairment by considering the length of time and extent to which market value has been less than cost or amortized cost, the financial condition and near-term prospects of the issuer as well as specific events or circumstances that may influence the operations of the issuer and the Company's intent to sell the security or the likelihood that it will be required to sell the security before recovery of the entire amortized cost. Once a decline in fair value is determined to be other-than-temporary, an impairment charge is recorded to other income (expense) and a new cost basis in the investment is established.

Concentrations of Credit Risk

The Company maintains its cash and cash equivalents and certificates of deposit with two financial institutions that are federally insured. Some of these financial instruments are in excess of federally insured limits and as a result, could potentially expose the Company to significant concentrations of credit risk. To date, the Company has not experienced any losses associated with this credit risk and continues to believe that this exposure is not significant. The Company invests its excess cash primarily in money market funds, certificates of deposit, and debt instruments of corporations and U.S. government agencies. These investments generally mature within a two year period from their purchase date, in line with the Company's investment policy that seeks to maintain adequate liquidity and preserve capital.

Inventory

Purchases of clinical materials stored for master and working viral banks that remain at the sites in anticipation of their future use at that site are charged to expense when they are incurred. Since the Company can use each of the raw materials in only a single product, each raw material is deemed to have no future economic value independent of the development status of that single drug.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

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. The Financial Accounting Standards Board ("FASB") Accounting Standard Codification ("ASC") Topic 820, Fair Value Measurements and Disclosures ("ASC 820"), establishes a hierarchy of inputs 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 those 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 financial instruments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and are 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.

Property and equipment

Property and equipment, consisting of laboratory equipment, furniture and fixtures, computer equipment and leasehold improvements, are recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which are generally three to seven years. Leasehold improvements are stated at cost and are amortized over the shorter of the estimated useful lives of the assets or the lease term, including any renewal periods that are deemed to be reasonably assured. Repair and maintenance costs that do not improve service potential or extend an asset's economic life are recorded as an expense when incurred.

Intangible assets

Intangible assets primarily include licenses and patents. The Company obtains licenses from third parties and capitalizes the costs related to exclusive licenses that have alternative future use in multiple potential programs. The Company also capitalizes costs related to filing, issuance, and prosecution of patents. The Company reviews its capitalized costs periodically to determine that such costs relate to patent applications that have future value and an alternative future use, and writes off any costs associated with patents that are no longer being actively pursued or that

have no future benefit.

Amortization expense is computed using the straight-line method over the estimated useful lives of the assets, which are generally eight to twenty years. The Company amortizes in-licensed patents and patent applications from the date of the applicable license and internally developed patents and patent applications from the date of the initial application. Licenses and patents converted to research use only are immediately written off to expense.

Impairment of long-lived assets

The Company reviews its long-lived assets for impairment when impairment indicators are present. If impairment indicators exist, management determines whether impairment in value has occurred by comparing the estimated undiscounted cash flows from future operations with the carrying values of the assets. Management considers several indicators in assessing impairment, including trends and prospects, as well as the effects of obsolescence, demand, competition and other economic factors. No impairment charges were recorded for each of the fiscal years ended June 30, 2016, 2015, and 2014.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

Revenue recognition

The Company has generated revenue primarily through collaboration agreements, sponsored research arrangements with nonprofit organizations for the development and commercialization of product candidates and revenues from federal research and development grant programs. The Company recognizes revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current liabilities. The Company recognizes revenue for reimbursements of research and development costs under collaboration agreements as the services are performed. The Company records these reimbursements as revenue and not as a reduction of research and development expenses, as the Company has the risks and rewards as the principal in the research and development activities.

The Company evaluates the terms of sponsored research agreement grants and federal grants to assess the Company's obligations and if the Company's obligations are satisfied by the passage of time, revenue is recognized on a straight-line basis. In situations where the performance of the Company's obligations has been satisfied when the grant is received, revenue is recognized upon receipt of the grant. Certain grants contain refund provisions. The Company reviews those refund provisions to determine the likelihood of repayment. If the likelihood of repayment of the grant is determined to be remote, the grant is recognized as revenue. If the probability of repayment is determined to be more than remote, the Company records the grant as a deferred revenue liability, until such time that the grant requirements have been satisfied.

Collaboration revenue

On July 1, 2015, the Company entered into a collaboration and license agreement (the "Collaboration Agreement") with a wholly owned subsidiary of Biogen Inc. This collaboration is discussed further in Note 7 of notes to the financial statements. The terms of this agreement and other potential collaboration or commercialization agreements the Company may enter into generally contain multiple elements, or deliverables, which may include, among others, (i) licenses, or options to obtain licenses, to its technology, and (ii) research and development activities to be performed on behalf of the collaborative partner. Payments made under such arrangements typically include one or more of the following: non-refundable, up-front license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Multiple element arrangements are analyzed to determine whether the deliverables within the agreement can be separated or whether they must be accounted for as a single unit of accounting. Deliverables under an agreement are required to be accounted for as separate units of accounting provided that (i) a delivered item has value to the customer on a stand-alone basis; and (ii) if the agreement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables within each agreement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price ("BESP") if neither VSOE nor TPE are available. Determining the best estimate of selling price for a deliverable requires significant judgment. The Company uses BESP to estimate the selling price related to licenses to its proprietary technology, since it often does not have VSOE or TPE of selling price for these deliverables. In those circumstances where it utilizes BESP to determine the estimated selling price of a license to its proprietary technology, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its best estimate of selling price, the Company evaluates whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration among multiple deliverables.

If the delivered element does not have stand-alone value, the arrangement is then accounted for as a single unit of accounting and the Company recognizes the consideration received under the arrangement as revenue on a straight-line basis over its estimated

period of performance. The Company's anticipated periods of performance, typically the terms of its research and development obligations, are subject to estimates by management and may change over the course of the collaboration agreement. Such changes could have a material impact on the amount of revenue recorded in future periods.

Milestone revenue

The Company applies the milestone method of accounting to recognize revenue from milestone payments when earned, as evidenced by written acknowledgement from the collaborator or other persuasive evidence that the milestone has been achieved and the payment is non-refundable, provided that the milestone event is substantive. A milestone event is defined as an event (i) that can only be achieved based in whole or in part on either the Company's performance or on the occurrence of a specific outcome resulting from the Company's performance; (ii) for which there is substantive uncertainty at the inception of the arrangement that the event will be achieved; and (iii) that would result in additional payments being due to the Company. Events for which the occurrence is either contingent solely upon the passage of time or the result of a counterparty's performance are not considered to be milestone events. A milestone event is substantive if all of the following conditions are met: (i) the consideration is commensurate with either the Company's performance to achieve the milestone, or the enhancement of the value to the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone; (ii) the consideration relates solely to past performance; and (iii) the consideration is reasonable relative to all the deliverables and payment terms (including other potential milestone consideration) within the arrangement.

The Company assesses whether a milestone is substantive at the inception of the arrangement. If a milestone is deemed substantive and the milestone payment is nonrefundable, the Company recognizes revenue upon the successful accomplishment of that milestone. Where a milestone is deemed non-substantive, the Company accounts for that milestone payment in accordance with the multiple element arrangements guidance and recognizes revenue consistent with the related units of accounting for the arrangement over the related performance period.

During the fiscal year ended June 30, 2016 the Company recognized milestone revenue in the amount of $5.0 million. No milestone revenues were recognized during the fiscal years ended June 30, 2015 or 2014.

Deferred revenue

Amounts received by the Company prior to satisfying the above revenue recognition criteria are recorded as deferred revenue on the balance sheet. Amounts not expected to be recognized within 12 months of the balance sheet date are classified as non-current deferred revenue.

Income taxes

The Company uses the asset and liability method for accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective income tax bases. Deferred tax assets and liabilities are measured using enacted rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled.

As required by U.S. GAAP, the Company recognizes the financial statement benefit of a tax position only after determining that the relevant tax authority would more likely than not sustain the position following an audit. For tax positions meeting the more-likely-than-not threshold, the amount recognized in the financial statements is the largest benefit that has a greater than 50 percent likelihood of being realized upon ultimate settlement with the relevant tax authority. The Company is subject to examination of its income tax returns in the federal and state income tax jurisdictions in which it operates. On December 28, 2015, the United States Internal Revenue Service, or IRS, notified the Company of an income tax audit for the tax period ending June 30, 2014. As of June 30, 2016, the Company had no liability recorded as an uncertain tax benefit. Currently, the Company cannot reasonably estimate the ultimate outcome of the IRS audit, however, it believes that it has followed applicable U.S. tax laws and will defend its income tax positions.

As of June 30, 2016 and 2015, the Company did not have any significant uncertain tax positions.

Research and development expenses

Research and development costs include costs incurred in identifying, developing and testing product candidates and generally comprise compensation and related benefits and non-cash share-based compensation to research related employees; laboratory

costs; animal and laboratory maintenance and supplies; rent; utilities; clinical and pre-clinical expenses; and payments for sponsored research, scientific and regulatory consulting fees and testing.

As part of the process of preparing financial statements, the Company is required to estimate its accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on its behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. The majority of the Company's service providers invoice the Company monthly in arrears for services performed or when contractual milestones are met. The Company makes estimates of its accrued expenses as of each balance sheet date in its financial statements based on facts and circumstances known to it at that time. The significant estimates in the Company's accrued research and development expenses are related to expenses incurred with respect to academic research centers, contract research organizations ("CROs"), and other vendors in connection with research and development activities for which it has not yet been invoiced.

There may be instances in which the Company's service providers require advance payments at the inception of a contract or in which payments made to these vendors will exceed the level of services provided, resulting in a prepayment of the research and development expense. Such prepayments are charged to research and development expense as and when the service is provided or when a specific milestone outlined in the contract is reached.

Prepayments related to research and development activities were $2.0 million and $958,000 at June 30, 2016 and 2015, respectively, and are included within the Prepaid and other current assets line item on the balance sheets.

Share-based compensation

The Company accounts for share-based awards issued to employees in accordance with ASC Topic 718, Compensation—Stock Compensation ("ASC 718") and generally recognizes share-based compensation expense on a straight-line basis over the periods during which the employees are required to provide service in exchange for the award. In addition, the Company issues stock options and restricted shares of common stock to non-employees in exchange for consulting services and accounts for these in accordance with the provisions of ASC Subtopic 505-50, Equity-Based Payments to Non-employees ("ASC 505-50"). Under ASC 505-50, share-based awards to non-employees are subject to periodic fair value re-measurement over their vesting terms.

For purposes of calculating stock-based compensation, the Company estimates the fair value of stock options using a Black-Scholes option-pricing model. The determination of the fair value of share-based payment awards utilizing the Black-Scholes model is affected by the Company's stock price and a number of assumptions, including expected volatility, expected life, risk-free interest rate and expected dividends. The expected volatility is primarily based on the historical volatility of peer company data while the expected life of the stock options is based on historical and other economic data trended into the future. The risk-free interest rate assumption is based on observed interest rates appropriate for the expected terms of the Company's stock options. The dividend yield assumption is based on the Company's history and expectation of no dividend payouts. If factors change and the Company employs different assumptions, stock-based compensation expense may differ significantly from what has been recorded in the past. If

there is a difference between the assumptions used in determining stock-based compensation expense and the actual factors which become known over time, specifically with respect to anticipated forfeitures, the Company may change the input factors used in determining stock-based compensation costs for future grants. These changes, if any, may materially impact the Company's results of operations in the period such changes are made.

Net loss per share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock, stock options, and warrants are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all annual periods presented. Therefore, basic and diluted net loss per share was the same for all annual periods presented.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

Comprehensive loss

Comprehensive loss consists of net loss and changes in equity during a period from transactions and other equity and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss for all periods presented.

New Accounting Pronouncements

In February 2016, the FASB issued Accounting Standards Update ("ASU") No. 2016-02, Leases (Topic 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet for those leases previously classified as operating leases under GAAP. The standard requires, in most instances, a lessee to recognize on its balance sheet a liability to make lease payments (the lease liability) and also a right-of-use asset representing its right to use the underlying asset for the lease term. The amendments are effective for fiscal years beginning after December 15, 2018, including interim periods within those periods, using a modified retrospective approach and early adoption is permitted. The Company is currently in the process of evaluating the impact of adoption of this standard on its financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Improvements to Employee Share-Based Payment Accounting, which amends ASC Topic 718, Compensation – Stock Compensation. The amendments simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, forfeitures, and classification on the statement of cash flows. The amendments are effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years and early adoption is permitted. The Company is currently in the process of evaluating the impact of adoption of this standard on its financial statements.

In November 2015, the FASB issued ASU No. 2015-17, Balance Sheet Classification of Deferred Taxes, requiring all deferred tax assets and liabilities, and any related valuation allowance, to be classified as noncurrent on the balance sheet. The classification change for all deferred taxes as noncurrent simplifies entities' processes as it eliminates the need to separately identify the net current and net noncurrent deferred tax asset or liability in each jurisdiction and allocate valuation allowances. The Company adopted the accounting standard with effect from the beginning of its third fiscal quarter ending March 31, 2016. The adoption of this standard did not have a material impact on the Company's financial statements.

In August 2014, the FASB issued Accounting Standard Update No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. The amendments require management to perform interim and annual assessments of an entity's ability to continue as a going concern and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. The standard applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. The Company adopted the accounting standard with effect from the beginning of its third fiscal quarter ending March 31, 2016. The adoption of this standard did not have a material impact on the Company's financial statements.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers. The guidance requires companies to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration to which the company expects to be entitled in exchange for those goods or services. It also requires enhanced disclosures about revenue, provides guidance for transactions that were not previously addressed comprehensively, and improves guidance for multiple-element arrangements. The guidance applies to any entity that either enters into contracts with customers to transfer goods or services or enters into contracts for the transfer of nonfinancial assets unless those contracts are within the scope of other standards. In July 2015, the FASB delayed the effective date of this guidance by one year. The guidance is now effective for public companies for annual periods beginning after December 15, 2017 as well as interim periods within those annual periods using either the full retrospective approach or modified retrospective approach. The Company is currently evaluating the impacts of the new guidance on its financial statements.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

(3) Investments:

Cash in excess of our immediate requirements is invested in accordance with the Company's investment policy that primarily seeks to maintain adequate liquidity and preserve capital.

The following table summarizes the Company's investments by category as of June 30, 2016 and 2015:

In thousands	June 30, 2016	June 30, 2015
Investments - Current:		
Certificates of deposit	$18,093	$10,776
Debt securities - held-to-maturity	51,571	11,678
	$69,664	$22,454
Investments - Noncurrent:		
Certificates of deposit	$2,544	$5,310
Debt securities - held-to-maturity	71,639	18,319
	$74,183	$23,629

A summary of the Company's debt securities classified as held-to-maturity is as follows:

	At June 30, 2016			
In thousands	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Investments - Current:				
U.S. government and agency obligations	$40,609	$ 12	$ (2)	$40,619
Corporate obligations	10,962	3	(1)	10,964
	$51,571	$ 15	$ (3)	$51,583
Investments - Noncurrent:				
U.S. government and agency obligations	$71,639	$ 53	$ (11)	$71,681
	$71,639	$ 53	$ (11)	$71,681

At June 30, 2015

In thousands	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Investments - Current:				
U.S. government and agency obligations	$5,244	$ 2	$ —	$5,246
Corporate obligations	6,434	1	(3)	6,432
	$11,678	$ 3	$ (3)	$11,678
Investments - Noncurrent:				
U.S. government and agency obligations	$16,816	$ 2	$ (8)	$16,810
Corporate obligations	1,503	—	—	1,503
	$18,319	$ 2	$ (8)	$18,313

The amortized cost and fair value of held-to-maturity debt securities as of June 30, 2016, by contractual maturity, were as follows:

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

In thousands	Amortized Cost	Fair Value
Due in one year or less	$51,571	$51,583
Due after one year through two years	71,639	71,681
	$123,210	$123,264

The Company believes that the unrealized losses disclosed above were primarily driven by interest rate changes rather than by unfavorable changes in the credit ratings associated with these securities and as a result, the Company continues to expect to collect the principal and interest due on its debt securities that have an amortized cost in excess of fair value. At each reporting period, the Company evaluates securities for impairment when the fair value of the investment is less than its amortized cost. The Company evaluated the underlying credit quality and credit ratings of the issuers, noting neither a significant deterioration since purchase nor other factors leading to an other-than-temporary impairment. Therefore, the Company believes these losses to be temporary. As of June 30, 2016, the Company did not have any intent to sell any of the securities that were in an unrealized loss position at that date.

(4) Fair Value Measurements:
Certain assets and liabilities are measured at fair value in the Company's financial statements or have fair values disclosed in the notes to the financial statements. These assets and liabilities are classified into one of three levels of a hierarchy defined by GAAP. The Company's assessment of the significance of a particular item to the fair value measurement in its entirety requires judgment, including the consideration of inputs specific to the asset or liability.

The following methods and assumptions were used to estimate the fair value and determine the fair value hierarchy classification of each class of financial instrument included in the table below:

Cash and Cash Equivalents. The carrying value of cash and cash equivalents approximates fair value as maturities are less than three months.

Certificates of Deposit. The Company's certificates of deposit are placed through an account registry service. The fair value measurement of the Company's certificates of deposit is considered Level 2 of the fair value hierarchy as the inputs are based on quoted prices for identical assets in markets that are not active. The carrying amounts of the Company's certificates of deposit reported in the balance sheets approximate fair value.

Debt securities – held-to-maturity. The Company's investments in debt securities classified as held-to-maturity generally include U.S. Treasury Securities, government agency obligations and corporate obligations. U.S. Treasury Securities are valued using quoted market prices. Valuation adjustments are not applied. Accordingly, U.S. Treasury Securities are considered Level 1 of the fair value hierarchy. The fair values of U.S. government agency obligations and corporate obligations are generally determined using recently executed transactions, broker quotes, market price

quotations where these are available or other observable market inputs for the same or similar securities. As such, the Company classifies its investments in U.S. government agency obligations and corporate obligations within Level 2 of the hierarchy.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

The following fair value hierarchy table presents information about each major category of the Company's financial assets and liabilities measured at fair value on a recurring basis:

In thousands	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)	Total Fair Value	Total Carrying Value
June 30, 2016					
Cash and cash equivalents	$28,868	$ —	$ —	$28,868	$28,868
Certificates of deposit	—	20,626	—	20,626	20,637
Held-to-maturity investments:					
Corporate obligations	—	10,964	—	10,964	10,962
U.S. government and agency obligations	73,809	38,491	—	112,300	112,248
Total assets	$102,677	$ 70,081	$ —	$172,758	$172,715
June 30, 2015					
Cash and cash equivalents	$39,187	$ —	$ —	$39,187	$39,187
Certificates of deposit	—	16,086	—	16,086	16,086
Held-to-maturity investments:					
Corporate obligations	—	7,935	—	7,935	7,937
U.S. government and agency obligations	3,824	18,232	—	22,056	22,060
Total assets	$43,011	$ 42,253	$ —	$85,264	$85,270

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

(5) Property and Equipment, Net:
Property and equipment consists of the following:

	At June 30,	
In thousands	2016	2015
Laboratory equipment	$2,414	$1,246
Leasehold improvements	883	8
Office equipment	514	152
Property and equipment, gross	3,811	1,406
Less: Accumulated depreciation and amortization	(1,184)	(928)
Property and equipment, net	$2,627	$478

Depreciation and amortization expense of $319,000, $126,000 and $92,000 was recorded for each of the fiscal years ended June 30, 2016, 2015 and 2014, respectively.

(6) Intangible Assets, Net:
Intangible assets subject to amortization consist of the following:

	At June 30, 2016		
In thousands	Cost	Accumulated Amortization	Net of Accumulated Amortization
Patents	$1,982	$ (1,035)	$ 947
Licenses	1,240	(907)	333
Other	87	(46)	41
Intangible assets, net	$3,309	$ (1,988)	$ 1,321

	At June 30, 2015		
			Net of

In thousands	Cost	Accumulated Amortization	Accumulated Amortization
Patents	$1,935	$ (875)	$ 1,060
Licenses	1,180	(832)	348
Other	73	(33)	40
Intangible assets, net	$3,188	$ (1,740)	$ 1,448

Amortization expense related to intangible assets for the years ended June 30, 2016, 2015 and 2014 was $248,000, $250,000 and $242,000, respectively.

Estimated amortization expense (in thousands) for the next five years and thereafter is as follows:

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

Fiscal Year Ending June 30,	Amount
2017	$ 246
2018	233
2019	188
2020	184
2021	159
Thereafter	311
	$ 1,321

(7) Collaboration with Biogen:

On July 1, 2015, the Company entered into a Collaboration Agreement with Biogen, pursuant to which the Company and Biogen will collaborate to develop, seek regulatory approval for and commercialize gene therapy products to treat XLRS, XLRP, and discovery programs targeting three indications based on the Company's adeno-associated virus vector technologies. The Collaboration Agreement became effective on August 14, 2015.

Under the Collaboration Agreement, the Company will conduct all development activities through regulatory approval in the United States for the XLRS program, and all development activities through the completion of the first in human clinical trial for the XLRP program. In addition, the Collaboration Agreement provides for discovery programs targeting three indications whereby the Company will conduct discovery, research and development activities for those additional drug candidates through the stage of clinical candidate designation, after which, Biogen may exercise an option to continue to develop, seek regulatory approval for and commercialize the designated clinical candidate. In February 2016, the Company announced Biogen's selection of adrenoleukodystrophy as the non-ophthalmic indication of the three discovery programs. Under the terms of the Collaboration Agreement, the Company, in part through its participation in joint committees with Biogen, will participate in overseeing the development and commercialization of these specific programs.

The Company has granted to Biogen with respect to the XLRS and XLRP programs, and upon exercise of the option for the applicable discovery program, an exclusive, royalty-bearing license, with the right to grant sublicenses, to use adeno-associated virus vector technology and other technology controlled by the Company for the licensed products or discovery programs developed under the Collaboration Agreement. Biogen and the Company have also granted each other worldwide licenses, with the right to grant sublicenses, of their respective interests in other intellectual property developed under the collaboration outside the licensed products or discovery programs.

Activities under the Collaboration Agreement were evaluated under ASC 605-25, Revenue Recognition—Multiple Element Arrangements, as amended by ASU 2009-13, Revenue Recognition ("ASC 605-25"), to determine if they represented a multiple element revenue arrangement. The Collaboration Agreement includes the following significant deliverables: (1) for each of the XLRS and XLRP programs, exclusive, royalty-bearing licenses, with the right to grant sublicenses, to use adeno-associated virus vector technology and other technology controlled by the Company for the purpose of researching, developing, manufacturing and commercializing licensed products developed under the arrangement (the "License Deliverables"); (2) for each of the three discovery programs, exercisable options to obtain

exclusive licenses to develop, seek regulatory approval for and commercialize any of the designated clinical candidates under such discovery programs (the "Option Deliverables"); and (3) the performance obligations to conduct research and development activities through (a) regulatory approval in the United States, in the case of the XLRS program; (b) completion of the first in human clinical trial, in the case of the XLRP program; and (c) the stage of clinical candidate designation, in the case of each of the three discovery programs (the "R&D Activity Deliverables").

The Company determined that all of the License Deliverables and Option Deliverables did not have stand-alone value and did not meet the criteria to be accounted for as separate units of accounting under ASC 605-25. The factors considered by the Company in making this determination included, among other things, the unique and specialized nature of its proprietary technology and intellectual property, and the development stages of each of the XLRS, XLRP and the discovery programs targeting three indications. Accordingly, the License Deliverables under each of the XLRS and XLRP programs and the Option Deliverables under each of the discovery programs have been combined with the R&D Activity Deliverables associated with each related program and as a result, the Company's separate units of accounting under its collaboration with Biogen, comprise the XLRS program, the XLRP program, and each of the three discovery programs.

Under the Collaboration Agreement, the Company received a non-refundable upfront payment of $94.0 million in August 2015 which it recorded as deferred revenue. This upfront payment of $94.0 million was allocated among the separate units of

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

accounting discussed above using the relative selling price method. In addition to the Collaboration Agreement, on July 1, 2015, the Company also entered into an equity agreement with Biogen. Under the terms of this equity agreement, Biogen purchased 1,453,957 shares of the Company's common stock at a price of $20.63 per share, for an aggregate cash purchase price of $30.0 million which the Company also received in August 2015. The shares issued to Biogen represented approximately 8.1% of the Company's outstanding common stock on a post-issuance basis, calculated on the number of shares that were outstanding at June 30, 2015, and constitute restricted securities that may not be resold by Biogen other than in a transaction registered under, or pursuant to an exemption from the registration requirements of, the Securities Act of 1933, as amended.

Accounting standards for multiple element arrangements contain a presumption that separate contracts negotiated or entered into at or near to the same time with the same entity were likely negotiated as a package and should be evaluated as a single agreement. The Company determined that the price of $20.63 paid by Biogen included a premium of $7.45 per share over the fair value of the company's stock price, calculated based upon the stock price on the date of close of the agreement and adjusted for lack of marketability due to restrictions. Accordingly, the total premium of $10.8 million was also recorded as deferred revenue and, together with the $94.0 million, allocated to the separate units of accounting identified above using the relative selling price method as discussed in Note 2 to these financial statements. The Company will record revenue based on the revenue recognition criteria applicable to each separate unit of accounting. For amounts received up-front and initially deferred, the Company will recognize the deferred revenue on a straight-line basis over the estimated service periods in which it is required to perform the research and development activities associated with each unit of accounting, anticipated to be between 2 and 3 years.

During the fiscal year ended June 30, 2016, the Company recognized revenue of approximately $46.8 million from its collaboration with Biogen. Below is a summary of the components of the collaboration revenue:

	Fiscal year ended June 30,		
	2016	2015	2014
	(dollars in thousands)		
Amortization of non-refundable upfront fees	$41,166	$ —	$ —
Milestone revenue	5,000	—	—
Other	585	—	—
Total collaboration revenue	$46,751	$ —	$ —

During the fiscal year ended June 30, 2016, the Company recorded and received $5.0 million of milestone revenue after having achieved a patient enrollment-based milestone under the Collaboration Agreement. Other revenue is primarily comprised of reimbursable costs for post-funding development activities that were conducted by the Company during the fiscal year.

As a result of the upfront payment of $94.0 million made by Biogen and achievement of the $5.0 million milestone as discussed above, the Company became liable to various research partner institutions for sub-license and other payments under existing agreements with such institutions. These agreements obligate the Company to pay to each research partner institution, amounts that range from 5% to 10% of certain proceeds received from collaboration and other arrangements, including any milestone payments received under such arrangements. Accordingly, the Company recorded total collaboration costs of approximately $12.0 million associated with such obligations, including $636,000 of expense that was settled during fiscal year 2016 by the issuance of 40,000 shares of the Company's common stock to a research partner institution, pursuant to the terms of the existing agreement with that institution. The remainder of these sub-license and milestone fees were fully paid in cash during the fiscal year ended June 30, 2016.

The Company is also eligible to receive payments of up to $467.5 million based on the successful achievement of future milestones under the two lead programs and up to $592.5 million based on the exercise of the option for and the successful achievement of future milestones under the three discovery programs. Biogen will pay revenue-based royalties for each licensed product at tiered rates ranging from high single digit to mid-teen percentages of annual net sales of the XLRS or XLRP products and at rates ranging from mid-single digit to low-teen percentages of annual net sales for the discovery products. Due to the uncertainty surrounding the achievement of the future milestones, such payments were not considered fixed or determinable at the inception of the Collaboration Agreement and accordingly, will not be recognized as revenue unless and until they become earned. The Company is not able to reasonably predict if and when the remaining milestones will be achieved.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

(8) Share-based Compensation Plans:

The Company uses stock options and awards of restricted stock to provide long-term incentives for its employees, non-employee directors and certain consultants. The Company has two equity compensation plans under which awards are currently authorized for issuance, the 2013 Employee Stock Purchase Plan and the 2013 Equity and Incentive Plan. No awards have been issued to date under the 2013 Employee Stock Purchase Plan and all of the 128,571 shares previously authorized under this plan remain available for issuance. As of June 30, 2016, the total number of shares available for issuance under the 2013 Equity and Incentive Plan was 534,730.

The Compensation Committee of the Board of Directors, as the plan administrator, has the authority to select the individuals to whom share-based awards are granted and to determine the terms of each award, including (i) the number of shares of common stock subject to a stock option or restricted share award; (ii) the date on which the stock option becomes exercisable; (iii) the option exercise price, which, in the case of incentive stock options, must be at least 100% (110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's stock) of the fair market value of the common stock as of the date of grant; (iv) the vesting term; and (v) the duration of the option (which, in the case of incentive stock options, may not exceed ten years). Employee options typically vest over a three- or four-year period.

A summary of the stock option activity is as follows:

	For the years ended June 30,					
	2016		2015		2014	
(In thousands, except per share amounts)	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding, beginning of year	1,484	$ 11.83	1,024	$ 6.21	380	$ 1.45
Granted	675	17.08	615	19.58	715	8.45
Exercised	(59)	4.77	(46)	3.24	(61)	3.24
Forfeited	(57)	13.90				
Expired	(6)	15.50	(109)	6.43	(10)	3.50
Outstanding, end of year	2,037	$ 13.71	1,484	$ 11.83	1,024	$ 6.21
Exercisable, end of year	872		424		200	
Weighted average fair value of options granted during the year	$11.83		$14.39		$6.18	

The following table summarizes information about stock options outstanding:

(Number of options in thousands; remaining lives in years)	At June 30, 2016		2015	
Exercise Price	Number of Options	Weighted Average Contractual Life Remaining	Number of Options	Weighted Average Contractual Life Remaining
$0.35 to $4.90	509	6.48	581	7.07
$12.00 to $15.90	412	8.35	288	8.72
$16.00 to $19.87	940	8.89	436	9.50
$20.00 to $24.62	176	8.58	179	9.58
	2,037		1,484	

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

The following table summarizes information about stock options exercisable:

	At June 30,	
	2016	2015
Exercise Price	Number of Options (in thousands)	
$0.35 to $4.90	396	333
$12.00 to $15.90	160	91
$16.00 to $19.87	239	—
$20.00 to $24.62	77	—
	872	424

As of June 30, 2016, the aggregate intrinsic value of all outstanding stock options was $6.1 million and for exercisable stock options was $4.7 million. The intrinsic value per option at June 30, 2016 is calculated as the difference between the exercise price of the underlying option and the closing price of the Company's common stock of $14.13 on that date, and applies only to those awards having an exercise price currently below this closing price. The total fair value of options that vested during the fiscal years ended June 30, 2016, 2015, and 2014 was $4.5 million, $1.9 million, and $280,000, respectively.

Unrecognized compensation expense related to non-vested employee stock options amounted to $11.5 million as of June 30, 2016. Such compensation expense is expected to be recognized over a weighted-average period of 2.71 years.

In accounting for stock options to non-employees, the fair value of services related to the options granted are generally recorded as an expense as these services are provided to the Company over the relating service periods. The Company re-measures any non-vested, non-employee options to fair value at the end of each reporting period using the Black-Scholes pricing model.

Share-based compensation expense related to stock options awarded to employees, non-employee directors and consultants amounted to $4.9 million, $2.3 million and $825,000 for the fiscal years ended June 30, 2016, 2015 and 2014, respectively.

Share-based compensation expense related to restricted shares of common stock awarded to employees and consultants amounted to $167,000 and $524,000 for the fiscal years ended June 30, 2016 and 2015, respectively. The Company did not record any share-based compensation expense associated with its restricted shares of common stock during the fiscal year ended June 30, 2014.

Total share-based expense associated with stock options and restricted shares of common stock was allocated as follows:

	For the fiscal years ended June 30,		
(In thousands)	2016	2015	2014
General and administrative	$2,860	$1,912	$748
Research and development	2,147	908	77
	$5,007	$2,820	$825

The fair value of each option granted is estimated on the grant date using the Black-Scholes stock option pricing model. The following assumptions were made in estimating fair value:

	Fiscal Years Ended June 30,		
Assumption	2016	2015	2014
Dividend yield	0.00 %	0.00 %	0.00 %
Expected term	6.00 to 6.25 years	6.00 to 10.00 years	6.00 to 10.00 years
Risk-free interest rate	1.41% to 1.86%	1.49% to 2.58%	2.04% to 2.31%
Expected volatility	78.85 %	85.68 %	85.00 %

The dividend yield is based upon the assumption that the Company will not declare a dividend over the life of the options. Since adopting ASC 718, the Company has been unable to use historical employee exercise and option expiration data to estimate the expected term assumption for the Black-Scholes grant-date valuation. The Company therefore has utilized the “simplified”

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

method, as prescribed by the SEC's Staff Accounting Bulletin No. 107, Share-Based Payment, to estimate on a formula basis the expected term of our stock options considered to have "plain vanilla" characteristics. The risk-free interest rate is based on the U.S. Treasury yield curve on the date of valuation. As a relatively new public company, the Company does not have sufficient history to estimate the volatility of its common stock price or the expected life of the options. The Company calculates expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of its common stock is sufficient to measure expected volatility for future option grants. The group of similar publicly traded companies was determined based upon companies considered to be direct competition or having been presented by independent parties as a "comparable" company based upon market sector. In determining this group, the Company has excluded "large-cap" entities. Forfeitures are estimated at the time of the grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Share-based compensation expense recognized in the statements of operations for the fiscal years ended June 30, 2016, 2015 and 2014 does not reflect tax related effects on stock-based compensation given the Company's historical and anticipated operating losses and offsetting changes in its valuation allowance that fully reserves against potential deferred tax assets.

(9) Commitments and Contingencies:
Operating Leases

Alachua, Florida

The Company's corporate headquarters are located in Alachua, Florida. In January 2016, the Company moved into a new combined-use facility consisting of approximately 21,000 square feet of laboratory and office space. The initial lease term for this facility is 10 years and the Company has options to extend the term of the lease for three additional five-year periods. The Company's prior leased facilities encompassed approximately 7,000 square feet of office and laboratory space. The operating leases associated with the prior facilities expired in December 2015.

Cambridge, Massachusetts

In August 2015, the Company entered into a two-year lease to occupy approximately 3,000 square feet of office and laboratory space in Cambridge, Massachusetts. This additional facility primarily focuses on business development, pharmacology, and basic research and development.

For the fiscal years ended June 30, 2016, 2015 and 2014, rent expense under these operating leases amounted to $587,000, $167,000 and $123,000, respectively. Future annual minimum lease payments (in thousands) under these non-cancelable operating leases are as follows:

Fiscal Year Ending June 30,	Amount
2017	$ 804
2018	582
2019	538
2020	538
2021	538
Thereafter	2,421
	$ 5,421

License and Other Agreements

Under various agreements, the Company will be required to pay royalties and milestone payments upon the successful development and commercialization of products. The Company has entered into funding agreements with various not-for-profit organizations. The Company may become obligated to pay royalties on net product sales of any collaboration product that it successfully develops and subsequently commercializes or, if it out-licenses rights to a collaboration product, a specified percentage of certain payments it receives from its licensee. The Company is not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. The Company’s obligation to make such payments would end upon its payment of a specified amount.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

The Company is also party to various agreements entered into in the ordinary course of its business, principally relating to licensed technology. At June 30, 2016, the Company had nine license agreements with six different entities, including five with the University of Florida Research Foundation. The Company is responsible for all costs related to preparation, filing, issuance, prosecution and maintenance of the underlying patents covered in the license agreements. The Company is required to pay minimum annual royalty and license maintenance for all licenses until such time when the license is terminated by either expiration of underlying patents or voluntary termination by either party per the agreement.

These license agreements also require future payments related to milestones or royalties on future sales of specified products. Payments under these agreements generally become due and payable only upon achievement of certain developmental, regulatory or commercial milestones. Because the achievement of these milestones had not occurred as of June 30, 2016, such contingencies have not been recorded in the Company's financial statements. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory and commercial milestones. There is uncertainty regarding the various activities and outcomes needed to reach these milestones, and they may not be achieved. The Company may terminate its license agreements with zero to ninety days written notice depending upon the terms of each specific agreement.

The Company's expense associated with annual royalty and milestone payments was $963,000, $122,000 and $87,000 for each of the fiscal years ended June 30, 2016, 2015 and 2014, respectively. All royalty and milestone payments are included within research and development expenses in the statement of operations.

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to these agreements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners or customers, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The term of these indemnification agreements is generally perpetual. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. From time to time, the Company may be involved in claims and legal actions that arise in the normal course of business. Management has no reason to believe that the outcome of any such legal actions would have a significant adverse effect on the Company's financial position, results of operations or cash flows.

(10) Income Taxes:

For the fiscal years ended June 30, 2016, 2015 and 2014, the Company did not record a current or deferred income tax expense or benefit.

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets (liabilities) are

comprised of the following:

In thousands	At June 30, 2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$27,103	$28,559
Research and development tax credit carryforwards	8,771	7,941
Accruals and other	1,599	418
Gross deferred tax assets	37,473	36,918
Deferred tax asset valuation allowance	(37,412)	(36,845)
Total deferred tax assets, net of valuation allowance	61	73
Deferred tax liabilities:		
Depreciation and amortization	(61)	(73)
Total deferred tax liabilities	(61)	(73)
Net deferred tax asset (liability)	$—	$—

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

As of June 30, 2016, the Company had net operating losses of approximately $70.0 million that may be applied against future taxable income and expire in various years ranging from 2022 to 2036. As of June 30, 2016, the Company also had research and development tax credits of approximately $8.8 million that may provide future tax benefits and expire from 2027 to 2045.

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on its history of operating losses, the Company has concluded that as of June 30, 2016, it is more likely than not that the benefit of its deferred tax assets will not be realized. Therefore, any tax benefits to be realized in future years as a result of the utilization of the Company's net operating loss carry forwards as of June 30, 2016, computed based on statutory federal and state rates, are completely offset by valuation allowances established because realization of the deferred tax benefits are not considered more likely than not as of that date. The valuation allowance increased by approximately $567,000 during the fiscal year ended June 30, 2016, due primarily to the impact of temporary differences and research and development tax credits generated in the fiscal year, partially offset by the utilization of net operating loss carryforwards to offset taxable income that was generated during the period. On July 1, 2015, the Company entered into a collaboration agreement with Biogen, under which it received a non-refundable upfront payment of $94.0 million. This collaboration agreement is discussed in more detail in Note 7 of notes to the financial statements. The Company has evaluated the income tax implications of this collaboration agreement and believes that while this transaction did not result in any current income tax liabilities, it could have an impact on management's assessment of the realizability of deferred tax assets in future periods.

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	For the years ended June 30,		
	2016	2015	2014
Federal income tax benefit at statutory rate	(34)%	(34)%	(34)%
State income tax, net of federal benefit	(4)%	(4)%	(4)%
Permanent differences	52 %	9 %	9 %
Research and development tax credits	(60)%	(18)%	(2)%
Other	85 %	1 %	1 %
Change in valuation allowance	(39)%	46 %	30 %
Effective income tax rate	0 %	0 %	0 %

Under the provisions of the Internal Revenue Code, the Company's net operating loss and tax credit carry forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carry forwards may become 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 percent, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount

of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Since its inception, the Company has completed several financings and sales of common stock which have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code. Subsequent ownership changes may further affect the limitation in future years.

For fiscal years through June 30, 2016, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development tax credit carry forwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position at June 30, 2016 and 2015. A full valuation allowance has been provided against the Company's research and development tax credits and, if an adjustment were to be required, this adjustment would be offset by an adjustment to the deferred tax asset established for the tax credit carry forwards and the valuation allowance.

The Company files income tax returns in the United States and in the states of Florida, Massachusetts and Oregon. The federal and state returns are generally subject to tax examinations for the tax years ended June 30, 2012 through June 30, 2016. To the extent the Company has tax attribute carry forwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service, or state authorities, to the extent such attributes are utilized in a future period. On December 28, 2015, the United States Internal Revenue Service, or IRS, notified the Company of an income tax audit for the tax period ending June 30, 2014. As of June 30, 2016, the Company had no liability recorded as an uncertain tax

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

benefit. Currently, the Company cannot reasonably estimate the ultimate outcome of the IRS audit, however, it believes that it has followed applicable U.S. tax laws and will defend its income tax positions.

The Company's policy is to recognize interest and penalties related to uncertain tax positions in income tax expense. As of June 30, 2016 and 2015, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations for any of the fiscal years ended June 30, 2016, 2015 and 2014.

(11) Accrued Expenses:

Accrued expenses as of June 30, 2016 and 2015 consisted of the following:

	At June 30,	
In thousands	2016	2015
Research and development-related	$4,923	$2,679
Compensation-related	1,591	772
	$6,514	$3,451

(12) Defined Contribution Plan:

The Company sponsors an employee 401(k) salary deferral plan ("401(k) Plan") that covers substantially all of its employees and is administered through its staff leasing company. Under the 401(k) Plan, employees may elect to defer up to 25% of their compensation per year (subject to a maximum limit prescribed by federal tax law) and the Company matches a portion of such employee contributions up to a maximum of 4% of the eligible salary. The Company's matching contributions to the 401(k) Plan amounted to $162,000, $90,000 and $60,000 for each of the fiscal years ended June 30, 2016, 2015 and 2014, respectively.

(13) Common Stock and Stockholders' Equity:

Reverse Stock Split

On March 4, 2014, the Company effected a 1-for-35 reverse stock split of its common stock, whereby each share of common stock, $0.001 par value, outstanding immediately prior to that date was combined, reclassified and changed

into one thirty-fifth (1/35) of a fully paid and non-assessable share of common stock. The accompanying financial statements and notes to the financial statements give retroactive effect to the reverse split for all periods presented.

Common Stock

On April 1, 2014, the Company completed its IPO in which it sold 4,166,667 shares of common stock at a price of $12.00 per share. The shares began trading on the Nasdaq Global Select Market on March 27, 2014. An additional 625,000 shares were sold pursuant to the exercise of the underwriters' over-allotment option, also at the offering price of $12.00 per share. The aggregate net proceeds received by the Company from the offering, including exercise of the over-allotment option, amounted to $51.6 million, net of underwriting discounts and commissions and other issuance costs incurred by the Company. Upon the closing of the IPO, all outstanding shares of convertible preferred stock converted into 9,120,081 shares of common stock; and warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for 49,811 shares of common stock, resulting in the reclassification of the related convertible preferred stock warrant liability of $551,000 to additional paid-in capital.

On July 30, 2014, the Company completed a public offering in which the Company sold 2,000,000 shares of common stock at a public offering price of $15.00 per share. On August 1, 2014, the Company sold an additional 300,000 shares of common stock at a public offering price of $15.00 per share pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the public offering that was completed in July 2014. The aggregate net proceeds received by the Company from the offering, including the exercise of the overallotment option, amounted to $32.0 million, net of underwriting discounts and commissions.

In connection with its entry into the Collaboration Agreement with Biogen described in note 7 of these financial statements, the Company also entered into an equity agreement with Biogen on July 1, 2015. Under the terms of this equity agreement, Biogen purchased 1,453,957 shares of the Company's common stock, at a price of $20.63 per share, for an aggregate cash purchase price of $30.0 million. These cash proceeds were received from Biogen in August 2015. The shares issued to Biogen constitute

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

restricted securities that may not be resold by Biogen other than in a transaction registered under the Securities Act of 1933, as amended, or pursuant to an exemption from such registration requirement.

As of June 30, 2016, there were 150,000,000 shares of $0.001 par value common stock that were authorized to be issued. As of that date, a total of 18,052,956 shares of common stock were issued, of which 18,047,956 shares were outstanding.

The following shares of common stock were reserved for future issuance as of June 30, 2016:

In thousands	June 30, 2016
Common stock warrants	17
Stock options issued and outstanding	2,037
Authorized for future grant under the 2013 Employee Stock Purchase Plan	129
Authorized for future grant under the 2013 Equity and Incentive Plan	535
	2,718

Former Series B purchase rights

In November 2012, the Company entered into a Series B-1, B-2 and B-3 Preferred Stock Purchase Agreement, or Series B Purchase Agreement, which authorized the sale of up to 290,781,972 shares of convertible preferred stock in three separate tranches of Series B-1, Series B-2 and Series B-3 preferred stock, respectively. Simultaneously with the execution of the Series B Purchase Agreement, the Company issued and sold an aggregate of 66,147,709 shares of Series B-1 preferred stock at a price per share of $0.1297. The Series B Purchase Agreement provided that the holders of the Series B-1 shares, or Series B holders, were also entitled to purchase up to an aggregate of 140,542,178 shares of Series B-2 preferred stock for an aggregate purchase price equal to $18.2 million, or second tranche, and up to an aggregate of 82,670,167 shares of Series B-3 preferred stock for an aggregate purchase price equal to $10.7 million, or third tranche. The price per share and number of shares to be issued in exchange for such amount was to be determined separately for each tranche by reference to which, if any, of three milestones specified in the agreement had been satisfied by the Company.

The purchase rights were legally separable and exercisable apart from the Series B-1 shares and, because representatives of the Series B holders held a majority of the seats on the board of directors, the decision to complete the second and third tranche was deemed to be outside the Company’s control. The Company therefore recorded, at the time of entry into the Series B Purchase Agreement, a Series B purchase rights liability of $1.7 million for the fair value of its obligation to sell the Series B-2 and Series B-3 preferred stock in the second and third tranche. The Series B purchase rights liability was valued separately for each series using the Black-Scholes option-pricing method to assign a value to the purchase right relating to that series under each of the possible applicable valuation scenarios, depending on which milestones were met, with each scenario being assigned an estimated probability as of the valuation date. The aggregate of these probability-weighted valuations was assigned as the value of the purchase right for each tranche. The initial fair value of the Series B purchase rights liability was estimated to be $0.6 million for the

second tranche and $1.1 million for the third tranche. The total value allocated to the Series B purchase rights reduced the amount allocated to the carrying value of the Series B-1 preferred stock on the Company's balance sheet.

The most significant and judgmental inputs driving the fair value of the Company's Series B purchase rights were the assumptions regarding the fair value of the underlying preferred shares and the volatility factor. With all other inputs constant, an increase or decrease in the assumed fair value of the preferred shares would have resulted in a higher or lower estimate of the fair value of the Series B purchase rights, respectively, although there would not have been a direct correlation. Similarly, an increase or decrease in the assumed volatility factor would have resulted in a higher or lower estimate of the fair value of the Series B purchase rights, respectively.

In October 2013, the Series B holders exercised their rights with respect to the third tranche and on November 5, 2013, the Company sold to the Series B holders an aggregate of 58,816,897 shares of its Series B-3 preferred stock at a price per share of $0.1823 (or $6.38 on an as-converted to common stock basis), for gross cash proceeds of $10.7 million. In connection with the closing of the third tranche, the Company and the Series B holders amended the terms of the Series B purchase agreement to provide that if the two remaining milestones specified in the Series B Purchase Agreement were not satisfied by September 2014, the Series B holders who continued to hold shares of Series B-3 preferred stock would be entitled to receive an aggregate of approximately 13,387,000 additional shares of Series B-3 preferred stock. This right was extinguished upon the conversion to common stock of all the outstanding shares of preferred stock upon closing of the Company's initial public offering.

APPLIED GENETIC TECHNOLOGIES CORPORATION

NOTES TO FINANCIAL STATEMENTS— (Continued)

FOR THE YEARS ENDED JUNE 30, 2016, 2015 AND 2014

During the year ended June 30, 2014, the Company recorded a change in value of the Series B purchase right liability of $2.9 million to other expense, and $5.0 million allocated to the Series B-3 purchase right immediately prior to the closing of the third tranche was reallocated to the carrying value of the Series B-3 preferred stock.

In connection with the consummation of the Company's IPO on April 1, 2014, all Series A Preferred Stock and Series B Preferred Stock converted into 9,120,081 shares of common stock on that date. As a result, none of the convertible series of preferred stock were issued or outstanding at June 30, 2016, 2015 and 2014.

Former warrant liabilities

As of June 30, 2013, the Company had warrants outstanding to purchase shares of its Series A-1, Series A-1A and Series B-1 preferred stock. Because the Series A-1, Series A-1A and Series B-1 preferred stock were subject to redemption under circumstances outside of the Company's control, the outstanding shares of these series of preferred stock were presented as temporary equity for those periods. Consequently, the warrants to purchase shares of Series A-1, Series A-1A and Series B-1 preferred stock were accounted for as liabilities and adjusted to fair value at the end of each reporting period. The fair value of the warrants classified as liabilities was estimated using the Black-Scholes option pricing model. The estimates in the Black-Scholes option pricing model were based, in part, on subjective assumptions, including stock price volatility, term of the warrants, risk free interest rate, dividend yield, and fair value of the preferred stock underlying the warrants. The gain or loss associated with the change in the fair value of the preferred stock warrant liability from the prior period was recognized as a component of other (expense) income, net. The fair value of the warrants on the date of issuance, and on each financial reporting date for those warrants classified as liabilities, was estimated using the Black-Scholes option pricing model.

Upon the closing of the Company's initial public offering, these warrants were converted into warrants exercisable for common stock.

(14) Quarterly Financial Information (Unaudited):

Summarized quarterly information for the two fiscal years ended June 30, 2016 and 2015, respectively, is as follows:

	Fiscal Year 2016 by Quarter:			
In thousands, except per share data	First	Second	Third	Fourth
Revenue	$11,062	$12,189	$11,997	$12,113
Income (loss) from operations	$(9,213)	$2,870	$1,767	$2,487
Net income (loss)	$(9,123)	$3,045	$1,969	$2,728
Net earnings (loss) per common share, basic and diluted	$(0.53)	$0.17	$0.11	$0.15

	Fiscal Year 2015 by Quarter:			
In thousands, except per share data	First	Second	Third	Fourth
Revenue	$705	$652	$284	$713
Loss from operations	$(5,409)	$(4,702)	$(6,391)	$(8,030)
Net loss	$(5,381)	$(4,650)	$(6,326)	$(7,961)
Net loss per common share, basic and diluted	$(0.34)	$(0.28)	$(0.38)	$(0.48)

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is recorded, processed, summarized and reported within the time periods specified in the rules and forms, and that such information is accumulated and communicated to us, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, we recognize that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, as ours are designed to do, and we necessarily were required to apply our judgment in evaluating whether the benefits of the controls and procedures that we adopt outweigh their costs.

As required by Rule 13a-15(b) under the Exchange Act, an evaluation of the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of June 30, 2016 was conducted under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. As a result of the material weakness in internal control over financial reporting relating to the design and operation of our closing and financial reporting processes disclosed below, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were not effective at the reasonable assurance level as of June 30, 2016.

Management's Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate "internal control over financial reporting," as such term is defined under Rule 13a-15(f) of the Exchange Act. We maintain internal control over financial reporting 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. Internal control over financial reporting includes maintaining records that in reasonable detail accurately and fairly reflect our transactions; providing reasonable assurance that transactions are recorded as necessary for preparation of our financial statements; providing reasonable assurance that receipts and expenditures of our assets are made in accordance with management's authorization; and providing reasonable assurance that unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements would be prevented or detected on a timely basis.

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. Therefore, internal control over financial reporting determined to be effective provides only reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Management assessed the effectiveness of the Company's internal control over financial reporting as of June 30, 2016. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control — Integrated Framework (2013). Based on this assessment, management has concluded that, as of June 30, 2016, a material weakness in internal control over

financial reporting relating to the design and operation of our closing and financial reporting processes still existed and, as a result, the Company did not maintain effective internal control over financial reporting as of June 30, 2016. Notwithstanding this material weakness in internal control over financial reporting relating to the design and operation of our closing and financial reporting processes, our management has concluded that the financial statements included in this Annual Report on Form 10-K present fairly, in all material respects, our financial position, results of operations and cash flows for the periods presented in conformity with accounting principles generally accepted in the United States.

We are not required to comply with the auditor attestation requirement of Section 404 of the Sarbanes-Oxley Act while we qualify as an “emerging growth company” as defined in the JOBS Act. Subject to earlier triggers and limitations, we expect to remain an emerging growth company under the JOBS Act for up to five years from the end of the fiscal year in which our initial public offering closed, which was April 1, 2014.

Material Weaknesses in Internal Control over Financial Reporting

Management previously identified and disclosed a material weakness in our internal control over financial reporting at June 30, 2015 which related to the design and operation of our closing and financial reporting processes. Specifically, management concluded

that this material weakness in our internal control over financial reporting was due to the fact that we did not have the appropriate resources with the appropriate level of experience and technical expertise to oversee our closing and financial reporting processes.

In order to address this material weakness, we took the following actions in fiscal year 2016:

- we hired an additional employee during the second half of fiscal year 2016 to provide further support to our finance and accounting team. The finance and accounting team now comprises of a total of six employees, including our Chief Financial Officer and our Controller;
- we continued to provide functional and system training to employees and to prepare detailed documentation to clearly define key tasks and actions, as well as the positions responsible for those tasks and actions . During fiscal year 2016, we also engaged the services of a consultant to assist in documenting and formalizing our accounting policies and internal control processes and to help strengthen supervisory reviews by our management; and
- we continued to design and implement monthly manual controls to manage our financial reporting close processes and to help ensure an adequate level of segregation of duties within our finance and accounting function. Also, with effect from the beginning of fiscal year 2016, we completed the implementation of and began using a new accounting software system and new equity compensation management software. We believe this automation has improved the level of our segregation of duties and further enhanced our processes associated with general accounting and financial reporting, including the accounting for our share-based compensation accounts.

We have completed the documentation and review of the corrective actions described above and, as of June 30, 2016, our management has concluded that there still existed significant flaws in the design and operation of our closing and financial reporting processes and therefore that this previously identified material weakness had not been fully remediated as of June 30, 2016. In order to fully remediate this material weakness, we will continue to implement the corrective actions described above, including additional procedures to improve the capture, review, approval, and recording of all transactions in the appropriate accounting period. Management will also continue to review and make necessary changes to the overall design of our internal control environment, and implement policies and procedures that improve the overall effectiveness of our internal controls over financial reporting.

Changes in Internal Control over Financial Reporting

Except for those remedial actions described above, there was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be set forth under the captions “Election of Directors,” “Executive Officers,” “Code of Ethics,” “Directors—Audit Committee Financial Expert” and “Corporate Governance” in an amendment to our Annual Report on Form 10-K/A to be filed with the Securities and Exchange Commission no later than 120 days after the end of our fiscal year (the “Annual Report Amendment”), and is incorporated herein by reference.

We are also required under Item 405 of Regulation S-K to provide information concerning delinquent filers of reports under Section 16 of the Securities and Exchange Act of 1934, as amended. This information will be set forth under the caption “Section 16(a) Beneficial Ownership Reporting Compliance” in our Annual Report Amendment, and is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be set forth under the captions “Executive Officers—Executive Compensation” in our Annual Report Amendment and is incorporated herein by reference.

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

The information required by Item 403 of Regulation S-K will be set forth under the caption “Security Ownership of Certain Beneficial Owners and Management” in our Annual Report Amendment, and is incorporated herein by reference.

We have two equity compensation plans under which awards are currently authorized for issuance, our 2013 Equity and Incentive Plan and our 2013 Employee Stock Purchase Plan. In connection with the consummation of our initial public offering in April 2014, our board of directors terminated any new offerings under our 2001 Stock Option Plan and our 2011 Stock Incentive Plan. Each of our 2013 Equity and Incentive Plan, our 2013 Employee Stock Purchase Plan, our 2001 Stock Option Plan and our 2011 Stock Incentive Plan was approved by our stockholders prior to our initial public offering in 2014. The following table provides information regarding securities authorized for issuance as of June 30, 2016 under our equity compensation plans.

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights, and vesting of outstanding restricted stock units (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (c)	
Equity compensation plans approved by security holders	2,054,237	$ 13.66	663,301	(1)
Equity compensation plans not approved by security holders	—	$ —	—	
Total	2,054,237	$ 13.66	663,301	

(1) Includes 534,730 shares issuable under our 2013 Equity and Incentive Plan, which may be issued in the form of options, restricted stock, unrestricted stock, performance share awards or other equity-based awards, and 128,571 shares issuable under our 2013 Employee Stock Purchase Plan.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTORS INDEPENDENCE

The information required by this item will be set forth under the caption “Executive Officers—Certain Relationships and Related Transactions” and “Corporate Governance” in our Annual Report Amendment, and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item will be set forth under the caption “Independent Registered Public Accounting Firm” in our Annual Report Amendment, and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) Documents filed as a part of this Report:

(1) Financial Statements —See Index to Financial Statements and Financial Statement Schedule at Item 8 on page 104 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules —See Index to Financial Statements and Financial Statement Schedule at Item 8 on page 104 of this Annual Report on Form 10-K. All other schedules are omitted because they are not applicable or not required.

(3) Index to Exhibits.

Exhibit number	Description
3.1	Fifth Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on April 1, 2014)
3.2	Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on April 1, 2014)
4.1	Specimen certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.1	Lease Agreement made as of April 10, 2015, by and between Alachua Foundation Park Holding Company, LLC and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.1 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))
10.2*	Employment Agreement dated as of May 27, 2015 between Applied Genetic Technologies Corporation and Mark S. Shearman (incorporated by reference to Exhibit 10.2 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))
10.3*	Employment Agreement dated as of January 29, 2015 between Applied Genetic Technologies Corporation and Stephen W. Potter (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 (File No. 001-36370))
10.4*	Separation Agreement dated as of March 3, 2015 between Applied Genetic Technologies Corporation and Daniel L. Menichella (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q/A (Amendment No. 1) for the quarter ended March 31, 2015 (File No. 001-36370))
10.5*	Employment Agreement dated as of September 26, 2014 between Applied Genetic Technologies Corporation and Susan B. Washer (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, event date September 26, 2014, filed on October 2, 2014 (File No. 001-36370))
10.6*	Employment Agreement dated as of September 26, 2014 between Applied Genetic Technologies Corporation and Jeffrey D. Chulay (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K, event date September 26, 2014, filed on October 2, 2014 (File No. 001-36370))
10.7†	Collaboration and License Agreement dated as of July 1, 2015 by and between Biogen MA Inc., and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.7 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))
10.8	Common Stock Purchase Agreement dated as of July 1, 2015 by and between Biogen MA Inc., and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))
10.9†	Manufacturing License and Technology Transfer Agreement dated as of July 1, 2015 by and between Biogen MA Inc., and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.9 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))

10.10† Second Amendment to Non-exclusive License Agreement, made and effective as of June 29, 2015, by and between The UAB Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.10 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))

10.11† Omnibus Amendment to Standard Exclusive License Agreement with Sublicensing Terms, made and effective as of July 1, 2015, by and between the University of Florida Research Foundation, Inc., the University of Florida Board of Trustees, John Hopkins University and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.11 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))

Exhibit number	Description
10.12†	Omnibus Amendment to Standard Exclusive License Agreement with Know How and Standard Non-Exclusive License Agreement, made and effective as of June 30, 2015, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.12 to the Company's Annual Report on Form 10-K for the year ending June 30, 2015 (File No. 001-36370))
10.13	Lease Agreement made as of September 19, 2011, by and between Thomson-Davis Enterprises, LLC and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.14†	Exclusive License Agreement with Sublicensing Terms, effective as of September 25, 2001, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.15†	Restated Amendment to License Agreement made and, effective as of January 31, 2005, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.16†	First Amendment After Restated Amendment to License Agreement, made and effective as of November 28, 2007, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.17†	Standard Exclusive License Agreement with Sublicensing Terms, effective as of October 7, 2003, by and between the University of Florida Research Foundation, Inc., Johns Hopkins University and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.18†	First Amendment to Standard Exclusive License Agreement with Sublicensing Terms, made as of November 2004, by and between the University of Florida Research Foundation, Inc., Johns Hopkins University and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.19†	Second Amendment to Standard Exclusive License Agreement with Sublicensing Terms, made as of February 25, 2009, by and among Applied Genetic Technologies Corporation, the University of Florida Research Foundation, Inc. and Johns Hopkins University (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.20†	Non-Exclusive License Agreement with Sublicensing Terms, made as of January 19, 2006, by and between The UAB Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.21†	Standard Non-Exclusive License Agreement, effective as of September 18, 2012, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No.

333-193309))

10.22† Standard Exclusive License Agreement with Know How, effective as of November 5, 2012, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-193309))

10.23 Amended and Restated Investor Rights Agreement, dated as of November 15, 2012 (incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1 (File No. 333-193309))

10.24* Applied Genetic Technologies Corporation 2001 Stock Option Plan, as amended (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1 (File No. 333-193309))

10.25* Applied Genetic Technologies Corporation 2011 Stock Incentive Plan, as amended, and forms of Incentive Stock Option Agreement and Nonstatutory Stock Option Agreement thereunder (incorporated by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1 (File No. 333-193309))

10.26* Applied Genetic Technologies Corporation 2013 Equity And Incentive Plan (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1 (File No. 333-193309))

10.27* Applied Genetic Technologies Corporation 2013 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1 (File No. 333-193309))

Exhibit number	Description
10.28	Form of Applied Genetic Technologies Corporation Warrant to Purchase Shares of Series A-1 Preferred Stock (incorporated by reference to Exhibit 10.17 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.29	Form of Applied Genetic Technologies Corporation Warrant to Purchase Shares of Series B-1 Preferred Stock (incorporated by reference to Exhibit 10.18 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.30	Warrant to Purchase Shares of Series A-1 Preferred Stock of Applied Genetic Technologies Corporation issued to Silicon Valley Bank and effective on September 23, 2005 (incorporated by reference to Exhibit 10.19 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.31	Warrant to Purchase Shares of Series A-1 Preferred Stock of Applied Genetic Technologies Corporation issued to Silicon Valley Bank and effective on June 30, 2006 (incorporated by reference to Exhibit 10.20 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.32	Warrant to Purchase Shares of Series A-1 Preferred Stock of Applied Genetic Technologies Corporation issued to Square 1 Bank on July 6, 2010 (incorporated by reference to Exhibit 10.21 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.33	Warrant to Purchase Shares of Series B-1 Preferred Stock of Applied Genetic Technologies Corporation issued to Square 1 Bank on August 31, 2012 (incorporated by reference to Exhibit 10.22 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.34	Form of Indemnification Agreement for Directors Associated with an Investment Fund (incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.35	Form of Indemnification Agreement for Directors Not Associated with an Investment Fund (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.36†	Second Amendment After Restated Amendment to License Agreement, made and effective as of January 10, 2014, by and between the University of Florida Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.37†	Fourth Amendment to Standard Exclusive License Agreement with Sublicensing Terms, made as of December 17, 2013 by and between the University of Florida Research Foundation, Inc., Johns Hopkins University and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.26 to the Company's Registration Statement on Form S-1 (File No. 333-193309))
10.38*	Letter Agreement dated July 22, 2013 by and between the Company and Dan Menichella (incorporated by reference to Exhibit 10.26 to the Company's Registration Statement on Form S-1 (File No. 333-197385))
10.39†	First Amendment to Non-Exclusive License, made as of March 28, 2014, by and between the UAB Research Foundation, Inc. and Applied Genetic Technologies Corporation (incorporated by reference to Exhibit 10.27 to the Company's Registration Statement on Form S-1 (File No. 333-197385))

10.40*	Letter Agreement dated January 22, 2014 by and between the Company and Larry Bullock (incorporated by reference to Exhibit 10.28 to the Company's Registration Statement on Form S-1 (File No. 333-197385))
23.1**	Consent of Independent Registered Public Accounting Firm
31.1**	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2**	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Exhibit number	Description
101.INS**	XBRL Instance Document
101.SCH**	XBRL Taxonomy Extension Schema Document
101.CAL**	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF**	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB**	XBRL Taxonomy Extension Label Linkbase Document
101.PRE**	XBRL Taxonomy Extension Presentation Linkbase Document

* Management contract or compensatory plan or arrangement
** Filed herewith
† We have omitted portions of this exhibit, for which confidential treatment has been granted.

SCHEDULE II—VALUATION AND QUALIFYING ACCOUNTS

In thousands	Beginning of Period	Additions Charge (Benefit) to Expenses	Additions To (from) Other Accounts	Deductions	End of Period
Deferred Tax Valuation Allowance					
Year 2016	$ 36,845	$567	$ —	$ —	$37,412
Year 2015	$ 24,086	$12,759	$ —	$ —	$36,845
Year 2014	$ 18,956	$5,130	$ —	$ —	$24,086

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

APPLIED GENETIC TECHNOLOGIES CORPORATION

By: /s/ Susan B. Washer
Susan B. Washer
President and Chief Executive Officer
Date: September 12, 2016

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report has been signed below by the following persons on behalf of the Company and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Susan B. Washer Susan B. Washer	Chief Executive Officer, President and Director (Principal Executive Officer)	September 12, 2016
/s/ Lawrence E. Bullock Lawrence E. Bullock	Chief Financial Officer (Principal Financial and Accounting Officer)	September 12, 2016
/s/ Scott Koenig Scott Koenig	Director	September 12, 2016
/s/ David Guyer David Guyer	Director	September 12, 2016
/s/ Ed Hurwitz Ed Hurwitz	Director	September 12, 2016
/s/ Ivana Magovcevic-Liebisch Ivana Magovcevic-Liebisch	Director	September 12, 2016
/s/ Arnold Oronsky Arnold Oronsky	Director	September 12, 2016

/s/ Anne VanLent Anne VanLent	Director	September 12, 2016
/s/ James Rosen James Rosen	Director	September 12, 2016