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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2014

or

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

For the transition period from _____ to _____

Commission File Number: 001-36579

Avalanche Biotechnologies, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**20-5258327**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

1035 O'Brien Drive, Suite A
Menlo Park, California 94025
(650) 272-6269
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.0001 per share	**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 ☐ No ☒

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

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

Indicate by check mark whether the registrant has submitted electronically 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files): Yes ☒ No ☐

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a smaller reporting company)	Smaller reporting company	☐

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

The registrant did not have a public float on the last business day of its most recently completed second fiscal quarter because there was no public market for the registrant's common equity as of such date.

As of February 28, 2015, the registrant had 25,221,495 shares of common stock, par value $0.0001 par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement (the Proxy Statement) for the 2015 Annual Meeting of Stockholders of the registrant are incorporated by reference into Part III of this Annual Report on Form 10-K. The Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31,

2014.

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In this report, unless otherwise stated or the context otherwise indicates, references to "Avalanche," "Avalanche Biotechnologies," "the Company," "we," "us," "our" and similar references refer to Avalanche Biotechnologies, Inc., a Delaware corporation.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "potential" or "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the anticipated timing, costs and conduct of our planned clinical trials for our AVA-101, AVA-201, AVA 311 and other product candidates in our development program;
- our ability to advance our viral vector manufacturing and delivery capabilities;
- the timing or likelihood of regulatory filings and approvals;
- our plans to explore potential applications of our Ocular BioFactory™ platform in other indications in ophthalmology;
- our expectations regarding the clinical effectiveness of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- our expectation regarding the potential market size for anti-vascular endothelial growth factor and wet age-related macular degeneration therapies;
- our intellectual property position;
- the potential benefits of strategic collaborations and our ability to enter into strategic arrangements;
- developments and projections relating to our competitors and our industry;
- our expectations regarding the time during which we will be an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Any forward-looking statement in this Annual Report on Form 10-K reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward looking statements speak only as of the date of this Annual Report on Form 10-K. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless

otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

PART 1.

Item 1. Business

Overview

We are a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. We have leveraged our next-generation gene therapy platform, the Ocular BioFactory™, to create a robust pipeline of product candidates. Our product candidates are designed to provide long-term benefit or a functional cure for these diseases by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye.

We are targeting ophthalmic diseases with significant unmet medical need, including prevalent ophthalmic diseases such as wet age-related macular degeneration (AMD), as well as rare genetic diseases. We believe that there are several important benefits to focusing on the development of therapies for ophthalmic diseases, including the following:

- well-understood disease biology, in which many conditions are caused by a defect in expression of a single gene;
- reduced risk of harmful immune responses and systemic side effects due to localized delivery in a self-contained organ;
- relatively easy access and visualization of the back of the eye, limiting the need for invasive procedures to deliver therapies and evaluate their impact;
- well-defined and objective clinical endpoints such as the ability to read an eye chart; and
- significant market demand for therapies that can offer long-term clinical benefit with one-time administration.

Our lead product candidate is AVA-101 for the treatment of wet AMD. Standard-of-care therapies include the anti-VEGF class, which inhibit vascular endothelial growth factor (VEGF), a protein that causes abnormal blood vessel growth in wet AMD. Anti-VEGF therapies, such as Lucentis®, marketed by Genentech, Inc. and Novartis AG, and EYLEA®, marketed by Regeneron Pharmaceuticals, Inc. in the United States and Bayer HealthCare LLC outside the United States, represented approximately $6.7 billion in worldwide sales in 2014, and we believe 65%-80% of those sales were for the treatment of wet AMD. Due to a variety of factors, including inconvenience and discomfort associated with frequent injections in the eye, patient compliance is a significant concern with anti-VEGF therapies. These treatments require continuous injections every four to eight weeks to maintain efficacy and patients often experience vision loss with reduced frequency of treatment. By contrast, AVA-101 is designed to enable retinal cells to continuously produce therapeutic levels of a naturally occurring anti-VEGF protein with a single administration. Accordingly, we believe that AVA-101 could transform the treatment paradigm and address a significant unmet need in this large wet AMD market. In addition to wet AMD, we believe that AVA-101 may have the potential to treat other neovascular diseases of the eye such as diabetic macular edema (DME) and retinal vein occlusion (RVO).

We have generated human proof-of-concept data for AVA-101 in a Phase 1 trial with eight wet AMD subjects conducted at Lions Eye Institute (LEI) in Australia. In that Phase 1 trial, AVA-101 was well tolerated with no drug-related adverse events. In addition, subjects treated with AVA-101 showed meaningful improvement in their visual acuity test scores (up to 15 letter improvement on an eye chart from baseline), and most subjects did not receive any rescue injections of standard-of-care therapy (required for subjects exhibiting disease progression) during the one-year trial period.

We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. Most adverse events that have been observed to date are mild and not related to AVA-101 or

the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015. We own exclusive rights to develop and commercialize AVA-101 worldwide.

In addition to AVA-101, our Ocular BioFactory platform has generated other promising product candidates for the treatment of severe ophthalmic diseases, including:

- **AVA-201.** We are developing AVA-201 as a next-generation product candidate for the prevention of wet AMD. AVA-201 produces the same anti-VEGF protein as AVA-101 using a proprietary, customized delivery mechanism, or vector, that can be administered earlier in the disease progression, before the onset of wet AMD. According to the Center for Disease Control (CDC), up to 7.3 million patients in the United States are at high risk of developing wet AMD, and we believe that the highest risk patients can be identified through a combination of clinical and genetic biomarkers. These high-risk patients, if treated early enough in the disease progression, could potentially maintain their visual acuity instead of experiencing sudden onset of vision loss characterized by wet AMD. We own exclusive rights to develop and commercialize AVA-201 worldwide.
- **AVA-311**. As part of our research collaboration with Regeneron, AVA-311 is being evaluated in preclinical studies for the treatment of juvenile X-linked retinoschisis (XLRS), a rare genetic disease of the retina with no approved therapy. There are approximately 10,000 boys and young men in the United States suffering from the disease. XLRS is caused by mutation of the RS1 gene and results in splitting of retinal layers and corresponding loss of vision. In preclinical studies in animals to date, AVA-311 has delayed the progression of XLRS and improved vision by delivering functional copies of the RS1 gene in retinal cells of mice.

In order to accelerate the pace of generating and developing product candidates for our pipeline, we entered into a broad research collaboration and license agreement (Collaboration Agreement), with Regeneron in May 2014. Under the terms of the collaboration, we will jointly discover novel product candidates based on our Ocular BioFactory platform for up to eight therapeutic targets including AVA-311. We received initial payments of $8.0 million as well as ongoing support for research and development. In addition, we are eligible to receive up to $80.0 million in development milestone payments for product candidates directed toward each therapeutic target, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single-digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits. See “License and Collaboration Agreements—Regeneron Research Collaboration and License Agreement” for more information regarding our collaboration agreement.

Our Ocular BioFactory platform seeks to treat the cause of ophthalmic diseases by enabling patients’ own cells to express a therapeutic protein for a sustained period of time. We use a vector derived from adeno-associated virus (AAV), which is a small, non-pathogenic virus. DNA encoding the AAV viral genes are removed and replaced with a therapeutic gene to treat a disease. The resulting vector is used to deliver and express, or transduce, a functional gene to the cells of the eye to promote continuous protein production. Although AAVs are widely used for gene therapy due to their safety, stability and sustained protein expression, our Ocular BioFactory platform has distinct characteristics that provide advantages over competing gene therapy technologies using AAVs as well as other viral and non-viral vectors.

Our Ocular BioFactory platform features two key proprietary components: a vector screening and optimization system referred to as directed evolution, and an industrialized manufacturing process. Through directed evolution, we generate a diverse library of millions of AAV variants and subsequently screen the variants in

multiple *in vitro* and *in vivo* tests to identify the optimal variant for a specific disease. Our directed evolution technology allows us to create proprietary vectors and optimize them to target cells in different layers of the retina. Each of these cell layers constitutes a potential therapeutic target for currently unmet medical needs, providing us with multiple opportunities to apply our directed evolution technology. Our industrialized manufacturing process, based on our proprietary system, is highly efficient and stable. It uses the baculovirus expression system (BVES), which is a technology for producing high levels of recombinant protein in insect-derived cells. Production yields are more than 50 times greater than those obtained using conventional AAV production systems. Therefore, we are able to manufacture commercial grade production for large markets such as wet AMD.

Our senior management team and board of directors have significant experience in the biotechnology industry, specifically in the areas of ophthalmology and gene therapy. Our Chief Executive Officer and co-founder, Thomas W. Chalberg, Jr., Ph.D., was a member of the ophthalmology team at Genentech that was responsible for the successful launch and commercialization of Lucentis. Furthermore, Dr. Chalberg was a Howard Hughes Medical Institute Fellow at Stanford University, where his research focused on retinal diseases and novel technologies for gene therapy.

Our Chairman and co-founder, Mark S. Blumenkranz, M.D., is an ophthalmologist, a trained vitreoretinal surgeon and the Chairman of the Byers Eye Institute at Stanford University. Dr. Blumenkranz was also a founding member of the Eyetech Pharmaceuticals Scientific Advisory Board. Dr. Blumenkranz also serves on the boards of directors of Vantage Surgical Systems Inc., Oculogics, Inc., Presbia Holdings, Digisight Technologies Inc. and Oculeve, Inc.

Our director and co-founder, Steven D. Schwartz, M.D., is an ophthalmologist and a trained vitreoretinal surgeon at the UCLA Jules Stein Eye Institute, where he has served as principal investigator in a number of early-stage clinical trials for retinal diseases, including the initial studies for Lucentis and novel product candidates in gene and cell therapy. Dr. Schwartz held various key positions at Eyetech, and has served on a number of Scientific Advisory Boards, including Genentech and Ophthotech Corporation.

Other members of our executive management team also have significant experience in the discovery and development of gene therapies including, expertise and/or prior experience at gene therapy companies in the following areas: regulatory, led by Samuel Barone, our Chief Medical Officer with prior experience at the Office of Cellular, Tissue and Gene Therapies at the Food and Drug Administration (FDA); translational medicine, led by Roman Rubio, our Senior Vice President and Head of Translational Medicine, with prior experience at Genentech; manufacturing and technical operations, led by Mehdi Gasmi, our Vice President, Pharmaceutical Development, with prior experience at Ceregene, Inc. and Généthon; finance, led by Linda Bain, our Chief Financial Officer with prior experience at bluebird bio, inc., Genzyme Corporation and AstraZeneca plc; and legal and business operations, led by Hans Hull, our Senior Vice President, Business Operations, with prior experience at Second Genome, Inc. and Aprecia Pharmaceuticals Company and as an attorney at Heller Ehrman White & McAullife LLP.

Strategy

Our goal is to transform the lives of patients suffering from blinding and sight-threatening diseases by discovering, developing and commercializing potentially curative therapies. The key elements of our strategy to achieve this goal are to:

- **Successfully advance AVA-101 through clinical development and commercial launch for wet AMD.** Global sales of Lucentis and EYLEA were approximately $6.7 billion in 2014 with approximately $3.4 billion in the United States and $3.3 billion in territories outside of the United States, of which we believe a significant portion occurred in the European Union, Japan and Australia. We believe 65%-80% of those sales were for the treatment of wet AMD. We intend to pursue a worldwide development and commercialization strategy of advancing AVA-101 in the United States

and these international markets. After the completion of our Phase 2a clinical trial in mid-2015, we plan to file an Investigational New Drug application (IND) in the United States and work with regulatory authorities to pursue a global regulatory strategy. We currently own worldwide rights to AVA-101. Given the small number of retina specialists globally, we believe we will have the opportunity to commercialize AVA-101 alone or with a partner. We will pursue a commercialization strategy that will increase the probability of AVA-101's ultimate success and maximize value for our stockholders.

- **Pursue additional indications for AVA-101.** There are other diseases in which VEGF plays a central role in disease biology, including DME and RVO. Anti-VEGF therapies such as Lucentis and EYLEA are already approved in these indications. Since patient compliance presents the same challenge in these indications, we believe that AVA-101 may offer an attractive alternative to the existing therapies in these markets.
- **Continue to identify and target ophthalmic diseases using our Ocular BioFactory platform.** We are focusing on both prevalent and rare ophthalmic diseases for which the disease biology is well characterized and for which the diseases themselves can be better treated by the sustained delivery of a therapeutic protein. These diseases include choroideremia, diabetic retinopathy, glaucoma, Leber's congenital amaurosis (LCA), macular telangiectasia, retinitis pigmentosa, wet AMD and XLRS, among others. We will continue to identify the most appropriate target indications based on emerging data from our platform, by leveraging our internal expertise and through relationships with thought leaders in ophthalmology.
- **Continue to invest in our Ocular BioFactory platform.** Our Ocular BioFactory platform has been validated by both preclinical and clinical data from our product candidates. We will continue to invest in our platform and employ directed evolution to create and manufacture next-generation vectors with higher efficiency and greater specificity that can potentially treat previously untreatable diseases. We believe this new class of therapeutics could emerge as a major treatment modality for ophthalmic diseases.
- **Build a balanced portfolio of proprietary and partnered programs.** We plan to develop and commercialize multiple product candidates independently. For targets outside our core area of interest or where a partner can contribute specific expertise, we intend to evaluate collaborations with strategic partners who can augment our industry-leading expertise in gene therapy for the eye. For example, in May 2014, we entered into a collaboration with Regeneron to leverage our Ocular BioFactory platform to discover and develop product candidates focused on up to eight therapeutic targets.

Gene Therapy Background

Gene therapy is a powerful treatment modality to address disease biology in a targeted and efficient way. Using gene therapy, physicians can introduce or re-introduce genes that encode a therapeutic protein. Instead of providing proteins or other therapies externally and dosing them over a long period, gene therapy offers the possibility of dosing once or a very limited number of times to achieve a long-term, durable benefit. Once a patient's cells have incorporated the therapeutic gene, the cells are able to continue to produce the therapeutic protein for years or, potentially, the rest of the patient's life.

Similar to existing classes of protein or biologic therapies such as monoclonal antibodies and drug-antibody conjugates, gene therapy has taken a number of years to evolve from a research tool into a viable and compelling treatment modality. There have been several recent advances in gene therapy, including the following:

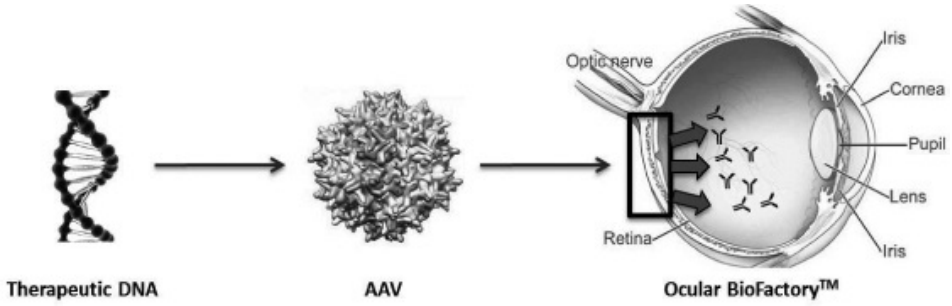
- **Clinical data.** Positive data from gene therapy have been reported in a variety of indications including adrenoleukodystrophy, beta-thalassemia, chronic lymphoid leukemia, hemophilia, HIV and Parkinson's disease, as well as several ophthalmic diseases such as LCA and wet AMD.
- **Increased investment by biopharmaceutical companies.** The modality of gene therapy has been further validated by growing interest and investments by biopharmaceutical companies. Large, global

biopharmaceutical companies, such as BioMarin Pharmaceutical Inc., Celgene Corporation, GlaxoSmithKline plc, Novartis, Sanofi, Regeneron and Shire Pharmaceuticals Group Plc, have increased their investment in the gene therapy field. Additionally, pure-play gene therapy companies, such as Applied Genetic Technologies Corporation, bluebird bio, Celladon Corporation, Spark Therapeutics, Inc., Biogen Idec Inc., Sangamo BioSciences, Inc. and uniQure N.V., have attracted recent investment in this growing field.

- **Regulatory clarity.** Although the FDA has not yet approved a gene therapy product, 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 within its Center for Biologics Evaluation and Research (CBER) to consolidate the review of gene therapy products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews.
- **First product approval.** In 2012, the European Medicines Agency (EMA) granted approval for Glybera® (developed by uniQure) for the orphan disease lipoprotein lipase deficiency. Glybera is the first gene therapy product approved in the Western world.

Our Ocular BioFactory Platform

Our Ocular BioFactory platform seeks to treat the cause of ophthalmic diseases by enabling patients' own cells to express a therapeutic protein for a sustained period of time. Our proprietary Ocular BioFactory platform features three key attributes: focus on the treatment of serious ophthalmic diseases; novel AAV vector discovery and optimization system; and our industrialized manufacturing process.



When injected into the eye, AAV creates a long-term Ocular BioFactory that secretes therapeutic protein over years following a single administration

Focus on the Treatment of Serious Ophthalmic Diseases

We believe that there are several important benefits to focusing our Ocular BioFactory platform on the development of therapies for ophthalmic diseases. These benefits include the following:

- **Unmet need.** There is a significant unmet medical need for patients suffering from various blinding or sight-threatening ophthalmic diseases. In certain degenerative eye diseases, such as wet AMD, there are effective therapies targeting factors established to be important in disease progression. However, the effectiveness of these therapies is limited by poor compliance due to the need for regular injections into the eye. For many rare genetic ophthalmic diseases, including XLRS, there are no approved therapies. In these diseases, serious sight-threatening symptoms arise early in patients' lives.
- **Well-understood disease biology.** Many ophthalmic diseases are caused by a defect in expression of a single gene or a small number of genes and the molecular mechanisms are well understood. As a result,

in many cases, highly predictive animal models are available for these disease states, which allow us to obtain proof-of-concept data for product candidates early in development.

- **Safety.** The eye is a small, self-contained organ, separated from the rest of the body by physical and biochemical barriers. Therefore, drugs delivered into the eye are much less likely to evoke a systemic immune response. Gene therapies can be delivered locally at concentrations that are highly effective in the eye and at the same time lead to little or no systemic distribution.
- **Accessibility.** The eye is easily accessible for treatment, in contrast to internal organs that can be accessed only via the bloodstream or by invasive procedures. Furthermore, the retina and surrounding structures can be visualized and targeted by clinicians in a non-invasive and localized manner, making it easy to evaluate both the delivery of therapy as well as its impact.
- **Well-defined and accepted clinical endpoints.** Clinical endpoints for ocular disease generally consist of objective, well-defined, performance-based parameters such as the ability to read an eye chart. These endpoints have been used for many years and are well understood and accepted by clinical investigators, regulatory agencies and practicing ophthalmologists.

Our Novel AAV Vector Discovery and Optimization System

Our Ocular BioFactory platform is based on AAV vectors, which offer numerous advantages over other viral and non-viral vector technologies used for gene therapy. These advantages, highlighted below, allow AAVs to be safe, applicable for a variety of indications and to exhibit long-term efficacy.

- **Non-pathogenic**. AAV vectors are not known to cause any disease in humans.
- **Low immunogenicity**. AAV vectors elicit only a mild immune response, if any, in humans, particularly when used in the eye.
- **Non-replicating**. Once inside the host cell, AAV vectors do not replicate, thereby preventing the spread to unwanted tissues.
- **Non-integrating**. AAV vectors do not readily integrate into the host cell's genome, mitigating the risk of potential safety concerns.
- **Ability to transduce non-dividing cells**. AAV vectors are able to transduce non-dividing cells and this is a significant advantage as many retinal cells cease to divide early in a person's life.
- **Long-term expression**. Once incorporated into the host cell, AAV vectors can continue to drive expression of a therapeutic protein for years.

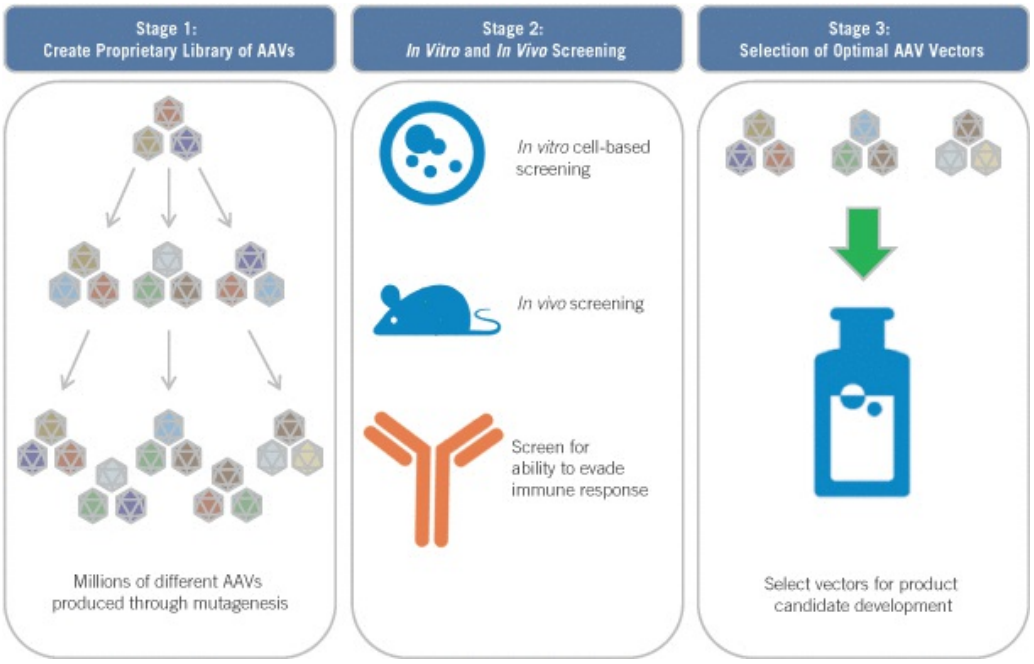
AAV is naturally occurring and has become a leading vector used in gene therapy. According to the *Journal of Gene Medicine*, AAV has been used in approximately 100 clinical trials as of January 2014 demonstrating the increasing acceptance of gene therapy as a safe and effective method for delivering therapeutic genes of interest. The most frequently studied variant of AAV is AAV2, which can preferentially infect a number of cell types, including those found in the retina. AAV2 is the basis for our lead product AVA-101.

As effective as existing AAV vectors are in gene therapy, we believe there is an opportunity to advance vector capabilities beyond those currently available. Naturally occurring AAV variants have evolved with particular characteristics, some of which pose limitations to their use in gene therapy in the eye. Consequently, there is significant room to improve AAV vectors to maximize utility for gene therapy in the eye. Therefore, our other product candidates have been created using our methodology that gives AAV new and powerful capabilities of cell penetration, gene delivery, protein expression and manufacturability. We believe we can target retinal cells even more precisely with these next-generation AAV vectors, to one or more of the eight cell layers found in the retina.

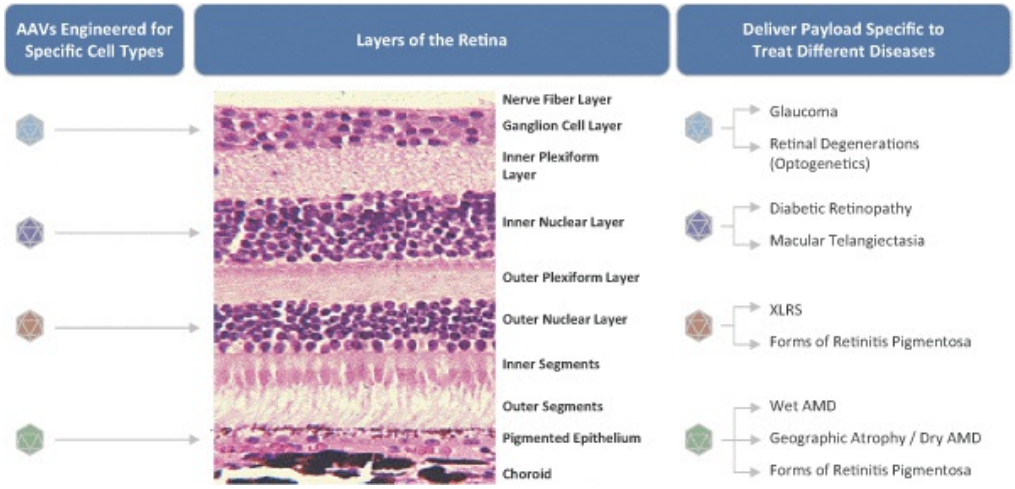
In order to create next-generation vectors, we use a multi-step process known as directed evolution. These vectors are designed to penetrate a specific cell type within the retina with high efficiency and transduce cells to express a therapeutic protein over a long duration.

Our directed evolution technology uses a library of genes coding for viral proteins found in a number of naturally occurring AAVs. We modify these genes in the laboratory to derive novel combinations of genes that produce vectors exhibiting different properties and capabilities. Once we have created an initial pool of millions of different AAVs, each with distinct genetic and chemical composition, we screen the AAVs in the pool for their potential therapeutic benefits. We also screen the pool to eliminate vectors that would lead to interference by a host's antibodies. After identifying a smaller pool of optimized vectors from this screening process, we repeat the steps of diversity generation and screening until we have identified a select number of ideal, engineered AAVs. These lab-created AAVs represent the basis for our therapeutic product pipeline. Furthermore, when we develop additional product candidates, we return to the initial pool of novel vectors, or to one or more of the adapted pools we created, and use further applications of directed evolution to create new AAVs.

Directed Evolution Technology for AAV Discovery and Optimization



Developing next-generation AAV vectors through directed evolution allows us to develop gene therapy product candidates that are able to enter the desired cell populations. Once the genes have transduced the appropriate cells, our product candidates can increase or initiate the production of therapeutic proteins in physiologically relevant amounts. Our directed evolution technology provides us with a toolkit to create AAV-based product candidates that we believe will be able to address any number of common and rare ophthalmic diseases.



Our Industrialized Manufacturing Process

Our AAV manufacturing method is industrialized, ready for adaptation to commercial processes and highly scalable. It is based on the BVES, which has been used in a number of FDA- and EMA-approved products. Our process provides the following advantages over competing systems:

- **Industrial-scale biologics production.** Our BVES system can produce commercial quantities by incorporating scalable, well-established process steps used throughout the industry for biologic products.
- **Safety advantages.** Our BVES system does not use mammalian cell cultures or tumorigenic cell lines, and the DNA sequences used in production are inactive in mammalian cells, which lowers the risk of off-target expression from our products.
- **High yield and low cost.** Our BVES system produces a high number of particles per cell, producing many thousand doses per manufacturing run. The yields are up to one hundred times greater than those obtained using conventional AAV production systems. This lowers the unit cost of goods, allowing us to meet global demand for large markets, such as wet AMD.
- **High purity.** Our BVES system produces a highly pure drug substance, which reduces the presence of unwanted contaminants in the final product.
- **Precedent regulatory framework.** Our BVES system is used for several FDA- and EMA-approved vaccines and gene therapy products including FluBlok®, Cervarix® and Glybera.

Our Product Candidates

Based on our Ocular BioFactory platform, we have developed a robust pipeline of proprietary and partnered programs across both major markets and rare diseases in the field of ophthalmology. Set forth below is a table summarizing our development programs:

AVA-101 for the Treatment of Wet AMD

We are developing our lead product candidate, AVA-101, to provide a safe and effective treatment for wet AMD that is durable and reduces the need for frequent injections. AVA-101 is currently being studied in a 40 subject Phase 1/2a trial that we are conducting together with LEI. One-year results from the Phase 1 portion (eight subjects) have been reported. The Phase 2a trial (32 subjects) is fully enrolled, and top-line data are expected in mid-2015.

We own exclusive rights to develop and commercialize AVA-101 worldwide. Regeneron has a time-limited right of first negotiation for certain rights to AVA-101 as part of our recent collaboration.

Wet AMD Overview

AMD is a progressive disease affecting the retinal cells in the macula, the region of the eye responsible for central vision. Disease progression results in the death of retinal cells and the gradual loss of vision. As people age, the likelihood of disease progression increases and the resulting condition is referred to as AMD.

Normal Vision

AMD Vision

Approximately 10% of total cases of AMD represent an advanced form of the disease called wet AMD, in which blood vessels begin to invade the cellular space between layers of cells in the retina. These new blood vessels are often leaky, which results in fluid and blood in the retina and causes vision loss.

While wet AMD represents only 10% of the number of cases of AMD overall, it is responsible for 90% of the AMD-related severe vision loss. Of untreated patients who are not already partially sighted or blind, over half will become partially sighted or blind within three years.

Wet AMD is a leading cause of vision loss with a prevalence of approximately three million people worldwide. The incidence of new cases of wet AMD in the United States is approximately 150,000 to 200,000 a year and this number is expected to grow significantly based on the aging of the population.

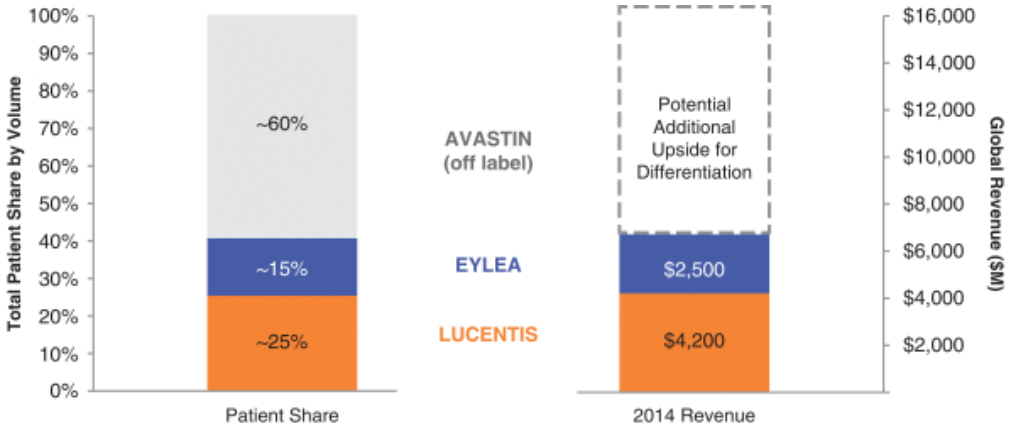
Current Therapies for Wet AMD

While the underlying molecular causes of AMD are not completely known, VEGF is known to play a central role in the growth of new blood vessels in wet AMD. A number of therapies have been developed to block the effects of VEGF by binding to and sequestering the protein. The standard-of-care therapies include the following:

- Lucentis is a recombinant humanized monoclonal antibody fragment that binds to and inhibits VEGF proteins in the eye. This product was approved in the United States in 2006 and in Europe in 2007. In 2014, Lucentis achieved worldwide sales of approximately $4.2 billion.
- EYLEA is a recombinant fusion protein containing portions of the human VEGF receptor that binds to soluble VEGF. Approved in the United States in 2011, EYLEA has exhibited strong adoption in the market due to its more convenient dosing regimen compared to Lucentis. In 2014, EYLEA achieved worldwide sales of approximately $2.5 billion.
- Avastin is a recombinant human monoclonal antibody that binds to VEGF and is approved as an anti-cancer agent. Avastin is widely prescribed off-label in ophthalmic diseases such as wet AMD. Avastin makes up approximately 60% of the wet AMD market by volume, but is insignificant in terms of revenue.

We believe a novel therapy that represents a functional cure is meaningfully differentiated from standard-of-care therapies and will have access to the entire wet AMD market, not just the 40% treated with on-label Lucentis and EYLEA, but also the large pool of patients currently using Avastin off-label.

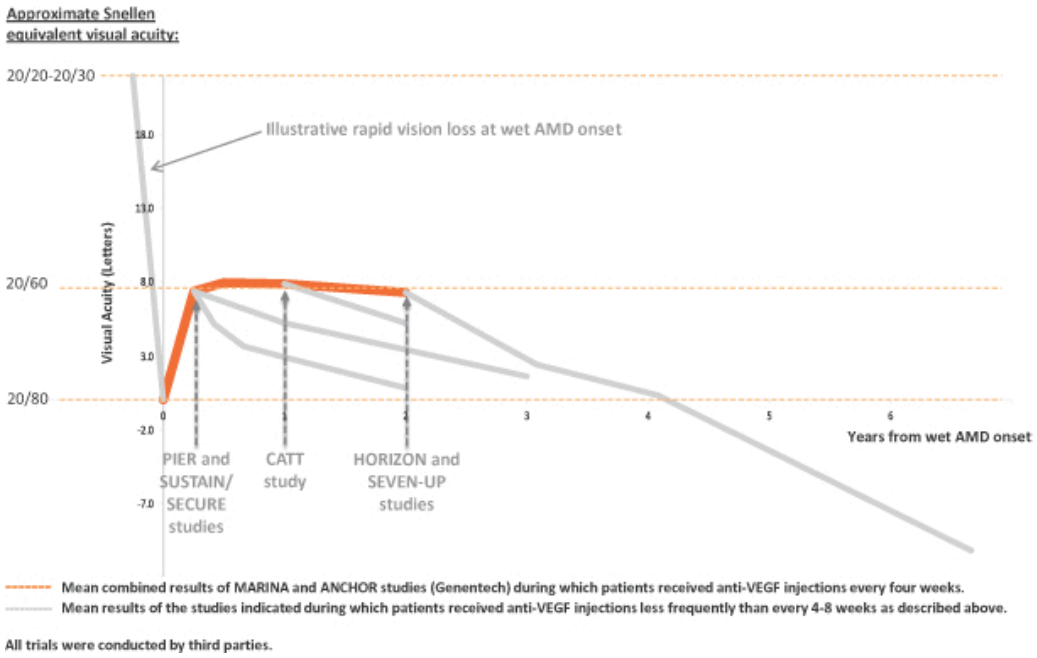
Comparison of Patient Share Volume and Global Revenues for Anti-VEGF Therapies



While standard-of-care treatments have proven to be effective, they do not offer a durable remission and require injections into the patient's eye every four to eight weeks. According to the journal *Ophthalmology* (2012), in the MARINA and ANCHOR trials (conducted by Genentech), a total of 599 subjects received Lucentis every four weeks. Treated subjects in these trials gained vision, averaging 9.0 letters on a standardized eye chart, and this gain was maintained with injections every four weeks for two years. When 388 of these subjects were subsequently moved to a less-frequent dosing regimen in the HORIZON study (Genentech), however, their vision declined by 7.0 letters over the next two years. In the SEVEN-UP study reported in the journal *Ophthalmology* (2013), 65 subjects from the HORIZON study were followed for an additional 3.3 years and injected less frequently, declining by an additional 10.3 letters.

Other clinical trials where subjects were treated less frequently than every 4 weeks have shown similar results. In the PIER study (Genentech), 61 subjects received three doses every 4 weeks, gaining 4.3 letters, but were then switched to 12-week dosing and declined 6.5 letters at two years (British Journal of Ophthalmology, 2009). In the SUSTAIN study (Novartis), 512 subjects received three doses every 4 weeks, gaining 5.8 letters, but were then switched to less frequent "as needed" dosing, and declined 2.2 letters at 12 months (*Ophthalmology*, 2011); 99 of these subjects continued to be followed in the SECURE study (Novartis) and were treated with less frequent "as needed" dosing and lost an additional 3.6 letters (*Ophthalmology*, 2013). Similarly, in CATT (United States National Eye Institute), 130 subjects were dosed monthly for 12 months, gaining 8.5 letters *(New England Journal of Medicine*, 2011), but then were switched to less-frequent "as needed" dosing and declined by 1.8 letters.

As summarized in the illustrative chart below, patients must comply with a burdensome treatment regimen every 4-8 weeks, or face a relative decline in visual acuity. The chart depicts the results for the MARINA and ANCHOR studies, compared to the decline in visual acuity from less frequent dosing in the other studies, as described above. When injections are given every four weeks, as in the MARINA and ANCHOR studies, patients initially gain vision and maintain that gain. However, when patients were relieved of injections every four weeks after three months (PIER and SUSTAIN/SECURE trials), twelve months (CATT trial), or two years (HORIZON and SEVEN-UP trials), the results were similar.



Despite sub-optimal outcomes with injections less than every four to eight weeks, patients often terminate treatment or do not comply with the prescribed regimen due to the burdensome frequency of administration. According to the *European Journal of Ophthalmology* (2011), 36% of patients who received anti-VEGF treatment for at least six months had stopped receiving therapy within a year. Of these patients, 59% had lost visual acuity. In addition, according to the journal *Ophthalmology* (2013), a study of a subset of 65 patients enrolled in Lucentis pivotal trials reported that only 23% of patients received more than 11 anti-VEGF treatments over the course of five years following the completion of the original trial. 59% of patients in this trial received fewer than six anti-VEGF injections during the follow up period and they lost an average of 9.3 letters of visual acuity. Studies examining treatment patterns in the real world report that patients are substantially under-treated, receiving an average of only five to seven injections per year; over time, this under-treatment has persisted despite evidence of worse visual outcomes (*American Journal of Ophthalmology*, 2014).

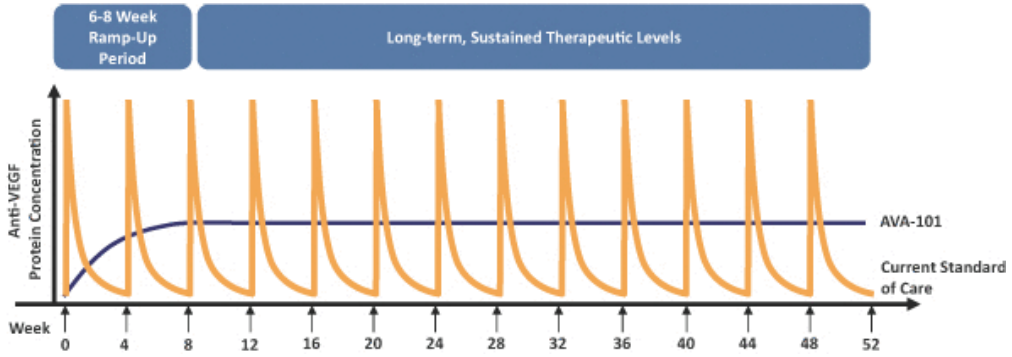
Our Solution: AVA-101

AVA-101 is comprised of the AAV2 vector, which contains a gene encoding sFLT-1, a naturally occurring anti-VEGF protein. When administered in the eye and expressed by the host retinal cells, the sFLT-1 protein inhibits the formation of new blood vessels and reduces vascular permeability by binding and blocking VEGF activity.

AVA-101 is designed to be administered via a single subretinal injection. The vector is placed into direct contact with retinal cells, which then produce sFLT-1. We believe that a majority of vitreoretinal surgeons are capable of performing the procedure to deliver AVA-101, which is an outpatient procedure performed under local anesthesia.

Based on data from preclinical studies, AVA-101 reaches a therapeutically beneficial level of continuous expression of sFLT-1 within six to eight weeks from administration. In animal models, AVA-101 expression has been shown to last up to 17 months, and data from other studies with AAV in the retina have shown gene expression to last more than five years. In humans, AVA-101 has been studied up to one year, and we believe it has the potential to last much longer.

Sustained Expression of sFLT-1 for AVA-101 Compared to Current Standard of Care



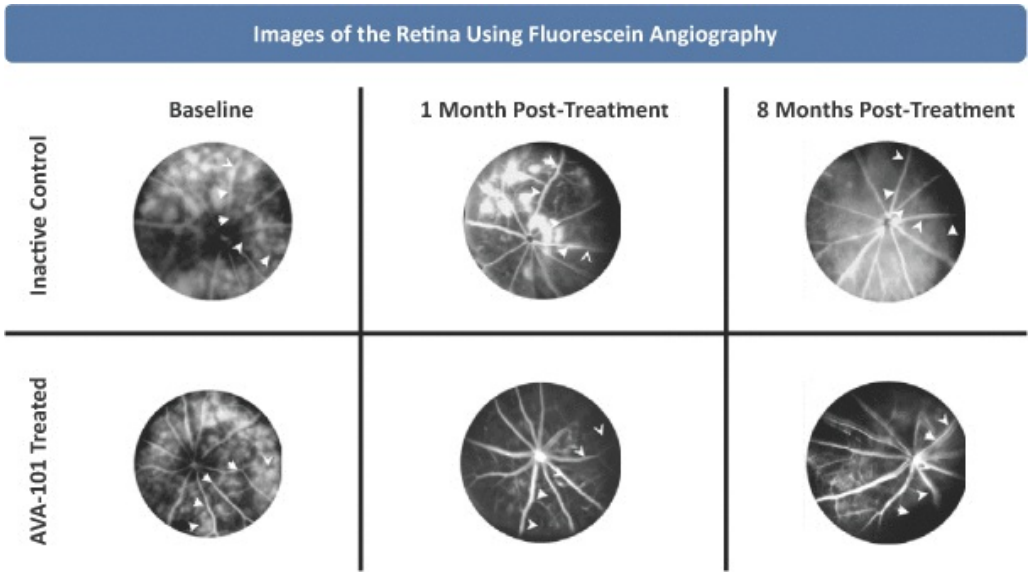
Above is an illustration of how our AVA-101 approach is designed to produce steady and sustained expression of sFLT-1 compared to the peaks and troughs experienced by patients on the current standard of care.

AVA-101 Preclinical Studies

Multiple preclinical studies of AVA-101 demonstrated no vector-specific adverse effects. For example, a study in 45 mice did not identify any systemic immune response subsequent to subretinal injections; the localized immune response in treated eyes was mild and transient and did not interfere with long-term efficacy or safety.

Highlighted below are results from a transgenic mouse model of wet AMD for AVA-101. The study demonstrated that the retinal neovascular lesions, a model for wet AMD, improved following treatment with AVA-101. An examination of eye tissues treated with AVA-101 also revealed that photoreceptors were preserved as compared to controls.

AVA-101: Transgenic Mouse Neovascularization Model



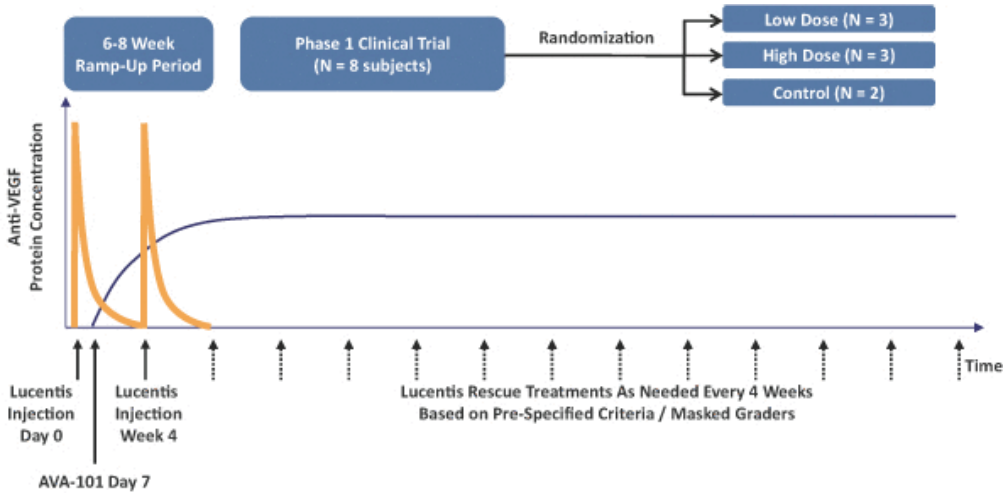
Transgenic mice expressing VEGF show symptoms of retinal neovascularization, including hyperpermeability, retinal degeneration, and scarring. Mice were treated with an inactive control vector (top row) or AVA-101 (bottom row) in the area demarcated by arrowheads. Mice treated with AVA-101 showed reduced neovascularization and scarring compared to those treated with an inactive control vector.

AVA-101 Phase 1/2a Clinical Trial

We are evaluating AVA-101 in a Phase 1/2a trial at LEI in Australia. The Phase 1 portion involving eight subjects completed the twelve-month endpoint and data has been reported. The Phase 2a portion involving 32 subjects is fully enrolled with top-line data expected in mid-2015.

The goal of the Phase 1 trial was to establish initial ophthalmic and systemic safety, as well as to investigate early efficacy as defined by improvement in visual acuity, reduction in retinal thickness and a reduced number of anti-VEGF (Lucentis) rescue injections. Participation in the trial was limited to subjects 55 years or older with confirmed neovascular leakage associated with AMD. Subjects were randomized into three groups: control, low AVA-101 dose (10^{10} vector genomes) and high AVA-101 dose (10^{11} vector genomes). All subjects received two initial doses of Lucentis at Day 0 and Week 4 and the subjects in the active arms received AVA-101 on Day 7. Beginning with the Week 8 visit, Lucentis was given as rescue therapy on an as-needed basis. The requirement for rescue therapy was based on objective criteria of disease recurrence as judged by personnel that were unaware of the subjects' treatment group. Subjects were assessed every four weeks for adverse events, retinal thickness, visual acuity and the need for Lucentis rescue injections.

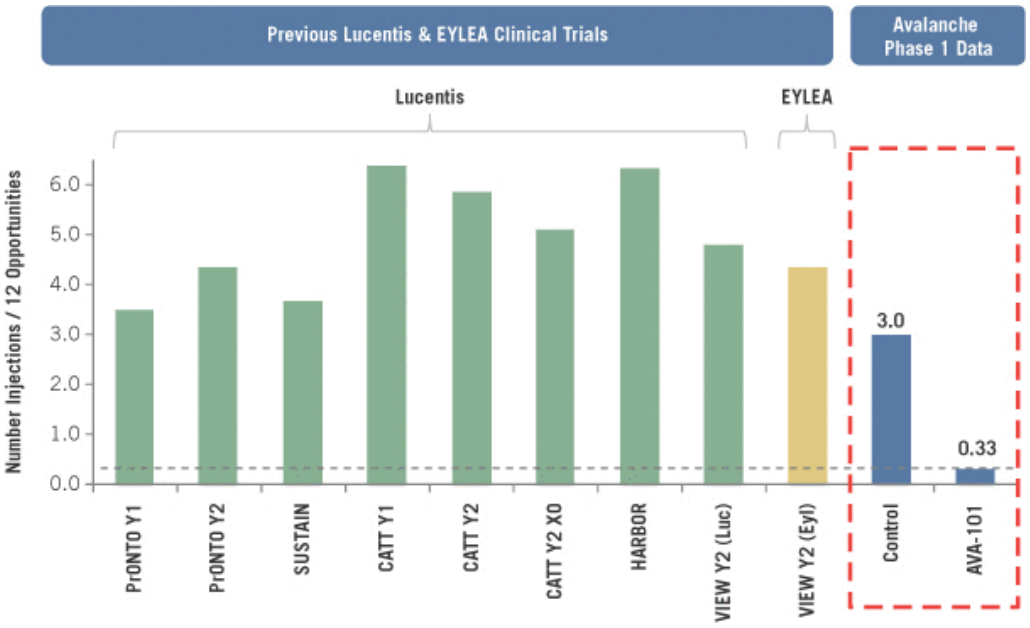
AVA-101 Phase 1 Illustrative Trial Design



All subjects received two initial doses of Lucentis on Day 0 and Week 4 and the subjects in the active arms received AVA-101 on Day 7. Beginning with the Week 8 visit, Lucentis was given as rescue therapy on an as-needed basis.

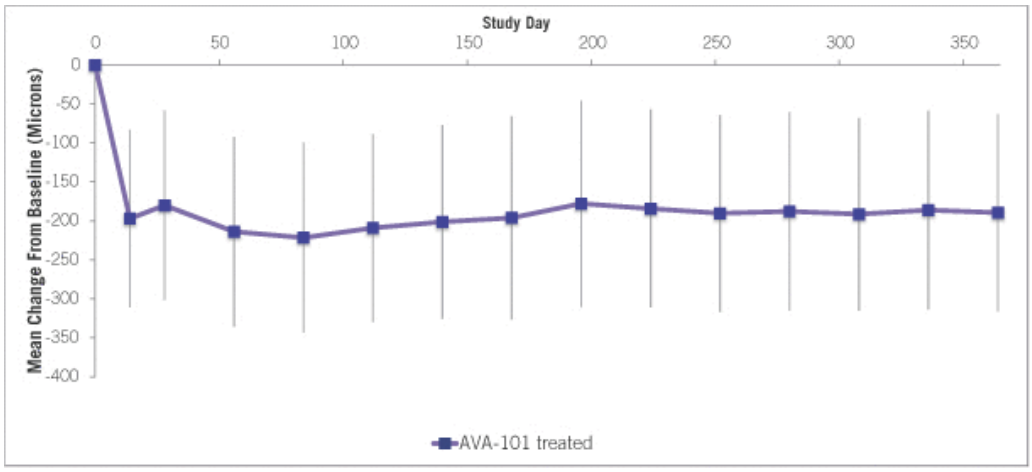
One-year follow up from the Phase 1 portion of the trial was completed in April 2013. No significant drug-related safety concerns were observed. There were mild and transient inflammatory responses related to the injection, but no effects that were deemed to be drug-related. There were no clinically significant adverse events detected systemically by clinical tests and no systemic anti-VEGF related events. The AAV vector was not detected outside of the treated eye.

Based on data from several previous clinical trials of Lucentis and EYLEA, when subjects are seen every four weeks and treated only as needed, they receive injections at 29% to 52% of visits. This translates to 3.5 to 6.4 injections out of 12 opportunities. In our Phase 1 trial, the control subjects needed 3.0 rescue treatments during the 12 opportunities from Week 8 to Week 52. By contrast, subjects receiving low or high dose of AVA-101 needed an average of only 0.33 rescue treatments over the same period. This equates to four of the six subjects in the active arms requiring no rescue injections, and two of the six subjects in the treatment arms requiring only a single rescue injection.



As shown in the graph below, the average retinal thickness for subjects treated with AVA-101 decreased meaningfully and this effect was maintained for the entire year of the trial.

AVA-101 Phase 1: Average Change in Retinal Thickness of Treated Subjects



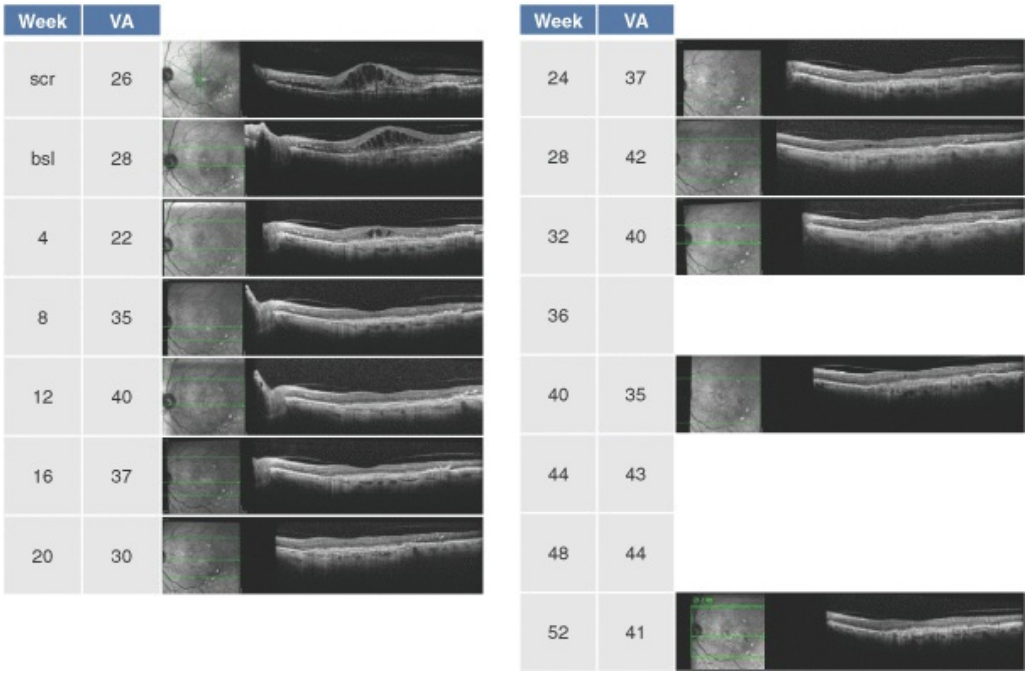
As highlighted in the table below, visual acuity improved in the high and low dose AVA-101 treated groups by an average of 8.7 and 6.3 letters from baseline, respectively. Despite an average of three extra injections of Lucentis, the control subjects lost 3.5 letters of visual acuity. Five of six subjects improved 5 letters from baseline, and three of six subjects improved 10 letters. One subject lost six letters from baseline; this subject had significant sub-foveal scarring at baseline, and consequently may not have had the ability to improve. Such subjects will be excluded from future trials designed to evaluate the efficacy of AVA-101.

AVA-101 Phase 1: Change in Visual Acuity

Group	Subject	Baseline Visual Acuity (ETDRS Letters)	Week 52 Visual Acuity (ETDRS Letters)	Change from Baseline	Change from Baseline
Low Dose	R1001	33	40	+7	+8.7
	R1002	28	41	+13	
	R1004	46	52	+6	
High Dose	R2005	56	50	-6	+6.3
	R2006	54	64	+10	
	R2008	34	49	+15	
Control	R1003	28	21	-7	-3.5
	R2007	39	39	+0	

Case Study of Subject Treated with AVA-101

The table below depicts one example of the therapeutic benefit of AVA-101 in the Phase 1 trial. This subject exhibited an advanced form of wet AMD, having received more than 20 injections of Lucentis prior to enrolling in the trial and with a visual acuity (VA) score of 26 at screening and 28 at baseline (approximately 20/250 on the Snellen scale). As evident from the scan below, the retina contained significant fluid, leading to increased retinal thickness. Pursuant to the trial protocol, the subject received Lucentis during the ramp-up phase on Day 0 and Week 4 and received one injection of low-dose AVA-101 on Day 7. By Week 8, the subject showed improved retinal anatomy and seven letter improvement in visual acuity. By Week 52, the subject's visual acuity increased by 13 letters from baseline to approximately 20/150 on the Snellen scale. In addition, the subject did not require a single rescue treatment of Lucentis following Week 4 throughout the duration of the trial.



Clinical Development for AVA-101

We initiated the Phase 2a portion of this trial in 32 subjects in August 2012. The trial design is similar to the Phase 1 trial. This portion of the study included subjects with less advanced disease compared to the Phase 1 subjects, including less extensive scarring and visual acuity up to 20/30. Subjects were randomized 2:1 to high dose AVA-101 and control with similar ramp up and re-treatment criteria as in the Phase 1 portion. The primary endpoint is safety and secondary endpoints include retinal thickness, visual acuity and the need for rescue injections with anti-VEGF therapy (Lucentis). The trial is fully enrolled and we expect to report top-line data in mid-2015.

Following the ongoing Phase 2a study, we plan to file an IND in the United States. Subsequently, we plan to conduct a Phase 2b trial in the United States in the second half of 2015. The planned trial will be a randomized, controlled, multi-center, double-masked study to assess the efficacy, safety and tolerability of a single subretinal injection of AVA-101 in subjects with wet AMD. The trial will include approximately 120 subjects and have endpoints similar to the Phase 2a trial.

Production of AVA-101 Phase 2b clinical drug substance using our proprietary baculovirus system and purification methods was completed in December 2014. Additionally, the in-life portion of the non-human primate study aimed at evaluating the toxicology and biodistribution of AVA-101 made in the baculovirus system was completed in November 2014. Preliminary data from this study suggest that AVA-101 made in baculovirus is well-tolerated. These activities remain on track to support initiation of the planned Phase 2b clinical trial in the second half of 2015.

Additional Markets for AVA-101

Beyond wet AMD, there are additional ophthalmic diseases where VEGF is known to play a central role, including DME and macular edema following RVO. Like wet AMD patients, these patients are currently treated with frequent injections into the eye with anti-VEGF agents.

DME is the leading cause of blindness in young adults in developed countries, affecting 12% and 28% of type 1 and type 2 diabetic patients, respectively, as published in the *World Journal of Diabetes* (2011). There are potentially many factors leading to the development of DME including poor control of diabetes, hypertension and dyslipidemia. These factors result in leakage of intravascular liquid into the interstitial space in the eye. Lucentis is currently approved for treatment of DME and Regeneron has recently filed for FDA approval of EYLEA for DME with the FDA.

There are an estimated 2.5 million patients in the world with RVO. In RVO, a retinal vein, which is responsible for draining blood from the eye, becomes obstructed. Both Lucentis and EYLEA have been approved in the United States, Europe and several other countries as treatments to alleviate symptoms of this disease.

AVA-201 for the Prevention of Wet AMD

According to the CDC, approximately 7.3 million patients in the United States are at high risk of developing wet AMD. Within this group, we believe that we can identify a subset of the patients at the highest risk of progressing to wet AMD through a combination of clinical and genetic factors. We believe these patients represent a highly motivated subgroup who could benefit from AVA-201 by preventing the progression from intermediate AMD to advanced wet AMD and the associated vision loss.

AVA-201 is our next generation anti-VEGF gene therapy product candidate, which we are developing for the prevention of wet AMD. AVA-201 delivers the same sFLT-1 expressing gene as AVA-101 but uses next-generation AAV vector delivery method. AVA-201 is administered by an intravitreal injection directly into the vitreous, the jelly-like substance inside the eye. Intravitreal injections are commonly performed, and represent a relatively convenient and low-risk procedure. Furthermore, AVA-201 uses an AAV vector that has been specifically selected through our proprietary directed evolution technology to overcome the physical barrier presented by the anatomy of the retina, leading to high rates of transduction of retinal cells. Based on the features of AVA-201, we are positioning this product candidate for prophylaxis use in patients with earlier forms of AMD. We expect to begin IND-enabling studies in 2015. We own exclusive rights for the development and commercialization of AVA-201 worldwide.

AVA-201 Preclinical Study

To establish proof of concept for the prevention of wet AMD, we tested whether sFLT-1 could prevent the onset of wet AMD symptoms in a non-human primate model. In this study, published in the journal *Molecular Therapy* (2005), non-human primates were transduced with AAV encoding sFLT-1 in one eye, and a control vector in the other eye. At 16 months, choroidal neovascularization, or growth of new blood vessels in the choroid of the eye, was induced by laser irradiation and assessed at two and four weeks. While 46% of control eyes developed lesions by Week 4, none of the treated eyes developed lesions. Therefore, a single dose of the treatment had prevented disease development 17 months later. This initial study, which used AVA-101 as a proof-of-concept, demonstrated that upregulation of sFLT-1 could effectively prevent development of choroidal neovascularization, a major symptom of wet AMD.

Long-Term Prevention of Choroidal Neovascularization in Non-Human Primates

Lesions Graded on Fundus Fluorescein Angiogram (Leaking / Total)		
Subject	Right Eye (sFLT-1 Treated)	Left Eye (Inactive Protein)
1	0 / 8	6 / 8
2	0 / 8	3 / 8
3	0 / 8	2 / 8

Future Clinical Development for AVA-201

We intend to initiate IND-enabling studies for AVA-201 in 2015, followed by a Phase 1 clinical trial. If AVA-201 demonstrates efficacy for the prevention of wet AMD, we intend to pursue other indications, such as DME and RVO.

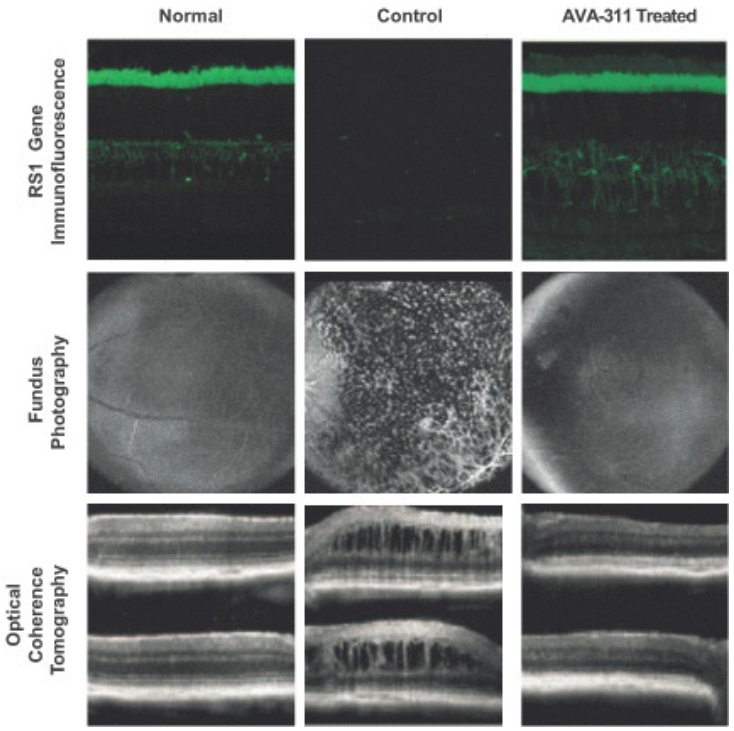
AVA-311 for the Treatment of Juvenile X-linked Retinoschisis

XLRS is an inherited retinal disease that occurs almost exclusively in males. It is caused by mutations in the RS1 gene located on the X chromosome. The RS1 protein binds to the surface of the photoreceptors and biopolar cells in the retina and is crucial in maintaining the tissue's integrity. Disruption in the production of the RS1 protein may cause schisis, or splitting, of the retinal layers or leakage in the blood vessels of the retina. These complications lead to severe vision impairment or blindness and often manifest early in childhood. We believe that approximately 10,000 boys and young men suffer from XLRS.

As part of our Collaboration Agreement with Regeneron, we are conducting studies on AVA-311 for the potential treatment of XLRS, a genetic disease affecting boys and young men with no approved therapy. Regeneron will be responsible for various preclinical studies of AVA-311 conducted as part of our collaboration. AVA-311 is comprised of an optimized AAV vector using our directed evolution technology that intravitreally delivers the RS1 gene in the eye to potentially achieve a functional cure for patients. As part of our collaboration with Regeneron, if it exercises its option it will be responsible for all preclinical studies and clinical trials for AVA-311 and will retain worldwide commercialization rights. We have the option to share up to 35% of the development costs and profits from this product candidate.

AVA-311 Preclinical Study

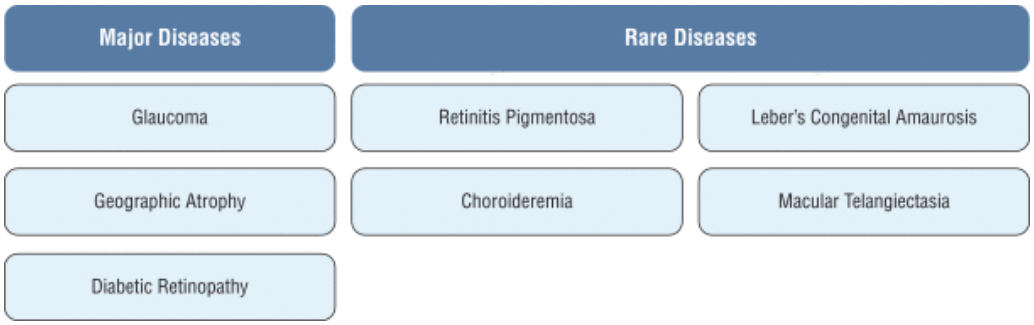
Working with collaborators, we completed a preclinical study with AVA-311 in a mouse model of XLRS that mimics many of the features of the disease by suppressing the RS1 gene in mice. The mice were given a single intravitreal injection of AVA-311 in one eye, and the other eye was left untreated. Mice were monitored for four months. As shown in the immunofluorescence images in Row 1 below, treated eyes exhibited high levels of RS1 protein expression, localized in photoreceptor outer segments of the retina, at levels that are comparable to those found in normal eyes. In addition, as shown in Row 2 by the fundus photographs of the retina and in Row 3 by cross-section images based on optical coherence tomography, AVA-311 restored the appearance of a normal retina.



To evaluate retinal function, electroretinography (ERG), which measures the electrical responses of various cell types in the retina, was used in the preclinical study of AVA-311. Treated eyes exhibited significant improvement in function after one month, and this improvement was maintained over four months. Conversely, retinal function in untreated eyes was lower and continued to decline over this four-month period.

Future Opportunities

In addition to AVA-101, AVA-201 and AVA-311, we are using our Ocular BioFactory platform to develop other undisclosed product candidates. These product candidates are focused on treating prevalent and rare ophthalmic diseases where a single administration of our therapy can potentially provide a functional cure. Some of these future opportunities are highlighted in the table below.



Manufacturing

We produce our AAVs using a proprietary manufacturing process based on insect cells and baculoviruses, a common family of viruses found in invertebrates. This approach is well suited for the production of large quantities of AAVs, as it takes advantage of efficiency of viral infection coupled with the high density and scalability of insect cells grown in serum-free suspension cultures. Compared to the mammalian cell-based approaches commonly used in the field, our manufacturing process is designed to produce higher yields of vectors in a cost-effective manner.

Our BVES manufacturing process is presented in the figure below.

1) The process begins with two DNA constructs, one encoding the therapeutic protein and the other encoding AAV helper components encoding the AAV capsid and for replication of vectors.

2) Each DNA construct is inserted into the genome of a baculorvirus to create two types of recombinant baculoviruses.

3) The two baculoviruses are used to transduce insect cells, which in turn produce large amounts of AAV vectors containing the therapeutic gene of interest.

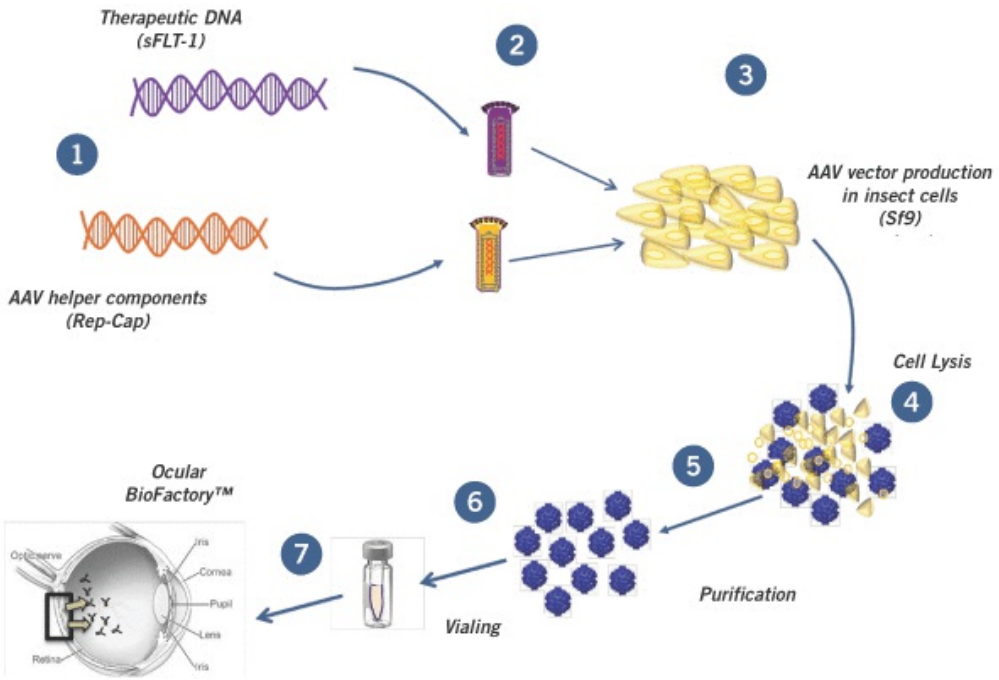
4) The transduced cells are then harvested and treated with a lysis buffer solution to burst the insect cells and release the AAV vectors.

5) AAV vectors are then purified to remove unwanted debris.

6) Following purification, the vectors are formulated in a physiological solution and placed in vials.

7) The resulting drug product is then used to create an Ocular BioFactory for the treatment of ophthalmic diseases.

BVES Manufacturing Process



We have entered into a manufacturing technology license agreement pursuant to which we and Lonza Houston, Inc. are assessing certain technology potentially useful for the manufacture of our products. The license agreement provides that the parties will conduct activities to evaluate such technology and that we may elect to engage Lonza to manufacture our products. We also granted to Lonza certain licenses to practice the manufacturing technology for products other than those being developed by us, our affiliates or sublicensees.

Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. 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 Ocular BioFactory platform, differentiated product candidates and scientific expertise in the field of gene therapy provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

AVA-101 will compete with a variety of therapies currently marketed and in development for wet AMD using therapeutic modalities such as biologics, small molecules and gene therapy. Existing anti-VEGFs, Lucentis, EYLEA and Avastin, are well established therapies and are widely accepted by physicians, patients and third-party payers as the standard of care for the treatment of wet AMD.

There are several other companies with marketed products or products in development for the treatment of wet AMD, including Allergan, Iconic Therapeutics, Inc., LPath Therapeutics Inc., Novartis, Ocular Therapeutix, Inc., Ophthotech Corporation, Hoffmann-La Roche Ltd., Neurotech Pharmaceuticals, Inc., Regeneron, Santen

Pharmaceuticals Co., Ltd., Valeant Pharmaceuticals North America LLC, ReGenX Biosciences LLC, Ohr Pharmaceuticals, Inc. and Mesoblast Limited.

Our preclinical product candidates are being developed for the treatment of prevalent or rare ophthalmic diseases, such as the prevention of wet AMD and XLRS, for which there are no approved therapies. However, there are multiple companies developing gene therapies for ophthalmic diseases, including Applied Genetic Technologies Coporation, Asklepios BioPharmaceutical Inc., Eos Neuroscience, Inc., GenSight Biologics, Genzyme Corporation, Hemera Biosciences, Inc., RetroSense Therapeutics, LLC, Spark Therapeutics, Inc., Oxford Biomedica plc, Sanofi-Aventis S.A., NightStaRx Limited and 4D Molecular Therapeutics, LLC.

Many of our competitors, either 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 commercializing those treatments. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. Our competitors' treatments may be more effective, or more effectively marketed and sold, than any treatment we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our treatments.

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

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

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. In addition, we expect that our therapeutic products, if approved, will be priced at a significant premium over competitive generic products and our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products.

License and Collaboration Agreements

Regeneron Research Collaboration and License Agreement

In May 2014, we entered into the Collaboration Agreement with Regeneron to research, develop and commercialize certain gene therapy products based on our proprietary viral vectors that express transgenes encoding molecules that modulate up to a total of eight specified targets, and encoding certain endogenous molecules known to bind to and modulate such targets. Such products, including AVA-311, are referred to collectively as "Products." Pursuant to the Collaboration Agreement, we and Regeneron will conduct a research program to identify potential Products for a specified time period. Regeneron will bear all costs of performing research under the Collaboration Agreement. Regeneron has a right to substitute a certain number of such targets and may, subject to a payment to us, expand the collaboration beyond the four initially designated targets to include up to four additional targets not currently being researched or developed by Avalanche, and endogenous

molecules known to bind to and modulate such additional targets, in the research program. Regeneron has an option, exercisable with respect to all Products containing transgenes expressing molecules that modulate one of the specified targets, to obtain an exclusive, worldwide license to research, develop, use, import, export, make, manufacture and commercialize such Products for the treatment, prevention or diagnosis of human disease or other medical disorders. Regeneron may exercise this option prior to the expiration of the term of the research program, within a certain time period after the acceptance for filing with the FDA of the IND for such Products. Regeneron must pay us an option fee each time it exercises an option.

Regeneron has the right to file an IND with the FDA for Products prior to exercising its option. If Regeneron exercises its option for specified Products, Regeneron will be primarily responsible for developing, obtaining and maintaining regulatory approval for, and commercializing such Products.

We have a right to co-fund costs of developing, manufacturing and commercializing Products containing transgenes encoding molecules capable of modulating a target with respect to which Regeneron has exercised its option, subject to certain exceptions. We may exercise this co-funding right up to two times. If we exercise such right, we may elect to bear up to 35% of all development costs incurred for such Products. For any co-funded Products, Regeneron's payment obligations extend until the Product is no longer sold in the applicable territory. For those Products for which we exercise this option, either party may opt out of sharing development costs for all Products containing transgenes encoding molecules capable of modulating a protein target, in which case the other party may continue to develop and commercialize such Products, subject to the payment of a royalty to the other party ranging from low-single digit to low double digit royalties. While Regeneron will record all revenue from sales of the co-funded Products, Regeneron will share in the net profits and losses of sales of any Products for which we exercised our co-funding right, with each party receiving a share of profits and bearing its share of losses in accordance with the share of development costs borne by each party for such Product, provided that neither party exercises its opt-out right for such Products.

Additionally, we granted to Regeneron a time-limited right of first negotiation for a potential license to develop and commercialize AVA-101. Such right may be exercised within a specified time period following the first Phase 1 clinical trial for AVA-101. If Regeneron wishes to exercise such right, it must make a payment to us. If Regeneron exercises its right to negotiate and makes such payment, but the parties do not enter into an agreement under which Regeneron obtains such a license, we shall be free to enter into negotiations with third parties provided that for a certain period after expiration of the negotiation period, we may not grant a third party such a license on terms that are less favorable, when taken as a whole, to us than the last proposed offer we made to Regeneron without first offering Regeneron the right to acquire or license AVA-101 on terms and conditions that provide us substantially the same economic value.

Under the Collaboration Agreement, Regeneron made an initial payment of $8.0 million dollars for collaboration research costs, a one-time option fee and a one-time license grant fee.

In addition to the initial payment, Regeneron may make the following payments to us:

- reimbursement for additional collaboration research costs;
- up to $80.0 million in development and regulatory milestones for product candidates directed toward each of the eight therapeutic candidates, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets subject to the Collaboration Agreement; and
- tiered, low- to mid-single digit royalties on annual net sales, subject to certain adjustments.

For each Product, Regeneron's payment obligations extend until the last to occur of the following: (i) the discontinuation of development of the Product or (ii) once a Product is approved by the FDA, the later of (x) the duration of patent coverage for the Product or (y) ten years after first commercial sale of the Product in a particular territory.

The Collaboration Agreement continues until the expiration of the option period for all Products, which occurs on May 1, 2017 if Regeneron has not exercised any options for a Product prior to such date. If Regeneron exercises an option for a Product prior to such date, the Collaboration Agreement continues in effect with respect to that Product on a country-by-country basis until the expiration of all payment obligations under the Collaboration Agreement. The Collaboration Agreement may also be terminated (i) by Regeneron at will, either in its entirety or on a target by target basis, upon 30 days' prior written notice to us, (ii) by either party, upon written notice in connection with a material breach remaining uncured 60 days after initial written notice, (iii) by us, if Regeneron challenges the patent rights licensed by us under the Collaboration Agreement or (iv) by either party, for insolvency of the other party.

University of California License Agreement

In May 2010, we entered into a license agreement with the Regents of University of California (Regents) as amended in September 2013. Under the license agreement, the Regents have granted to us an exclusive (even as to the Regents) license, with the right to grant sublicenses, under the Regents' undivided interest in patent rights covering a method of using recombinant gene delivery vectors for treating or preventing diseases of the eye, to develop, make, have made, use offer for sale, import, export and sell products covered by such patent rights in all fields of use in the United States. The licensed patent rights are jointly owned by the Regents and Chiron Corporation, but our license extends only to the Regents' interest in such patent rights.

Under the license agreement, we are required to diligently proceed with the development, manufacture and sale of licensed products, which includes obligations to meet certain development-stage milestones within specified periods of time, and to market the resulting licensed products in sufficient quantity to meet market demand. We have the right and option to extend the date by which we must meet any milestone by six-months up to two times by paying an extension fee for each such extension.

We have paid the Regents a license fee of $100,000. We are also obligated to make milestone payments totaling up to $900,000 upon reaching certain stages of development of the licensed products for one indication, and totaling up to $500,000 for each subsequent indication for which licensed products are developed, for up to a maximum of two additional indications. We must pay the Regents a low single-digit royalty on net sales of the licensed products by us or our sublicensees, subject to a minimum annual royalty payment of $50,000 beginning in the calendar year after the first commercial sale of a licensed product, until the patent rights upon which such royalties are based expire or are held invalid, which is currently expected to occur in 2020, subject to any potential patent term extensions. We are obligated to reimburse the Regents for expenses associated with the prosecution and maintenance of the licensed patents. Finally, we are obligated to pay the Regents a mid-teen percentage of non-royalty licensing revenue we receive from sublicensees.

Our license agreement with the Regents continues until the expiration of our royalty obligations. We may terminate this agreement without cause at any time upon 30 days' prior written notice to the Regents. The Regents may terminate this agreement for a breach by us that remains uncured for 60 days, if we become insolvent, if we directly or through a third party file a claim that a licensed patent right is invalid or unenforceable or if we fail to meet or extend the date for meeting certain diligence milestones.

Intellectual Property

Overview

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. 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. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

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 licenses, patents or trade secrets that cover these activities. In some cases, these rights may need to be enforced by third party licensors. 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 60 patent applications pending in the United States and foreign jurisdictions. At least 38 patent applications have been filed in the United States and foreign jurisdictions by or on behalf of universities which have granted us exclusive license rights to the technology. To date, 12 patents have issued to us or to our licensors that are active. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek United States and international patent protection for a variety of technologies, including: research tools and methods, methods for transferring genetic material into cells, AAV-based biological products, methods for treating diseases of interest and methods for manufacturing our AAV-based products. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel biological products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use specific technologies in our research and development.

Company Owned IP

We own a family of patent applications that are directed to AAV-based compositions and methods for treating or preventing eye diseases associated with neovascularization. The applications in this family relate to the AVA-101 composition, various unit dosages, dosing regimens and routes of administration. Four applications in this family are pending in the United States, and corresponding patent applications are pending in Australia, Brazil, Canada, China, Europe, Israel, India, Japan, South Korea, Mexico, New Zealand, Russia, Singapore, Thailand, Taiwan and South Africa. Patents that grant from this patent family are generally expected to expire in 2033, subject to possible patent term extensions.

We are also pursuing innovative ways to regulate the expression of transgenes in tissues. To that end, we have, in collaboration with Stanford University, filed a U.S. patent application that is directed to methods for regulating gene expression in a subject. Any patents that grant from this application are expected to expire in 2033, subject to possible patent term extensions.

Licensed IP

We have obtained exclusive licenses to patents directed to both compositions of matter and methods of use.

For example, we have exclusively licensed the rights of the Regents to a U.S. patent directed to methods of treating ocular disease that relate to methods of using AVA-101. This patent is co-owned by the Regents and by Chiron Corporation, and will expire in 2020, unless a term extension is obtained for such patent. There are no foreign patents in this patent family.

We have exclusively licensed several families of patents and applications that relate to variant rAAV virions having desirable characteristics, such as increased infectivity, as well as novel methods to screen for such variants.

One patent family that we have exclusively licensed includes granted patents in Australia, Germany, France, the United Kingdom and Spain; three pending U.S. patent applications; and a pending patent application in Canada. The patents are projected to expire in 2024, subject to possible patent term extensions, as are any patents that granted from the pending applications.

Another patent family that we have exclusively licensed includes a granted U.S. patent that is projected to expire in 2031 and a pending U.S. patent application which, if granted, is also projected to expire in 2031, in both cases subject to possible patent term extensions.

A third patent family that we have exclusively licensed includes three pending U.S. patent applications and pending corresponding applications in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, South Korea, Mexico, Russia, Singapore and South Africa. Patents that grant from this patent family are generally expected to expire in 2032, subject to possible patent term extensions.

We have also nonexclusively licensed rights to a patent family that includes an issued European patent and related Chinese and U.S. patent applications directed to methods of manufacturing. The European patent is expected to expire in 2027, as are any patents that may grant from the related patent applications.

Trademark Protection

We have registered trademarks in connection with our biological products. We may pursue additional registrations for future products in markets of interest. 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.

Trade Secret Protection

Finally, we may rely, in some circumstances, on trade secrets to protect our technology. 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.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of our product candidates. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling, and export and import of our product candidates.

In the United States, the FDA regulates drug and biologic products under the Federal Food, Drug, and Cosmetic Act (FFDCA), and the FDA implements regulations and other laws, including, in the case of biologics, the Public Health Service Act. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, the approval process or after approval, we may become subject to

administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us. Our product candidates may be subject to regulation by the FDA as biologics. Biologics require the submission of a Biologics Licensing Application (BLA) and approval by the FDA before being marketed in the United States. Similarly, FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States.

The process required by the FDA before our product candidates may be marketed in the United States generally involves:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies all performed in accordance with the FDA's current Good Laboratory Practice regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials in the United States may begin;
- approval by an independent IRB at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- prior to commercialization satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP regulations;
- submission to the FDA of a BLA or a new drug application (NDA);
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the BLA or NDA prior to any commercial marketing, sale or shipment of the product.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of pre-clinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must grant permission, either explicitly or implicitly by not objecting before each clinical trial can begin.

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND. An IRB for each medical center

proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice (GCP) requirements, including the requirements for informed consent.

All clinical research performed in the United States in support of a BLA or an NDA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA or an NDA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Clinical Trials

For purposes of BLA or NDA submission and approval, clinical trials are typically conducted in three or four sequential phases, which may overlap or be combined.

- Phase 1: Clinical trials are initially conducted in a limited population of subjects to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.
- Phase 2: Clinical trials are generally conducted in a limited subject population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the product candidate for specific targeted indications in subjects with the disease or condition under study.
- Phase 3: Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as “pivotal” studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. Phase 3 clinical trials are generally undertaken with large numbers of subjects, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse subject population at multiple, geographically-dispersed clinical trial sites.
- Phase 4: In some cases, the FDA may condition approval of a BLA or an NDA for a product candidate on the sponsor’s agreement to conduct additional clinical trials after the product’s approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the product. Such post approval trials are typically referred to as Phase 4 clinical trials.

These phases of testing may not be completed successfully within any specified period, if at all. Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the product candidate in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Biologics License Applications and New Drug Applications

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the product, are submitted to the FDA in the form of a BLA or an NDA requesting approval to market the product for one or more specified indications. The FDA reviews a BLA or an NDA to determine, among other things, whether a product is safe and effective for its intended use.

Once a BLA or an NDA has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. However, the review process is often significantly extended by FDA requests for additional information or clarification. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to BLAs and NDAs within ten months of the filing date for standard review, but this timeframe is also often extended and FDA review may not occur in a timely basis at all. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of a BLA or an NDA if the applicable statutory and regulatory criteria are not satisfied, or it may require additional clinical data or an additional Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the BLA or NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. Moreover, even if a product receives approval, the approval may be significantly limited to specific disease and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Once the FDA approves a BLA or an NDA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. Where a withdrawal may not be appropriate, the FDA still may seize existing inventory of such product or require a recall of any biologic or drug already on the market. In addition, the FDA may require testing, including Phase IV clinical trials and surveillance programs to monitor the effect of approved biologics or drugs which have been commercialized. The FDA has the authority to prevent or limit further marketing of a biologic or drug based on the results of these post-marketing programs.

Drugs and biologics may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the product, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement or a new NDA or NDA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Before approving an application, the FDA will inspect the facility or the facilities at which the finished biologic or drug product, and sometimes, for drug products, the active drug ingredient, is manufactured, and will not approve the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance, and will not approve the product unless compliance with GCP requirements is satisfactory.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our product candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Preclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the biologics or drugs. After approval, certain changes to the approved product, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval. Depending on the nature of the change proposed, a BLA supplement or an NDA supplement must be filed and approved before the change may be implemented. For many proposed

post-approval changes to a BLA or an NDA, the FDA has up to 180 days to review the application. As with new BLAs and NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

Other Regulatory Requirements

Any biologics or drugs manufactured or distributed by us or our collaborators pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the product. Biologic and drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. Adverse event reporting and submission of periodic reports are also required following the FDA approval of a BLA or an NDA. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a product from distribution or withdraw approval of the BLA for that biologic or the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of biologics and drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

Other Healthcare Laws and Regulations

If we obtain regulatory approval for any of our product candidates, we may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
- HIPAA, as amended by HITECH, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and impact our financial results.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payers. Third-party payers include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payer will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payers do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, contains provisions that

may reduce the profitability of drug products, including, for example, increased the minimum rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care plans, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payers fail to provide adequate coverage and reimbursement. In addition, emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

International Regulation

In addition to regulations in the United States, we or our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our future drugs. Whether or not we obtain FDA approval for a drug, we or our collaborators must obtain approval of a drug by the comparable regulatory authorities of foreign countries before commencing clinical trials or marketing of the drug in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized, decentralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marking authorization that is valid for all European Union member states. The decentralized procedure includes selecting one reference member state (RMS), and submitting to more than one member state at the same time. The RMS National Competing Authority conducts a detailed review and prepares an assessment report, to which concerned member states provide comment. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marking authorization may submit an application to the remaining member states post-initial approval. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we or our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of our future drugs.

Environmental Regulation

We are subject to numerous foreign, federal, state and local environmental, health and safety laws and regulations relating to, among other matters, safe working conditions, product stewardship and end-of-life handling or disposition of products, and environmental protection, including those governing the generation, storage, handling, use, transportation and disposal of hazardous or potentially hazardous materials. Some of these laws and regulations require us to obtain licenses or permits to conduct our operations. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, including requirements in the European Union relating to the restriction of use of hazardous substances in products, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits.

Employees

As of February 28, 2015, we had 52 full-time employees, including a total of 18 employees with M.D. or Ph.D. degrees. Within our workforce, 35 employees are engaged in research and development and 17 in business development, finance, legal, human resources, facilities, information technology and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements.

Corporate and Available Information

We were incorporated in Delaware in 2006. We completed the initial public offering of our common stock in August 2014. Our common stock is currently listed on The NASDAQ Global Market under the symbol "AAVL." We are an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012, and therefore we are subject to reduced public company reporting requirements.

Our principal executive offices are located at 1035 O'Brien Drive, Suite A, Menlo Park, CA 94025, and our telephone number is (650) 272-6269. Our website address is www.avalanchebiotech.com. We make available on our website, free of charge, our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. Further, a copy of this Annual Report on Form 10-K is located at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D. C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov. The information found on our website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC.

Item 1A. Risk Factors

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. The risks described below are not the only risks facing the Company. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, results of operations and/or prospects.

Risks Related to Our Financial Position and Need for Capital

We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since we were founded in 2006 and expect to incur significant losses for the foreseeable future as we continue our clinical trial and development programs for AVA-101, a gene therapy product targeting vascular endothelial growth factor (VEGF) currently under development for the treatment of wet age-related macular degeneration (AMD), and our other product candidates. For the year ended December 31, 2014, we reported a net loss of $25.4 million. As of December 31, 2014, we had an accumulated deficit of $36.7 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities and, if AVA-101 or any of our other product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize AVA-101 or other future product candidates. We do not currently have the required approvals to market AVA-101 or any other future product candidates, and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize AVA-101 and our other product candidates.

We will require substantial future capital in order to complete the remaining clinical development for AVA-101 and our other product candidates and to potentially commercialize these product candidates. We expect our spending levels to increase in connection with our clinical trials of AVA-101, as well as other corporate activities. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the type, number, scope, progress, expansion costs, results of and timing of our planned clinical trials of AVA-101 or any of our other product candidates which we are pursuing or may choose to pursue in the future;
- the need for, and the progress, costs and results of, any additional clinical trials of AVA-101 and our other product candidates we may initiate based on the results of our planned clinical trials or discussions with the FDA, including any additional trials the FDA or other regulatory agencies may require evaluating the safety of AVA-101 and our other product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining or maintaining manufacturing for AVA-101 and our other product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales and marketing capabilities and enhanced internal controls over financial reporting;

- the terms and timing of establishing collaborations, license agreements and other partnerships;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- the effect of competing technological and market developments;
- our ability to establish and maintain partnering arrangements for development; and
- the costs associated with being a public company.

Some of these factors are outside of our control. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of our clinical trials and remaining development program through commercial introduction. We expect that we will need to raise additional funds in the future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through collaboration agreements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we will be unable to complete the planned clinical trials for AVA-101 and our other product candidates and we may be required to significantly curtail some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or some of our technologies or otherwise agree to terms unfavorable to us.

Risks Related to the Discovery and Development of Our Product Candidates

Our business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed.

Our product candidates are in the early stage of development and will require additional preclinical studies, substantial clinical development and testing, manufacturing bridging studies and process validation and regulatory approval prior to commercialization. We have only one product candidate that has been the focus of advanced development efforts: AVA-101, a recombinant adeno-associated vector type 2 (AAV2) encoding the anti-VEGF protein sFLT-1. Successful continued development and ultimate regulatory approval of AVA-101 is critical for our future business success. We have invested, and will continue to invest, a significant portion of our time and financial resources in the development of AVA-101. We will need to raise sufficient funds for, and successfully enroll and complete, our planned clinical trials of AVA-101 in wet AMD subjects. The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for AVA-101;
- we may not be able to provide evidence of efficacy and safety for AVA-101;
- we do not know the degree to which AVA-101 will be accepted as a therapy for wet AMD, even if approved;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;
- subjects in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to AVA-101;

- if approved for treatment of wet AMD, AVA-101 will likely compete with other treatments then available, including the off-label use of products already approved for marketing and other therapies currently available or which may be developed; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Of the large number of biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a Biologics Licensing Application (BLA) or a New Drug Application (NDA) to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market AVA-101, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development

programs, we cannot assure you that AVA-101 will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, AVA-101, we may not be able to generate sufficient revenue to continue our business.

We are conducting, and may in the future conduct, clinical trials for AVA-101 and other product candidates in sites outside the United States and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. For example, we are currently conducting a Phase 1/2a trial for AVA-101 with LEI in Australia.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The study population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical studies conducted outside of the United States must be representative of the population for whom we intend to label the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the studies also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials for AVA-101 or any other product candidates, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of AVA-101 or any other product candidates. The FDA may also determine that additional safety or other data are needed before we may commence a Phase 2b clinical trial which could require us to conduct additional trials before we proceed.

Our Ocular BioFactory is based on a novel gene therapy 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 one gene therapy product has been approved in Europe.

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

In addition, the clinical study requirements of the FDA, the European Medicines Agency (EMA) and other regulatory agencies and the criteria these regulators may use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. As of the date of this Annual Report on Form 10-K, the FDA has not approved any gene therapy products for sale and only one gene therapy product has been approved in the Western world, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either Europe or the United States. Approvals by the EMA may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products may 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 (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 studies conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health (NIH) may also be subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee (RAC). Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation.

Conversely, the FDA can put an Investigational New Drug application (IND) on clinical hold even if the RAC has provided a favorable review. Also, before a clinical study can begin at an NIH-funded institution, that institution's institutional review board (IRB) and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. 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 treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we may 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. 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.

All of our product candidates are still in preclinical or early-stage clinical development. If we are unable to commercialize our product candidates or if we experience significant delays in obtaining regulatory approval for, or commercializing, any or all of our product candidates, our business will be materially and adversely affected.

All of our product candidates are still in preclinical and early-stage clinical development. Our ability to generate product revenue will depend heavily on our ability to successfully develop and commercialize these product candidates. We do not expect that such commercialization of any of our product candidates will occur for at least the next several years, if ever. Our ability to commercialize our product candidates effectively will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our product candidates;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States;

- establishing commercial manufacturing capabilities, for example, by making arrangements with third-party manufacturers;
- successfully launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payers;
- establishing market share while competing with other therapies;
- a continued acceptable safety profile of our products following regulatory approval;
- maintaining compliance with post-approval regulation and other requirements; and
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates.

If we, or our collaborators, do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to commercialize our product candidates, which would materially and adversely affect our business, financial condition and results of 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 products based on our Ocular BioFactory platform. Although our AVA-101 product candidate is currently in clinical development, our research programs, including those subject to our collaboration with Regeneron, may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, 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.

We have not tested any of our internally-developed viral vectors, or product candidates derived from these viral vectors, in clinical trials.

Drug development has inherent risk. Our lead product AVA-101 produced in mammalian-cell based manufacturing system is currently being evaluated in a Phase 1/2a human clinical trial. However, neither AVA-101 manufactured in the baculovirus expression system (BVES) system nor our other product candidates have ever been evaluated in human clinical studies, and we may experience unexpected results in the future. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates containing our proprietary vectors are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including AVA-101, may not have favorable results in later clinical trials, if any, or receive regulatory approval.

If our proprietary vectors are not shown to be safe and effective in targeting retinal tissue, we may not realize the value of our investment in directed evolution technology. In addition, success in early clinical trials does not

mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

We cannot be certain that any of our planned clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

AVA-101 and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials;
- we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;
- we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates.

If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. We will be required to identify and enroll a sufficient number of subjects with wet AMD for each of our planned clinical trials of AVA-101. Potential subjects for AVA-101 may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies. We also may encounter difficulties in identifying and enrolling wet AMD subjects with a stage of disease appropriate for our planned clinical trials. In addition, we and our collaboration partner, Regeneron, are developing AVA-311 for the treatment of X-linked retinoschisis (XLRS), an orphan indication. Enrollment of eligible subjects with orphan diseases may be limited or slower than we anticipate in light of the small subject populations involved. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or other foreign regulatory agencies. In addition, the process of finding and diagnosing subjects may prove costly.

We expect to initiate a Phase 2b clinical trial for AVA-101 in the United States in the second half of 2015. 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 or available approved therapies, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed.

Trials using early versions of retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events. For example, generalized public backlash developed against gene therapy following the death in September 1999 of an 18-year-old who had volunteered for a gene therapy experiment at the University of Pennsylvania. Researchers at the university had infused the volunteer's liver with a gene aimed at reversing a rare metabolic disease of the liver. The procedure triggered an extreme immune-system reaction that caused multiple-organ failure in a very short time, leading to the first death to occur as a direct result of a gene therapy experiment. In addition, in 2003, 20 subjects treated for X-linked severe combined immunodeficiency in two gene therapy studies using a murine gamma-retroviral vector showed correction of the disease, but the studies were terminated after five subjects developed leukemia (four of whom were subsequently cured). The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer (often leukemia). Using molecular diagnostic techniques, it was determined that clones from these subjects showed retrovirus insertion in proximity to the promoter of the LMO2 proto-oncogene. Earlier generation retroviruses like the one used in these two studies have been shown to preferentially integrate in regulatory regions of genes that control cell growth. Our inability to enroll a sufficient number of subjects for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

We believe we have appropriately accounted for the above factors in our trials when determining expected clinical trial timelines, but we cannot assure you that our assumptions are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

The occurrence of serious complications or side effects in connection with use of our product candidates, either in clinical trials or post-approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business, prospects, operating results and financial condition.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Various illnesses, injuries, and discomforts have been reported from time-to-time during clinical trials of our product candidates. It is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, operating results and financial condition.

AVA-101 is being studied in diseases of the eye in addition to AMD. There are many potential safety concerns associated with significant blockade of VEGF that may limit our ability to successfully develop and/or commercialize AVA-101. These serious and potentially life-threatening risks, based on clinical and preclinical experience of VEGF inhibitors, include bleeding, intestinal perforation, hypertension, proteinuria, congestive heart failure, heart attack, stroke and geographic atrophy. In addition, patients given infusions of any protein may develop severe hypersensitivity reactions or infusion reactions. Other VEGF inhibitors have reported side effects that became evident only after large-scale trials or after marketing approval when large numbers of patients were treated. There are risks in treating patients with gene therapy vectors, including adeno-associated virus (AAV), such as inflammation, cytotoxic T-cell response, anti-AAV antibodies and immune response to the expressed transgene, including T-cell responses and/or auto-antibodies against sFLT-1. There are risks inherent in the subretinal administration of drugs like AVA-101, which can cause injury to the eye and other complications. For example, in our Phase 1/2a trials of AVA-101 in wet AMD, the most frequent ocular adverse events to date have been subconjunctival hemorrhage, vitreous hemorrhage, cataract progression and intra-ocular inflammation.

There are also risks inherent in subretinal injections, including subretinal injections with AVA-101, such as intraocular inflammation, cataract, sterile and culture positive endophthalmitis, retinal detachment, retinal tear and other side effects. Serious complications or serious, unexpected side effects in connection with the use of AVA-101 could materially harm our business, prospects' operating results and financial condition.

Risks Related to Our Reliance on Third Parties

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

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We are dependent on third parties to conduct the Phase 2 and Phase 3 clinical trials for AVA-101 and preclinical and clinical trials for our other future product candidates, and, therefore, the timing of the initiation and completion of these trials is controlled by such third parties and may occur at times substantially different from our estimates. Specifically, we use clinical research organizations (CROs) to conduct our clinical trials and rely on medical institutions, clinical investigators, CROs and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data.

There is no guarantee that any CROs, investigators or other third parties on which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, fails to meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit by the FDA. Any such delay or rejection could prevent us from commercializing AVA-101 or our other future product candidates.

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

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols.

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 plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies required to support future IND submissions and approval of our product candidates.

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;
- 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 study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products.

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

We currently have relationships with a single supplier for the manufacturing of our viral vectors and product candidates. The supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities. All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturer for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with current Good Manufacturing Practice (cGMP). These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturer must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current Good Laboratory Practice regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Our contract manufacturer has not produced a commercially-approved product and therefore has not obtained the requisite FDA approvals to do so. 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 or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect our manufacturing facilities or those of our third-party contractors involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If the facility does not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

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

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

Additionally, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies 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 studies, 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 studies may be delayed or we could lose potential revenue.

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

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

Risks Related to Commercialization of Our Product Candidates

Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials in the United States for our product candidates, we need to submit the results of preclinical testing to the FDA, along with other information including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND. We may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our plans for our clinical trials. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND, which may lead to additional delays and increase the costs of our preclinical development. Delays in the commencement or completion of our planned clinical trials for AVA-101 or other product candidates could significantly affect our product development costs. We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA failing to grant permission to proceed or placing the clinical trial on hold;
- subjects failing to enroll or remain in our trial at the rate we expect;

- subjects choosing an alternative treatment for the indication for which we are developing AVA-101 or other product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- a facility manufacturing AVA-101, any of our other product candidates or any of their components being ordered by the FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of cGMP or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practice or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;
- inspections of clinical trial sites by the FDA or the finding of regulatory violations by the FDA or an IRB that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire trial or that prohibit us from using some or all of the data in support of our marketing applications;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of AVA-101 or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of our clinical trials, or if we, the FDA or other regulatory authorities, the IRB, other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for a product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. For example, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of AVA-101 or other product candidates could be significantly reduced.

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

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones will be based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline.

Final marketing approval for AVA-101 or our other product candidates by the FDA or other regulatory authorities for commercial use may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenue.

After the completion of our clinical trials and, assuming the results of the trials are successful, the submission of a BLA, we cannot predict whether or when we will obtain regulatory approval to commercialize AVA-101 or our other product candidates, and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize AVA-101 or our other product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for AVA-101 or our other product candidates. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. If marketing approval for AVA-101 or our other product candidates is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

Even if we obtain marketing approval for AVA-101 or any other product candidate, they could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. Following approval, if at all, of AVA-101 or any other product candidates, such candidate will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. 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, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for AVA-101 or any other product candidate that may receive regulatory approval, if any, fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- 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 pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product or request us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue.

The FDA has the authority to require a risk evaluation and mitigation strategy plan as part of a BLA or NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry.

In addition, if AVA-101 or any of our other product candidates is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Even if we receive regulatory approval we still may not be able to successfully commercialize AVA-101 or any other product candidate, and the revenue that we generate from its sales, if any, could be limited.

Even if AVA-101 or any of our other product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payers or the medical community. Coverage and reimbursement of our product candidates by third-party payers, including government payers, is also generally necessary for commercial success. The degree of market acceptance of our product candidates will depend on a number of factors, including:

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

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payers or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payers on the benefits of AVA-101 or any of our other product candidates may require significant resources and may never

be successful. In addition, our ability to successfully commercialize our product candidate will depend on our ability to manufacture our products, differentiate our products from competing products and defend and enforce our intellectual property rights relating to our products.

If the market for AVA-101 for the treatment of wet AMD is smaller than we believe it is, our future revenue may be adversely affected, and our business may suffer.

If the size of the market for wet AMD is smaller than we anticipate, we may not be able to achieve profitability and growth. While we are initially targeting AVA-101 for the treatment of wet AMD, a disease we believe to be the most common cause of vision loss in adults over the age of 50 in developed countries, our projections of the number of people who have wet AMD, as well as the subset of people with these diseases who have the potential to benefit from treatment with wet AMD, are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations and market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payers for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payer may depend upon a number of factors including the third-party payer's determination that use of a product candidate 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 candidate from a government or other third-party payer is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of the applicable product candidate to the payer. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, reimbursement amounts may reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payers are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. By way of example, the Medicare Prescription Drug Improvement and Modernization Act of 2003 (MMA) changed the way Medicare covers and pays for pharmaceutical products. The

legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs, including drugs currently on the market used by physicians to treat wet AMD and likely AVA-101, if approved. As a result of this legislation and the expansion of federal coverage of drug products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payers. These cost reduction initiatives and other provisions of the MMA could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively referred to as the Affordable Care Act, was enacted with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, addressed 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, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care organizations and established annual fees and taxes on manufacturers of certain prescription drugs.

Other legislative changes have also been proposed and adopted in the U.S. since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 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 included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken.

We expect that additional healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our products, if approved, or additional pricing pressures.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of health care may adversely affect:

- the demand for any product candidates for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our product candidates;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

Our product candidates are designed to provide therapeutic benefit after a single administration and, therefore, the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of AVA-101 for the treatment of wet AMD is our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to ocular diseases. We will evaluate internal opportunities from our compound libraries, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from ocular diseases such as diabetic macular edema (DME), retinal vein occlusion (RVO), glaucoma, XLRS or other disorders with high unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

We are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

The process of manufacturing our products is complex, highly regulated and subject to several risks, including:

- The manufacturing of biologics is extremely susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment or vendor or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing facility in which our products are made, such manufacturing facility may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facility in which our products are made could be adversely affected by equipment failures, labor shortages, contaminants, raw materials shortages, natural disasters, power failures and numerous other factors.
- We and our contract manufacturer must comply with the FDA's cGMP regulations and guidelines. We and our contract manufacturer may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our contract manufacturer are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or any delay, interruption or other issues that arise in the manufacture, fill-finish, packaging or storage of our products as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products. This may lead to significant delays in the availability of products for our clinical studies or the termination or hold on a clinical study, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could be costly and damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our products and/or may be subject to product recalls, seizures, injunctions or criminal prosecution.
- Our product candidates are biologics and require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be adequately characterized prior to manufacturing the final product. As a result, an assay of the finished product is

not sufficient to ensure that the product will perform in the intended manner. Accordingly, we expect to employ multiple steps to attempt to control our manufacturing process to assure that the process works and the product or product candidate is made strictly and consistently in compliance with the process.

- Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory.
- Some of the raw materials required in our manufacturing process are derived from biological sources. Such raw materials are difficult to procure and may also be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt commercialization.
- Any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. We may encounter problems achieving adequate or clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

We may not be successful in establishing and maintaining development or other strategic collaborations, which could adversely affect our ability to develop and commercialize product candidates.

We have entered into development or other strategic collaborations with major biotechnology or pharmaceutical companies. For example, our research collaboration and license agreement with Regeneron, which was announced in May 2014, covers up to eight distinct therapeutic targets, in which we could earn up to $80.0 million in development and regulatory milestones for product candidates directed toward each therapeutic target, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

Some of our strategic partners may terminate any agreements they enter into with us, and we may not be able to adequately protect our rights under these agreements. Furthermore, our strategic partners have negotiated for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do.

Moreover, if we fail to maintain development or other strategic collaborations related to our product candidates that we may choose to enter into:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly, and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development of any such product candidates.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of our product candidates. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that

dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for AVA-101 or our other product candidates because third parties may view the risk of failure in future clinical trials as too significant or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such development partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are disappointing. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market.

If our competitors develop treatments for the target indications of our product candidates that are approved more quickly than ours, marketed more successfully or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

We operate in highly competitive segments of the biopharmaceutical markets. We face competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies as well as with new treatments that may be introduced by our competitors. There are a variety of drug candidates in development for the indications that we intend to test. Many of our competitors have significantly greater financial, product candidate development, manufacturing and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. In addition, universities and private and public research institutes may be active in wet AMD research, and some could be in direct competition with us. We also may compete with these organizations to recruit management, scientists and clinical development personnel. We will also face competition from these third parties in establishing clinical trial sites, registering subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

New developments, including the development of other pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. Competition in drug development is intense. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available.

Even if we obtain regulatory approval for our product candidates, the availability and price of our competitors' products could limit the demand, and the price we are able to charge, for our product candidates. For example, EYLEA is currently available in the United States for treatment of wet AMD and macular edema following central retinal vein occlusion (CRVO), and in the United Kingdom, Germany, Switzerland, Australia, Japan and certain other countries for the treatment of wet AMD. Additionally, marketing approval has been obtained in the EU for EYLEA for the treatment of visual impairment due to macular edema secondary to CRVO. We will not achieve our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances. Our inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, prospects, financial condition and results of operations.

Our potential competitors in these diseases may be developing novel immune modulating therapies that may be safer or more effective than AVA-101 or our other product candidates. For example, AVA-101 will compete with a variety of therapies currently marketed and in development for wet AMD, using therapeutic modalities

such as biologics, small molecules and gene therapy. Lucentis, EYLEA and Avastin® are anti-VEGF therapies that are well established and widely accepted by physicians, patients and third-party payers as the standard of care for the treatment of wet AMD. There are several other companies with marketed products or products in development for the treatment of wet AMD, including Allergan, Iconic Therapeutics, Inc., LPath Therapeutics Inc., Novartis, Ocular Therapeutix, Inc., Ophthotech Corporation, Hoffmann-La Roche Ltd., Neurotech Pharmaceuticals, Inc., Regeneron, Santen Pharmaceuticals Co., Ltd., Valeant Pharmaceuticals North America LLC, ReGenX Biosciences LLC, Ohr Pharmaceuticals, Inc. and Mesoblast Limited.

Our preclinical product candidates are being developed for the treatment of prevalent or rare ophthalmic diseases, such as the prevention of wet AMD and XLRS, for which there are no approved therapies. However, there are multiple companies developing gene therapies for ophthalmic diseases, including Applied Genetic Technologies Coporation, Asklepios BioPharmaceutical Inc., Eos Neuroscience, Inc., GenSight Biologics, Genzyme Corporation, Hemera Biosciences, Inc., RetroSense Therapeutics, LLC, Spark Therapeutics, Inc., Oxford Biomedica plc, Sanofi-Aventis S.A., NightStaRx Limited and 4D Molecular Therapeutics, LLC.

We have no sales, marketing or distribution capabilities, and we may have to invest significant resources to develop these capabilities.

We have no internal sales, marketing or distribution capabilities. If AVA-101 or any of our other product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We may have to invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that AVA-101 or any of our other product candidates will be approved, if at all. We may not be able to hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms or at all. Even if we determine to perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by AVA-101 or any other product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product candidates. In some foreign countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Risks Related to Our Business Operations

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of AVA-101 and our product candidates or adversely affect our ability to conduct our business or obtain further marketing approvals for AVA-101 and marketing approvals for our product candidates.

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 symptomatic 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, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. Although none of our current product candidates utilize the gamma-retroviruses used in the 2003 studies, our product candidates do use a viral vector delivery system. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

Adverse events in our clinical trials or those conducted by other parties, 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 potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any such adverse events occur, commercialization of AVA-101 or further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

We are dependent on the services of our President and Chief Executive Officer, Thomas W. Chalberg, Jr., Ph.D., and other key executives, and if we are not able to retain these members of our management or recruit additional management, clinical and scientific personnel, our business will suffer.

We are dependent on the principal members of our management and scientific staff. The loss of service of any of our management could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management, particularly our President and Chief Executive Officer, Dr. Chalberg, and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including Dr. Chalberg, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our clinical development and commercialization efforts. Our success also depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior

management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations.

Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

If we fail to effectively integrate our new executive officers into our organization, the future development and commercialization of our product candidates may suffer, harming future regulatory approvals, sales of our product candidates or our results of operations.

Our current management team has only been working together for a relatively short period of time and some of our current management team have been employed by us for less than a year. Moreover, we expect to continue to expand our management team in the future. Our future performance will depend, in part, on our ability to successfully integrate recently and subsequently hired executive officers into our management team and their ability to develop and maintain an effective working relationship. Our failure to integrate these individuals with other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. In addition to the competition for personnel, the San Francisco Bay Area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

We may encounter difficulties in managing our growth and expanding our operations successfully.

Because as of February 28, 2015 we have only 52 full-time employees, we will need to grow our organization substantially to continue development and pursue the potential commercialization of AVA-101 and our other product candidates, as well as function as a public company. As we seek to advance AVA-101 and other product candidates, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain additional internal capabilities. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, clinical and regulatory, financial, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to so accomplish could prevent us from successfully growing our company.

If we fail to comply with applicable state and federal healthcare laws, we may be subject to civil or criminal penalties and/or exclusion from federal healthcare programs.

In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include anti-kickback, false claims, physician payment transparency and privacy and security laws and regulations. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the

purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced price items and services. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formula managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Many states have similar laws that apply to their state health care programs as well as private payers.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. The Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statute governing healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provided 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 False Claims Act.

Additionally, the False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. The period between August 1, 2013 and December 31, 2013 was the first reporting period, and manufacturers were required to report aggregate payment data by March 31, 2014, and to report detailed payment data and submit legal attestation to the accuracy of such data by June 30, 2014. Thereafter, manufacturers must submit reports by the 90th day of each subsequent calendar year. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

In the course of conducting our business, we may also obtain certain confidential patient health information including retinal scans from subjects participating in our clinical trials. In the event of an inadvertent disclosure or security breach, we could be subject to enforcement measures, including civil and criminal penalties and fines

for violations of state and federal privacy or security standards, such as HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations, including the final omnibus rule published on January 25, 2013. Additionally, certain states have adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. HIPAA, HITECH and comparable state laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. Any liability from failure to comply with the requirements of these laws, to the extent such requirements are deemed to apply to our operations, could adversely affect our financial condition. The costs of complying with privacy and security related legal and regulatory requirements are burdensome and could have a material adverse effect on our results of operations.

The need to build and maintain a robust compliance program with different compliance and/or reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. 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.

We and our development partners, third-party manufacturer and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and our development partners, third-party manufacturer and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of AVA-101 or our other product candidates.

We face an inherent risk of product liability as a result of the clinical testing of AVA-101 and our other product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if AVA-101 or our other product candidates allegedly cause injury or are found to be otherwise unsuitable during product 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 candidate, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for AVA-101 or our other product candidates;

- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize AVA-101 or our other product candidates; and
- a decline in our stock price.

We do not currently maintain product liability insurance. However, we are named as a beneficiary on the product liability insurance policy maintained by one of our trial sponsors, with up to $10.0 million in coverage as a beneficiary under such policy. In the future, we plan to obtain additional product liability insurance coverage in an amount and on terms and conditions that are customary for similarly situated companies and that are satisfactory to our board of directors. 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 AVA-101 or our other product candidates. Although we plan to maintain such insurance, 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. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We and any of our future development partners will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we and any of our future development partners or CROs are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our future development partners report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our future development partners may fail to report adverse events we become aware of within the prescribed timeframe. We and any of our future development partners may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we and any of our future development partners fail to comply with our reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our internal computer systems, or those of our development partners, third-party clinical research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an

event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce AVA-101 and our other product candidates. Our ability to obtain clinical supplies of AVA-101 or our other product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to regulatory authorities, (2) manufacturing standards, (3) federal and state health care fraud and abuse laws and regulations or (4) laws that require the reporting of financial information or data accurately. Specifically, sales, marketing, and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, 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. Activities subject to these laws also involve improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Relating to Our Intellectual Property

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies and universities.

We currently are heavily reliant upon licenses of certain patent rights and proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology

related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide adequate rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. For example, the license granted to us by the Regents to make, have made, use, offer for sale, import, export and sell products covered by certain patent rights licensed to us under our agreement with the Regents is limited to the United States. The license is also limited to the Regents' interest in the licensed patent rights which are co-owned by Chiron Corporation (Chiron). As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories not included in our licenses to patents.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, we must obtain consent from the Regents before we can enforce patent rights licensed to us by the Regents. While such consent may not be unreasonably withheld, the Regents may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

The patent rights subject to our exclusive license with the Regents are jointly owned by Chiron Corporation.

We currently have a license to the Regents' undivided interest in certain patent rights relating to the use of recombinant gene delivery vectors for treating or preventing diseases of the eye. The licensed patent rights are jointly owned by the Regents and Chiron but our license extends only the Regents' interest in such patent rights. As a result, Chiron has a right to develop and commercialize products and technology using these patent rights, and to license to third parties the right to do so. This may lead to the development and commercialization of products and technology by others that are based on technology similar to our Ocular BioFactory platform, which may impair our competitive position in the marketplace and have an adverse impact on our business.

Joint ownership of these patent rights may also limit our ability to effectively enforce our rights in these patents against alleged infringers. First, Chiron may be required to participate in any potential suit against such third party infringers but may not agree to do so. Additionally, Chiron may choose to license its interest in these patent rights to any such infringers without our consent in certain countries. Further, Chiron's joint ownership may limit the Regents' ability to prosecute related patent rights in foreign jurisdictions without the cooperation of Chiron. As a result, our business may be adversely impaired.

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and their uses as well as our ability to operate without infringing upon the proprietary rights of others. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. While we have an issued composition-of-matter patent in the United States for AVA-101, we cannot be certain that the claims in our patent applications covering composition-of-matter of our other product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged.

In addition to our composition of matter patent and applications, we have an issued method-of-use patent in the United States that encompasses AVA-101. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. However, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of AVA-101 or our other product candidates. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing AVA-101 or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this Annual Report on Form 10-K, others may hold proprietary rights that could prevent AVA-101 or our other product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market AVA-101 or our other product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing AVA-101 or our other product candidates, which could harm our business, financial condition and operating results.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control the prosecution and maintenance of the patents relating to our product candidates, there may be times when the filing and prosecution activities for platform technology patents that relate to our product candidates are controlled by our licensors. For example, we do not have the right to prosecute and maintain the patent rights licensed to us under agreements with each of the Regents and Virovek Corporation, and our ability to have input into such filing and prosecution activities is limited. If these licensors or any of our future licensors fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates or companion diagnostic, our ability to develop and commercialize those product candidates and companion diagnostic may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. 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 and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO 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. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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

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 (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 will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, inter-partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

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

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations 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 as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. 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 option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

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

We may fail to comply with any of our obligations under existing agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- 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;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties 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 be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these employees and consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that our company, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. 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 these claims, litigation could result in substantial costs and be a distraction to our management team.

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future 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.

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

Depending upon the timing, duration and specifics of FDA marketing approval of AVA-101 or other product candidates, one or more of our United States patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (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, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

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

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

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

While we have issued patents directed at AVA-101 in the United States and pending patent applications directed at AVA-101 and other product candidates in the United States and other countries, filing, prosecuting and defending patents on AVA-101 and our other 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 product candidates, 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 and other intellectual property protection, particularly those relating to biopharmaceuticals, 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.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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

- others may be able to make gene therapies that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Our Common Stock

We previously identified and have remediated a material weakness in our internal control over financial reporting. If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to prepare accurate and timely consolidated financial statements being prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with the annual report for our fiscal year ending December 31, 2015. When we lose our status as an "emerging growth company" and if we reach an accelerated filer threshold, our independent registered public accounting firm will also be required to attest to the effectiveness of our internal control over financial reporting, and the related report will also be required to be included in our annual reports filed with the SEC. However, for so long as we remain an emerging growth company and also not an accelerated filer, we intend to take advantage of an exemption available to companies meeting these criteria from these auditor attestation requirements. Section 404 of the Sarbanes-Oxley Act of 2002 compliance requirements are complex and require significant documentation, testing, and possible remediation.

To comply with the requirements of being a reporting company under the Exchange Act, we will need to upgrade our financial reporting systems including our information technology systems; implement additional financial reporting controls, and hire additional accounting and finance staff. If we (or our auditors if they are required to assess and attest to the effectiveness of our internal control over financial reporting) are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting, and the trading price of our common stock may decline.

Our management previously identified deficiencies in our internal control over financial reporting that constituted a material weakness in our internal control over financial reporting as of December 31, 2013 and which related to the design and operation of our control environment. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis. We did not maintain an effective control environment, which is the foundation for effective internal control over financial reporting, as evidenced by: (i) an insufficient number of personnel to perform control monitoring activities, (ii) an insufficient number of personnel with an appropriate level of knowledge of U.S. GAAP to determine that our consolidated financial statements were properly prepared in accordance with U.S. GAAP, (iii) insufficient management involvement to identify and resolve errors in recording transactions and (iv) inadequate processes for the preparation and review of our consolidated financial statements.

Subsequent to the identification of the material weakness, we hired an experienced Chief Financial Officer, Corporate Controller and additional skilled accounting and finance staff members, (b) formalized and implemented our accounting policies and internal controls and the related documentation and (c) strengthened our accounting systems, financial statements review procedures and the supervisory reviews by our management that are performed during the financial close process and which support the accurate and timely preparation of consolidated financial statements that are fairly presented in accordance with US GAAP. These improvements to our internal control infrastructure were implemented during 2014, and were in place in connection with the preparation of our consolidated financial statements for the year ended December 31, 2014. As such, we believe that these initiatives have remediated the material weakness in internal control over financial reporting as of December 31, 2014.

Although we have determined that our internal control over financial reporting was effective as of December 31, 2014 we cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The NASDAQ Stock Market, the Securities and Exchange Commission (SEC) or other regulatory authorities. Failure to implement and maintain effective internal control over financial reporting, including failure to remediate any material weaknesses we or our auditors identify, could also restrict our future access to the capital markets.

An active public market for our common stock may not persist.

We completed our initial public offering (IPO) on August 5, 2014. Prior to that offering, there had been no public market for shares of our common stock, and an active public market for our shares may not persist. The lack of an active market may impair our stockholders' ability to sell their shares at the time they wish to sell them or at a price they consider reasonable. The lack of an active market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including those discussed in this "Risk Factors" section of this Annual Report on Form 10-K and other such as:

- our ability to enroll subjects in our planned clinical trials;
- results of the clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory developments in the United States and foreign countries;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations;
- sales of our stock by insiders and stockholders;
- trading volume of our common stock;
- general economic, industry and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our quarterly operating results may fluctuate significantly.

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

- variations in the level of expenses related to our clinical trial and development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting AVA-101 and our other product candidates;
- our execution of any collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- nature and terms of stock-based compensation grants; and
- derivative instruments recorded at fair value.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our failure to meet the continued listing requirements of The NASDAQ Global Market could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of The NASDAQ Global Market, such as the corporate governance requirements or the minimum closing bid price requirement, NASDAQ may take steps to de-list our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we would expect to take actions to restore our compliance with NASDAQ's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the NASDAQ minimum bid price requirement or prevent future non-compliance with NASDAQ's listing requirements.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert control over matters subject to stockholder approval.

As of February 28, 2015, our executive officers, directors and greater than 5% stockholders, in the aggregate, own approximately 55.43% of our outstanding common stock. As a result, such persons, acting together, have the ability to control our management and affairs and substantially all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction. These persons also have the ability to control our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include:

- the authorization of the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- the limitation of the removal of directors by the stockholders;
- a staggered board of directors;

- the prohibition of stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- the elimination of the ability of stockholders to call a special meeting of stockholders;
- the ability of our board of directors to accelerate the vesting of outstanding option grants upon certain transactions that result in a change of control; and
- the establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

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

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

As of February 28, 2015, we have a total of 25,221,495 shares of common stock outstanding. Of these shares, approximately 4,820,426 shares of our common stock are currently subject to contractual lock-up agreements entered into by certain of our stockholders with the underwriters in connection with our public offering consummated on January 13, 2015 and will become freely tradeable on April 7, 2015, subject to certain provisions of the lock-up agreement, and to volume limitations under Rule 144 of the Securities Act of 1933, as amended. Jefferies LLC and Cowen and Company, LLC, however, may, in their sole discretion, permit our officers, directors and stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

In addition, as of February 28, 2015, 8,224,024 shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of 11,217,978 shares of our outstanding common stock, or approximately 44.48% of our total outstanding common stock as of February 28, 2015, will be entitled to rights with respect to the registration of

their shares under the Securities Act, subject to the 90-day lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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 Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until the last day of the fiscal year following the fifth anniversary of our IPO, although circumstances could cause us to lose that status earlier, including if we become a large accelerated filer (in which case we will cease to be an emerging company as of the date we become a large accelerated filer, which, generally, would occur if, at the end of a fiscal year, among other things, the market value of our common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter), if we have total annual gross revenue of $1.0 billion or more during any fiscal year (in which cases we would no longer be an emerging growth company as of December 31 of such fiscal year), or if we issue more than $1.0 billion in non-convertible debt during any three year period before that time (in which case 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 Sarbanes-Oxley and reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements. 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.

We have incurred and will continue to 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. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently adopted by the SEC, and The NASDAQ Global Market to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC to adopt additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. 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.

The rules and regulations applicable to public companies have substantially increased our legal and financial compliance costs and make some activities more time-consuming and costly. To the extent 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. 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. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

Our ability to use net operating loss carryforwards and other tax attributes may be limited by the Internal Revenue Code.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2014, the Company had U.S. federal NOL carryforwards of approximately $39.6 million to offset future federal income. NOLs expire at various years beginning with 2026. As of December 31, 2014, the Company also had U.S. state NOL carryforwards of approximately $41.0 million to offset future state income. U.S. State NOLs expire at various years beginning with 2016. If over a rolling three-year period, the cumulative change in our ownership exceeds 50 percentage points (as determined under applicable Treasury regulations) under Section 382 of the Internal Revenue Code of 1986, as amended (Code), our ability to utilize our U.S. federal net operating loss (NOL) carryforwards and other pre-change tax attributes (such as research tax credits) to offset future taxable income or taxes may be limited. We have experienced at least two ownership changes since inception and our utilization of NOL carryforwards will therefore be subject to annual limitation. Our ability to utilize our NOL carryforwards may be further limited as a result of subsequent ownership changes. Similar rules may apply under state tax laws. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our corporate headquarters are located in Menlo Park, California, where we lease and occupy approximately 36,000 square feet of office space. The current term of our lease expires on May 8, 2020, with an option to extend the term through May 8, 2024. We believe that our existing facilities are adequate for our current needs. When our lease expires, we may exercise our renewal option or look for additional or alternate space for our operations and we believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issue Purchases of Equity Securities

Our common stock has been listed on The NASDAQ Global Market under the symbol "AAVL" since July 31, 2014. Prior to July 31, 2014, there was no public trading market for our common stock. The following table sets forth for the periods indicated the high and low sales prices per share of our common stock as reported on The NASDAQ Global Market:

YEAR ENDED DECEMBER 31, 2014	HIGH	LOW
Third Quarter (beginning July 31, 2014)	$36.78	$22.00
Fourth Quarter	$57.37	$28.74

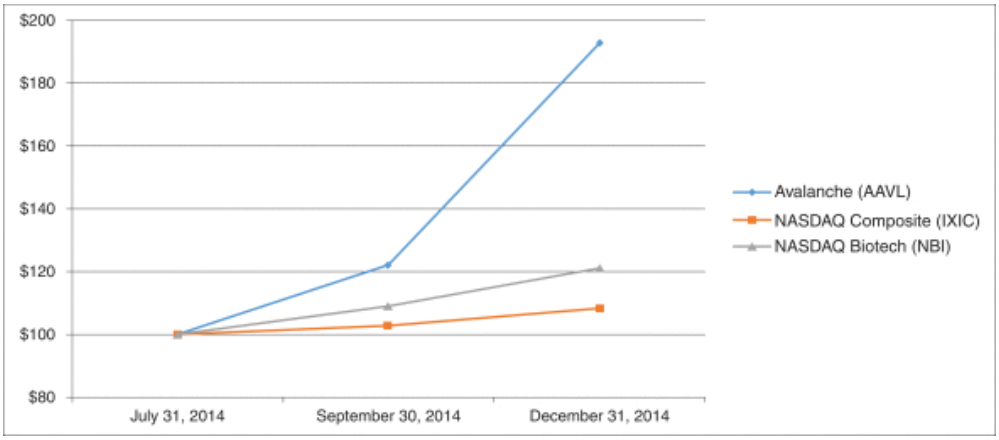
As of February 28, 2015, we had approximately 24 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

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

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return of an investment of $100 in cash on July 31, 2014, which is the date our common stock first began trading on the NASDAQ Global Market, through December 31, 2014 for (i) our common stock, (ii) the NASDAQ Composite Index and (iii) the NASDAQ Biotech Index. Pursuant to applicable SEC rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



$100 investment in stock or index	July 31, 2014	September 30, 2014	December 31, 2014
Avalanche Biotechnologies, Inc. (AAVL)	$ 100.00	$ 122.15	$ 192.93
NASDAQ Composite Index (IXIC)	$ 100.00	$ 102.83	$ 108.38
NASDAQ Biotech (NBI)	$ 100.00	$ 108.98	$ 121.12

Recent Sales of Unregistered Securities

From January 1, 2014 to December 31, 2014, we sold and issued the following unregistered securities:

1. Prior to filing our registration statement on Form S-8 in October 2014, we sold an aggregate of 213,021 shares of common stock to a consultant for cash consideration in the aggregate amount of $2,673.99 upon the exercise of stock options and stock awards.

2. Prior to filing our registration statement on Form S-8 in October 2014, we granted stock options and stock awards to employees, directors and consultants under our Amended and Restated 2006 Equity Incentive Plan covering an aggregate of 1,492,600 shares of common stock, at an average exercise price of $8.83 per share through July 30, 2014. Of these, options covering 55,000 shares were cancelled without being exercised.

3. Prior to filing our registration statement on Form S-8 in October 2014, we granted stock options and stock awards to employees under our 2014 Equity Incentive Award Plan covering an aggregate of 197,500 shares of common stock, at an average exercise price of $33.70 per share through October 13, 2014.

4. In January and April 2014, we issued unsecured subordinated convertible promissory notes to one accredited investor in an aggregate principal amount of $2.0 million. In April 2014, the aggregate principal amount on such convertible promissory notes converted into 295,115 shares of our Series B convertible preferred stock.

5. In March 2014, we issued warrants to purchase an aggregate of 25,000 shares of our common stock at a price per share of $2.75 to one accredited investor.

6. In April 2014, we repurchased an aggregate of 531,208 shares of our Series A convertible preferred stock from one accredited investor at a price per share of $7.53 for an aggregate purchase price of approximately $4.0 million.

7. In April 2014, we sold an aggregate of 7,321,003 shares of our Series B convertible preferred stock for $55 million, which included conversion of the aggregate principal amount on convertible promissory notes described above, to 45 accredited investors.

Use of Proceeds

On August 5, 2014, we closed our IPO and issued 6,900,000 shares of our common stock at an initial offering price of $17.00 per share. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File Nos. 333-197133 and 333-197739), which was declared effective by the SEC on July 30, 2014. The joint book-running managers for the IPO were Jefferies LLC, Cowen and Company, LLC and Piper Jaffray & Co. The aggregate offering price to the public for the shares sold in the IPO was $117.3 million. We received net proceeds from the IPO of approximately $106.5 million, after deducting underwriting discounts and commissions of approximately $8.2 million and expenses of approximately $2.6 million payable by us. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates.

There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus filed with the SEC on July 31, 2014 pursuant to Rule 424(b) of the Securities Act. We invested the funds received in short-term, interest-bearing investment-grade securities and government securities.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not repurchase any of our equity securities during the fourth quarter of the fiscal year ended December 31, 2014.

Item 6. Selected Financial Data

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

We derived the consolidated financial data for the years ended December 31, 2014, 2013 and 2012 and as of December 31, 2014 and 2013 from our consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. Historical results are not necessarily indicative of the results to be expected in future periods.

	YEARS ENDED DECEMBER 31,		
(In thousands, except per share data)	2014	2013	2012
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS DATA:			
Revenue:			
Collaboration and license revenue	$ 572	$ —	$ —
Government grant revenue	—	480	30
Total revenue	572	480	30
Operating expenses:			
Research and development	16,976	2,151	1,310
General and administrative	7,998	1,783	536
Total operating expenses	24,974	3,934	1,846
Operating loss	(24,402)	(3,454)	(1,816)
Other (expense) income:			
Interest expense	(18)	(73)	(8)
Other (expense) income, net	(21)	(4)	(6)
Changes in fair value of embedded derivative	—	18	6
Changes in fair value of warrant liabilities	(759)	(92)	13
Loss on extinguishment of related-party convertible notes	(204)	(1,671)	—
Total other (expense) income, net	(1,002)	(1,822)	5
Net loss	(25,404)	(5,276)	(1,811)
Deemed dividend (1)	(3,230)	—	—
Net loss attributable to common stockholders	(28,634)	(5,276)	(1,811)
Foreign currency translation adjustment	(17)	19	8
Comprehensive loss	$(25,421)	$(5,257)	$(1,803)
Net loss per share attributable to common stockholders —basic and diluted	$ (2.46)	$ (1.44)	$ (0.50)
Weighted-average common shares outstanding —basic and diluted	11,651	3,673	3,643

(1) In April 2014, we repurchased 531,208 shares of Series A convertible preferred stock for $4.0 million. The difference between the repurchase price of $7.53 per share and original issuance price of $1.45 per share was recorded as a deemed dividend of $3.2 million to a preferred stockholder and effected the calculation of net loss attributable to common stockholders and net loss per share for the year ended December 31, 2014.

(In thousands)	YEARS ENDED DECEMBER 31, 2014	2013	2012
CONSOLIDATED BALANCE SHEET DATA:			
Cash and cash equivalent	$159,404	$ 564	$ 357
Working capital	154,807	(340)	(457)
Total assets	161,906	1,085	386
Common stock warrant liability	—	42	5
Convertible preferred stock warrant liability	—	91	36
Convertible preferred stock	—	7,992	2,471
Accumulated deficit	(36,715)	(8,869)	(3,593)
Total stockholders' equity (deficit)	149,483	(8,210)	(3,468)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion of our financial condition and results of operations in conjunction with the financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. 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 on Form 10-K, particularly in "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

We are a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. We have leveraged our next-generation gene therapy platform, Ocular BioFactory™, to create a robust pipeline of product candidates. Our product candidates are designed to provide long-term efficacy or a functional cure for these diseases by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye.

We are targeting a variety of prevalent and rare genetic ophthalmic diseases with significant unmet medical need. Our lead product candidate is AVA-101 for the treatment of wet age-related macular degeneration (AMD). We believe that this product candidate could transform the treatment paradigm and address the unmet need in the large wet AMD market.

We have generated human proof-of-concept data for AVA-101 in a Phase 1 trial with eight wet AMD subjects conducted at Lions Eye Institute (LEI) in Australia. In that Phase 1 trial, AVA-101 was well tolerated with no drug-related adverse events. In addition, subjects treated with AVA-101 showed meaningful improvement in their visual acuity test scores (up to 15 letter improvement on an eye chart from baseline), and most subjects did not receive any rescue injections of standard-of-care therapy (required for subjects exhibiting disease progression) during the one-year trial period. We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. Most adverse events that have been observed to date are mild and not related to AVA-101 or the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015. We own exclusive rights to develop and commercialize AVA-101 worldwide.

In addition to AVA-101, our Ocular BioFactory platform has generated other promising product candidates for the treatment of severe ophthalmic diseases, including AVA-201 and AVA-311. We are developing AVA-201 as a next-generation product candidate for the prevention of wet AMD. AVA-201 produces the same anti-vascular endothelial growth factor (VEGF) protein as AVA-101 using a proprietary, customized delivery mechanism, or vector, that can be administered earlier in the disease progression, before the onset of wet AMD. We own worldwide rights to AVA-201. AVA-311 is being developed in collaboration with our partner Regeneron Pharmaceuticals, Inc. (Regeneron) for the treatment of X-linked retinoschisis (XLRS), a rare genetic disease of the retina with no approved therapy. Based on preclinical studies to date, AVA-311 has been shown to delay the progression of XLRS and improve vision by effectively delivering functional copies of the RS1 gene in retinal cells of mice.

In order to accelerate the pace of generating and developing product candidates for our pipeline, we entered into a broad research collaboration and license agreement with Regeneron in May 2014. Under the terms of the agreement, we intend to jointly discover novel product candidates based on our Ocular BioFactory platform for up to eight therapeutic targets including AVA-311. We have received initial payments of $8.0 million as well as ongoing support for research and development, and we are eligible to receive up to $80.0 million in development

and regulatory milestone payments for product candidates directed toward each therapeutic target, for a combined total of up to $640 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single-digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

On August 5, 2014, we completed our initial public offering (IPO). As a result, the following transactions were recorded in our consolidated financial statements in the third quarter of 2014:

- the sale of 6,900,000 shares of common stock, including 900,000 from the exercise by the underwriters of their option to purchase additional shares, at an offering price of $17.00 per share, for net proceeds of $106.5 million, after deducting the underwriters' discounts, commissions and offering expenses;
- concurrent with the IPO, the private placement of 588,235 shares of our common stock to Regeneron at the offering price of $17.00 per share for gross proceeds of $10.0 million and no underwriting discounts or commissions;
- immediately prior to the completion of the IPO, all the outstanding shares of our convertible preferred stock were converted into 10,689,027 shares of common stock; and
- immediately prior to the completion of the IPO, all outstanding warrants for convertible preferred stock and common stock were exercised into 407,131 shares of common stock for $0.6 million.

On January 13, 2015, we completed a public offering of 2,369,375 shares of our common stock (Follow-on Offering), which includes 359,918 shares we issued pursuant to the underwriters' exercise of their option to purchase additional shares, and we received net proceeds of approximately $130.5 million, after underwriting discounts, commissions and estimated offering expenses.

Financial Overview

Summary

We have not generated positive cash flow or net income from operations since our inception and, at December 31, 2014, we had an accumulated deficit of $36.7 million, primarily as a result of research and development and general and administrative expenses. We expect to incur substantial losses from operations in the foreseeable future as we continue our research and development efforts, advance AVA-101 and other product candidates through preclinical and clinical development, manufacture clinical study materials, seek regulatory approval and prepare for, and if approved, proceed to commercialization. We are at an early stage of development and may never be successful in developing or commercializing our product candidates.

See "Risk Factors—Risks Related to Our Financial Position and Need for Capital—We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability."

While we may in the future generate revenue from a variety of sources, including license fees, milestone and research and development payments in connection with strategic partnerships, and potentially revenue from approved product sales, we have not yet generated any revenue from approved therapeutic product candidates.

Prior to the IPO, we financed our operations through private placements of convertible notes and preferred stock with our investors, funding under our government grants and revenue from research collaboration and license agreements. We entered into our first license revenue generating agreement during the first quarter of 2014. We have never been profitable and have incurred net losses in each year since commencement of our operations.

We have no manufacturing facilities, and all of our manufacturing activities are contracted out to a third party. Additionally, we currently utilize third-party clinical research organizations (CROs) to carry out our clinical development and we do not yet have a sales organization.

We expect to incur significant and increasing losses from operations for the foreseeable future, and we can provide no assurance that we will ever generate significant revenue or profits. In April 2014, we received gross proceeds of $52.9 million from the sale of shares of Series B convertible preferred stock, of which $4.0 million was used to repurchase outstanding shares of Series A convertible preferred stock from an existing investor. We also converted the outstanding balance under our related-party convertible notes of $2.0 million into shares of Series B convertible preferred stock. In May 2014, we received initial payments of $8.0 million in connection with our collaboration with Regeneron. On August 5, 2014, we completed our IPO of shares of our common stock, sold stock in a concurrent private placement and received net proceeds of $116.5 million after deducting underwriting discounts, commissions and offering expenses. As of December 31, 2014, we had $159.4 million in cash and cash equivalents. We believe we will have sufficient funds to operate through at least December 31, 2015.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of AVA-101 and any additional product candidates. Specifically, we have incurred and we expect to continue to incur substantial expenses in connection with our existing Phase 2a clinical trial and any Phase 2b and Phase 3 clinical trials that we may conduct for AVA-101. We will need substantial additional funding to support our operating activities as we advance AVA-101 and other potential product candidates through clinical development, seek regulatory approval and prepare for, and if approved, proceed to commercialization. Adequate funding may not be available to us on acceptable terms, or at all.

Revenue

To date we have not generated any revenue from the sale of our products. In May 2014, we entered into a multi-year license and development agreement with Regeneron. Under the terms of the agreement, we received initial payments of $8.0 million that included payment for research license fees, prepaid collaboration research costs and the right of first negotiation for a potential license to develop and commercialize AVA-101. As the agreement provides for multiple deliverables, we account for this agreement as a multiple elements revenue arrangement. If deliverables do not appear to have a standalone fair value, they were combined with other deliverables into a unit of accounting with standalone fair value. We allocated the $8.0 million received to the fair values of the two units of accounting identified in the arrangement. We expect to recognize $6.5 million for research licenses and related research and development services ratably over the associated period of performance, which is the maximum research period of eight years. As there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, we will recognize revenue on a straight-line basis over the eight-year performance period. The remaining $1.5 million allocated to the second unit of accounting for the time-limited right of first negotiation for AVA-101 is deferred and will be recognized during the period when Regeneron has exclusive access to the results of Phase 2a clinical trials.

During the year ended December 31, 2014, we recognized $0.5 million under the Regeneron agreement. Prior to that period, we had previously only recognized revenue in connection with a license agreement for our technology and under government grants.

Our ability to generate product revenue and become profitable depends upon our ability to successfully develop and commercialize our product candidates. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the amount or timing of product revenue. Even if we are able to generate revenue from the sale of our products, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Research and Development Expenses

Conducting a significant amount of research and development is central to our business model. Research and development expenses include certain payroll and personnel expenses, stock-based compensation expense, laboratory supplies, consulting costs, external contract research and development expenses, including expenses

incurred under agreements with CROs, the cost of acquiring, developing and manufacturing clinical study materials and overhead expenses, including rent, equipment depreciation, insurance and utilities.

Research and development costs are expensed as incurred. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

We estimate preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. We estimate the amounts incurred through communications with third party service providers and our estimates of accrued expenses as of each balance sheet date are based on information available at the time. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly.

As we pursue the clinical development of our lead product candidate, AVA-101, the amount of research and development expenses will continue to grow. Product candidates in later stages of clinical development have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late-stage clinical trials. Accordingly, we plan to increase our research and development expenses for the foreseeable future as we seek to complete the development and commercialization of AVA-101. The successful development and commercialization of AVA-101 is highly uncertain and we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of AVA-101 at this time. Clinical development timelines, the probability of success and development and commercialization costs can differ materially from expectations.

We received refundable tax credits from the Australian tax authorities in connection with certain research costs incurred by our subsidiary conducting research in Australia. These refunds do not depend on our taxable income or tax position and therefore we do not account for them under an income tax accounting model. We recognize such refunds as government grants in the period when qualified expenses are incurred as a reduction of research expenses. We have recorded the reimbursement from the Australian tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss for the applicable period.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, stock-based compensation, professional fees for legal, consulting, audit and tax services, rent and other general operating expenses not otherwise included in research and development expenses. We anticipate general and administrative expenses will increase in future periods as we invest in the infrastructure needed to support continued research and development activities and potential commercialization of our product candidates. We also anticipate increased expenses related to audit, legal and regulatory functions, as well as director and officer insurance premiums and investor relations costs associated with being a public reporting company.

Other Income (Expense), Net

Other income (expense), net is comprised mainly of changes in the fair value of common stock warrant liabilities and preferred stock warrant liabilities. For a description of our valuation methods, see "—Estimated fair value of obligation to issue a common stock warrant and convertible preferred stock warrant liabilities" under "Critical accounting policies, significant judgments and use of estimates." At the time of the IPO, all outstanding warrants were exercised, and as a consequence, we do not expect to have any other income (expense), net related to changes in the fair value of warrant liabilities in future periods.

In April 2014, we recorded a $0.2 million loss related to the conversion of all outstanding convertible notes into Series B convertible preferred stock and we do not expect such charges in future periods.

Critical Accounting Policies, Significant Judgments and Use of Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

We have primarily generated revenue through a research and collaboration arrangement with a strategic partner for the development and commercialization of product candidates, and a license agreement related to the licensing of certain of our intellectual property. Additionally, we have historically generated grant revenue from research and development programs.

We recognize revenue in accordance with Accounting Standards Codification Topic 605, *Revenue Recognition* (ASC 605). Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- Persuasive evidence of an arrangement exists;
- Delivery has occurred or services have been rendered;
- The seller's price to the buyer is fixed or determinable; and
- Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

In May, 2014, we entered into a research collaboration and license agreement with Regeneron. As a result, we have updated our revenue recognition accounting policy and we are recognizing revenue under the agreement as discussed in Note 2 of the accompanying consolidated financial statements.

Government grants provide funds for certain types of expenditures in connection with research and development activities over a contractually defined period. Revenue related to government grants is recognized in the period during which the related costs are incurred and the related services are rendered, provided that the applicable performance obligations under the government grants have been met. We intend to continue to evaluate pursuing additional government grant opportunities on a case-by-case basis.

Funds received under government grants are recorded as revenue if we are deemed to be the principal participant in the contract arrangements because the activities under the contracts are part of our development programs. If we are not the principal participant, the funds from government grants are recorded as a reduction to research and development expense. Funds received from government grants are not refundable and are recognized when the related qualified research and development expenses are incurred and when there is reasonable assurance that the funds will be received. Funds received in advance of the performance of the services are recorded as deferred revenue.

Accrued Research and Development Expense

We estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing contracts and purchase orders, reviewing the terms of our license agreements, communicating with our applicable personnel to identify 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 actual cost. The majority of our service providers invoice us monthly in arrears for services performed. Expenses that are paid in advance of performance are deferred as a prepaid expense and expensed as the services are provided.

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

- contract manufacturers in connection with the production of clinical trial materials;
- CROs and other service providers in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors in connection with preclinical development activities; and
- services providers for professional service fees such as consulting and related services.

Our understanding of the status and timing of services performed relative to the actual status and timing may vary and may result in our reporting changes in estimates in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred. However, due to the nature of these estimates, we cannot assure you that we will not adjust our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies or other research activities.

Stock-Based Compensation Expense

We recognize compensation costs related to stock-based awards granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes valuation model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. We have used the Black-Scholes valuation model to assist us in determining the fair value of stock-based awards. The Black-Scholes valuation model requires the use of subjective and highly complex assumptions which determine the fair value of stock-based awards.

Stock Options Granted to Employees

The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Expected volatility	79%	80%	82%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	1.9%	1.0%	0.9%
Expected dividend yield	0.0%	0.0%	0.0%

As of December 31, 2014, there was $15.1 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 3.5 years.

Stock Options Granted to Non-Employees

We used the following weighted-average assumptions in estimating non-employees stock-based compensation expense:

	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Expected volatility	79%	79%	78%
Expected term (in years)	7.5	7.9	9.0
Risk-free interest rate	2.2%	1.8%	1.6%
Expected dividend yield	0.0%	0.0%	0.0%

As of December 31, 2014, there was $3.4 million of unrecognized stock-based compensation expense related to non-employees' awards that is expected to be recognized over a weighted-average period of 2.9 years.

Expected volatility. We estimate expected volatility based on the average historical volatility of a peer group of comparable publicly traded life sciences and biotechnology companies with product candidates in similar stages of clinical development, as we do not have sufficient trading history for our common stock. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Expected term. We derived the expected term using the "simplified" method (the expected term is determined as the average of the time-to-vesting and the contractual life of the options), as we have limited historical information to develop expectations about future exercise patterns and post vesting employment termination behavior. Expected term for non-employee awards is based on the remaining contractual term of an option on each measurement date.

Risk-free interest rate. The risk-free interest rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term on the options.

Expected dividend yield. We have never paid any dividends and do not plan to pay dividends in the foreseeable future, and, therefore, used an expected dividend yield of zero in the valuation model.

Forfeitures. We estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent actual forfeitures differ from the estimates, the difference will be recorded as a cumulative adjustment in the period that the estimates are revised.

The following table sets forth our total stock-based compensation expense for awards granted in the years ended December 31, 2014, 2013 and 2012:

(in thousands)	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Research and development	$ 7,331	$ 362	$ 54
General and administrative	1,236	153	22
Total	$ 8,567	$ 515	$ 76

Fair value of common stock. The fair value of the shares of common stock underlying our stock options has historically been determined by our board of directors. Because there has been no public market for our common stock and in the absence of recent arm's-length cash sales transactions of our common stock with independent third parties, our board of directors has determined the fair value of our common stock by considering at the time

of grant a number of objective and subjective factors, including the following: independent third-party valuations as of December 31, 2012, March 31, 2013, June 30, 2013, September 30, 2013, December 31, 2013, March 31, 2014 and June 30, 2014; progress of research and development activities; our operating and financial performance, including our levels of available capital resources; rights and preferences of our common stock compared to the rights and preferences of our other outstanding equity securities; equity market conditions affecting comparable public companies, as reflected in comparable companies' market multiples, initial public offering (IPO) valuations and other metrics; the achievement of enterprise milestones, including our progress in clinical trials and potential collaborations with partners; the likelihood of achieving a liquidity event for the shares of common stock, such as an IPO given prevailing market and biotechnology sector conditions; sales of our convertible preferred stock in arms-length transactions; the illiquidity of our securities by virtue of being a private company; business risks; and management and board experience.

The independent third-party valuations used the income, guideline and transaction approaches based on our expected future cash flows and applied a discount for lack of marketability. The guideline approach measures value on a minority-interest basis; the transaction and income approaches measure value on a controlling basis. This approach is outlined in the American Institute of Certified Public Accountants (AICPA) Practice Aid, "*Valuation of Privately-Held-Company Equity Securities Issued as Compensation*" as the probability-weighted expected return method (PWERM). Enterprise values were calculated based on three exit scenarios, including an IPO, a partnership for the development of our product candidate either in an earlier stage or a late stage of clinical development and a corporate failure. Each value was weighted based on the probability of each event's occurrence to arrive at an indicated enterprise value. In estimating the value of equities, management estimated a term for each of the IPO, partnership or corporate failure scenarios.

Following the completion of our IPO in August 2014, the fair value of our common stock generally is determined by reference to the closing sales price of a share of our common stock on the grant date.

Estimated Fair Value of Our Convertible Preferred Stock

In connection with the preparation of our consolidated financial statements for the year ended December 31, 2013 included in this Annual Report on Form 10-K, we prepared retrospective valuations of the fair value of our Series A convertible preferred stock for financial reporting purposes as of September 30, 2013, November 12, 2013 and December 31, 2013 to assist our board of directors in reevaluating the fair value of our convertible preferred stock. The estimated fair value of our Series A convertible preferred stock was determined using a PWERM model, as discussed above in the fair value of common stock. On August 28, 2012, we entered into a convertible note payable agreement with a related party investor for the issuance and sale of up to an aggregate principal amount of $2.0 million of convertible notes (2012 Notes). On November 12, 2013, we issued 1,419,959 shares of Series A convertible preferred stock upon the conversion of the 2012 Notes, and issued 689,655 shares of Series A convertible preferred stock to a potential collaborator for cash, in each case at a price of $1.45 per share. The estimated fair value of Series A convertible preferred stock was $2.63 per share on the issuance date. In fiscal 2013, we recorded a loss on extinguishment of the 2012 Notes of $1.7 million, and an expense of $0.8 million associated with collaboration acquisitions costs which are recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2013.

In connection with the completion of the IPO in August 2014, all outstanding shares of convertible preferred stock were converted into common stock on a one-for-one basis.

Estimated Fair Value of Obligation to Issue a Common Stock Warrant and Convertible Preferred Stock Warrant Liabilities

We previously issued warrants to purchase shares of our convertible preferred stock to certain investors in connection with convertible note purchase agreements entered into between 2006 and 2009. In addition, as of December 31, 2013, we had an obligation to issue a warrant to purchase common stock in connection with the

license agreement we entered into with LEI in 2010. Both the convertible preferred stock warrants and the obligation to issue a warrant to purchase common stock were accounted for as liabilities and were initially recorded at fair value. We have recorded the obligation to issue a warrant to purchase common stock as a derivative liability as the terms of the warrants are not fixed due to potential adjustments in the exercise price issuable under the warrants. At each balance sheet date, gains and losses arising from changes in fair value of these liabilities are recognized in other income (expense), net in the consolidated statements of operations and comprehensive loss while such instruments are outstanding and classified as liabilities. The fair value of the liabilities is determined using an option pricing model, based on inputs as of the valuation measurement dates, including the estimated fair value of our stock, the estimated volatility of the price of our stock, the expected term of the warrants and the risk-free interest rates. Refer to Note 10, Warrants, for key assumptions used in the valuation at each reporting period, in our consolidated financial statements included this Annual Report on Form 10-K. The convertible preferred stock and common stock warrant liabilities will increase or decrease each period based on the fluctuations of the fair value of the underlying security. A significant fluctuation in the common or convertible preferred stock fair value would result in a material change in the fair values of the convertible preferred stock and common stock warrant liabilities.

We adjusted the obligation to issue a warrant to purchase common stock liability for changes in fair value on an ongoing basis until the warrant was issued in March 2014 and the exercise price for the warrants became fixed. At such time we reclassified the liability to additional paid-in capital and no further change in fair value were recorded. In connection with the completion of the IPO in August 2014, all of the outstanding warrants to purchase convertible preferred stock were exercised. As a result of the exercises, we recorded a $0.8 million loss related to the change in fair value in our consolidated statements of operations and comprehensive loss and reclassified the fair value of $0.9 million to stockholders' equity.

Income Tax

We recognize deferred income taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. We periodically evaluate the positive and negative evidence bearing upon realizability of our deferred tax assets. Based upon the weight of available evidence, which includes our historical operating performance, reported cumulative net losses since inception and difficulty in accurately forecasting our future results, we maintained a full valuation allowance on the net deferred tax assets as of December 31, 2014 and 2013 of approximately $12.5 million and $2.5 million, respectively. We intend to maintain a full valuation allowance on the federal, state and foreign deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance.

As of December 31, 2014, the Company had U.S. federal NOL carryforwards of approximately $39.6 million to offset future federal income. NOLs expire at various years beginning with 2026. As of December 31, 2014, the Company also had U.S. state NOL carryforwards of approximately $41.0 million to offset future state income. U.S. State NOLs expire at various years beginning with 2016. At December 31, 2014, the Company also had approximately $0.2 million of foreign net operating loss carryforwards which may be available to offset future foreign income; these carryforwards do not expire.

Under Section 382 of the Code, our ability to utilize NOL carryforwards or other tax attributes such as research tax credits, in any taxable year may be limited if we have experienced an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who own at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. We believe that we have experienced at least two ownership changes under Section 382 which will result in limitations in our ability to utilized net operating losses and credits. In addition, we may experience ownership changes as a result of our previous or future offerings or other changes in the ownership of our stock. As a result, the amount of the NOL carryforwards and research and credit carryforwards presented in our financial statements could be limited and may expire unutilized.

We record unrecognized tax benefits as liabilities and adjust these liabilities when our judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from our current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. Our policy is to recognize interest and penalties related to income taxes as a component of income tax expense. No interest and penalties related to income taxes have been recognized in the statements of operations and comprehensive loss in 2014, 2013 and 2012.

Emerging Growth Company Status

Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can 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 extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for companies that are not emerging growth companies.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

The following table summarizes our results of operations for the periods indicated:

	YEARS ENDED DECEMBER 31,		INCREASE/ (DECREASE)
(in thousands)	**2014**	**2013**	
Collaboration and license revenue	$ 572	$ —	$ 572
Government grant revenue	—	480	(480)
Total revenue	572	480	92
Operating expenses:			
Research and development	16,976	2,151	14,825
General and administrative	7,998	1,783	6,215
Total operating expenses	24,974	3,934	21,040
Operating loss	(24,402)	(3,454)	(20,948)
Other (expense) income:			
Interest expense	(18)	(73)	55
Other (expense) income, net	(21)	(4)	(17)
Changes in fair value of embedded derivative	—	18	(18)
Changes in fair value of warrant liabilities	(759)	(92)	(667)
Loss on extinguishment of related party convertible notes	(204)	(1,671)	1,467
Net loss	$ (25,404)	$ (5,276)	$ (20,128)
Deemed dividend	(3,230)	—	(3,230)
Net loss attributable to common stockholders	$ (28,634)	$ (5,276)	$ (23,358)

Revenue

Collaboration and license revenue increased by $0.6 million for the year ended December 31, 2014, as we recognized revenue from the Regeneron agreement and from a license agreement entered into during the first

quarter of 2014. Government grant revenue decreased to zero for the year ended December 31, 2014 from $0.5 million for the year ended December 31, 2013, as we completed the work performed under the government grants during the 2013 fiscal year.

Research and Development Expense

Research and development expense increased to $17.0 million for the year ended December 31, 2014 from $2.2 million for the year ended December 31, 2013. The increase in research and development expense was primarily due to increases of $7.0 million in stock-based compensation expenses, $3.0 million in expenses related to an increase in our employee headcount, $2.5 million in drug product process development expenses and laboratory supplies and $1.6 million in external consulting expenses and research studies. Expenses during the year ended December 31, 2013 benefited from reimbursement of $0.8 million from the Australian tax authorities recorded as a reduction in research and development expense as compared to $0.1 million during 2014. For the periods presented, substantially all of our research and development expense related to our development activity for AVA-101 for the treatment of wet AMD, and the other potential product candidates in our development program. We expect research and development expenses to increase in future periods as we continue to invest in our pipeline products and AVA-101 in late-stage clinical trials.

General and Administrative Expense

General and administrative expense increased to $8.0 million for the year ended December 31, 2014 from $1.8 million for the year ended December 31, 2013. The increase in general and administrative expense was primarily due to increases of $1.8 million related in an increase in our employee headcount, $1.1 million in stock-based compensation expenses, $1.6 million in public company-related expenses and overhead and $2.5 million in consulting and professional service expenses, as we expanded our operations. We also recorded a $0.8 million non-cash one-time charge of collaboration acquisition costs in 2013 related to the issuance of 689,655 shares of Series A convertible preferred stock to a potential collaborator for cash at a price per share below the fair value of such shares. We expect general and administrative costs to increase in future periods, reflecting both the increased costs in connection with the future commercialization of AVA-101 and our pipeline products, as well as an expanded infrastructure and increased professional fees associated with being a public company.

Interest Expense

Interest expense decreased to $18,000 for the year ended December 31, 2014 from $73,000 for the comparable period in 2013 as outstanding convertible notes were converted into Series B convertible preferred stock in April 2014.

Changes in Fair Value of Embedded Derivative

We recorded an embedded derivative liability in connection with our 2012 Notes. For the year ended December 31, 2013, we recorded income of $18,000 for the change in fair value of the embedded derivative liability. In November 2013, upon conversion of the 2012 Notes into Series A convertible preferred stock, the embedded derivative was reversed.

Changes in Fair Value of Warrant Liabilities

We recorded changes in the fair value of warrant liabilities of ($0.8) million for the year ended December 31, 2014, compared to ($92,000) for the year ended December 31, 2013. In connection with the completion of the IPO in August 2014, all of the outstanding warrants to purchase convertible preferred stock were exercised. As a result of the exercises, we recorded a $0.8 million loss related to the change in fair value in our consolidated statements of operations and comprehensive loss.

Loss on Extinguishment of Related Party Convertible Notes

In April 2014, we converted the outstanding balance under our related-party convertible notes of $2.0 million into 295,115 shares of Series B convertible preferred stock at 90% of the purchase price paid by other investors, in accordance with the terms of the agreement. As a result, we recorded a loss on the extinguishment of convertible notes of $0.2 million in 2014.

In November 2013, we amended the terms of the convertible notes agreement to accelerate their conversion into shares of Series A convertible preferred stock, which we determined represented an extinguishment. As a result, we recorded a loss on the extinguishment of convertible notes of $1.7 million in 2013.

Deemed Dividend

In April 2014, we repurchased 531,208 shares of Series A convertible preferred stock for $4.0 million. The difference between the repurchase price of $7.53 per share and original issuance price of $1.45 per share was recorded as a deemed dividend of $3.2 million to a preferred stockholder and effected the calculation of net loss attributable to common stockholders and net loss per share for the year ended December 31, 2014.

Comparison of the Years Ended December 31, 2013 and 2012

The following table summarizes our results of operations for the periods indicated:

(in thousands)	YEARS ENDED DECEMBER 31, 2013	2012	INCREASE/ (DECREASE)
Government grant revenue	$ 480	$ 30	$ 450
Operating expenses:			
Research and development	2,151	1,310	841
General and administrative	1,783	536	1,247
Total operating expense	3,934	1,846	2,088
Operating loss	(3,454)	(1,816)	(1,638)
Other (expense) income:			
Interest expense	(73)	(8)	(65)
Other (expense) income, net	(4)	(6)	2
Changes in fair value of embedded derivative	18	6	12
Changes in fair value of warrant liabilities	(92)	13	(105)
Loss on extinguishment of related party convertible notes	(1,671)	—	(1,671)
Net loss	$ (5,276)	$ (1,811)	$ (3,465)

Revenue

Government grant revenue increased by $450,000 to $480,000 in 2013 from $30,000 in 2012, due to our performance of an increased amount of reimbursed research under government grants in the 2013 period as compared to 2012.

Research and Development Expense

Research and development expense increased to $2.2 million for 2013 from $1.3 million for 2012. The increase in research and development expense was primarily due to an increase in clinical development costs incurred during 2013 for our clinical trials, including:

- $0.2 million increase for clinical supply manufacturing and drug product process development activities in preparation for the AVA-101 clinical studies;

- $0.3 million increase to contractor-related expenses to support the increased development activities in 2013;
- $0.4 million increase in employee salaries and other personnel expenses as we increased our headcount during 2013;
- $0.3 million increase in stock-based compensation expenses during 2013; and
- $0.2 million increase in facilities expense during 2013.

The increase in research and development expense was partially offset by a reimbursement of $0.8 million from the Australian tax authorities recorded as a reduction in research and development expense in 2013. For the years ended December 31, 2013 and 2012, substantially all of our research and development expense related to our development activity for AVA-101 for the treatment of wet AMD.

General and Administrative Expense

General and administrative expense increased $1.2 million, to $1.8 million in 2013 from $0.5 million in 2012. The increase in general and administrative expense was primarily due to the recognition of $0.8 million of collaboration acquisition costs related to the issuance of 689,655 shares of Series A convertible preferred stock to a potential collaborator for cash at a price per share below the fair value of such shares. We also experienced an increase in stock-based compensation and consulting and professional services expenses of $0.5 million, and an increase in facility expense of $0.2 million during 2013 as we expanded our operations.

Interest Expense

Interest expense increased by $65,000 in 2013 as compared to the 2012 period. The increase was due to an increase in the balance of convertible notes outstanding during 2013 as compared to 2012.

Change in Fair Value of Embedded Derivative

We recorded an embedded derivative liability in connection with our 2012 Notes. We recorded change in the fair value of this derivative in our consolidated statements of operations and comprehensive loss. In November 2013, upon conversion of the convertible notes into Series A convertible preferred stock, the embedded derivative was terminated.

Changes in Fair Value of Warrant Liabilities

Changes in the fair value of warrant liabilities decreased $0.1 million as compared to year 2012 due to the remeasurement of the fair value of the common stock warrant and preferred stock warrant liabilities.

Loss on Extinguishment of Related Party Convertible Notes

In November 2013, we amended the terms of the convertible notes agreement to accelerate their conversion into shares of Series A convertible preferred stock, which we determined represented an extinguishment. As a result, we recorded a loss on the extinguishment of convertible notes of $1.7 million in 2013.

Liquidity, Capital Resources and Plan of Operations

Prior to the IPO, we financed our operations through private placements of convertible notes and preferred stock with our investors, funding under our government grants and revenue from research collaboration and license agreements. In April 2014, we received gross proceeds of $52.9 million from the sale of Series B convertible preferred stock, of which $4.0 million was used to repurchase outstanding shares of Series A convertible preferred stock from an existing investor. We also converted the outstanding balance under our convertible notes into shares of Series B convertible preferred stock. In May 2014, we received initial payments of $8.0 million in connection with our research collaboration.

In August 2014, we received net proceeds of $116.5 million from the sale of common stock in our IPO and the concurrent private placement from Regeneron. In January 2015, we completed a follow-on offering of 2,369,375 shares of our common stock, which includes 359,918 shares we issued pursuant to the underwriters' exercise of their option to purchase additional shares, and we received net proceeds of approximately $130.5 million, after underwriting discounts, commissions and estimated offering expenses.

We expect that our existing cash balance of $159.4 million as of December 31, 2014 and cash received from the follow-on public offering in January 2015 will be sufficient to fund our operations through at least December 31, 2016.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates and ongoing internal research and development programs. In order to complete our planned preclinical and clinical trials and complete the process of obtaining regulatory approval for our lead product candidate, as well as to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital in the future could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials for AVA-101 and our other product candidates in development;
- the outcome, timing of, and costs involved in, seeking and obtaining approvals from the FDA and other regulatory authorities, including the potential for the FDA and other regulatory authorities to require that we perform more studies than those that we currently expect;
- the ability of our product candidates to progress through clinical development activities successfully;
- our need to expand our research and development activities;
- the rate of progress and cost of our commercialization of our products;
- the cost of preparing to manufacture our products on a larger scale;
- the costs of commercialization activities including product sales, marketing, manufacturing and distribution;
- the degree and rate of market acceptance of any products launched by us or future partners;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need to implement additional infrastructure and internal systems;
- our ability to hire additional personnel;
- our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
- the emergence of competing technologies or other adverse market developments.

If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license other technologies or clinical product candidates or programs that we would prefer to develop and commercialize ourselves.

Cash Flows

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

(in thousands)	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Net cash (used in) provided by:			
Operating activities	$ (5,648)	$(2,175)	$(1,267)
Investing activities	(943)	(91)	(3)
Financing activities	165,442	2,480	500
Net increase (decrease) in cash	$158,840	$ 207	$ (761)

Cash Used in Operating Activities

Net cash used in operating activities was $5.6 million and $2.1 million for 2014 and 2013, respectively. Net cash used in operating activities for the year ended December 31, 2014 was $5.6 million, primarily the result of the net loss of $25.4 million offset by the $7.5 million related to the upfront payments received from our research collaboration and license agreement with Regeneron, $9.5 million of non-cash charges related to stock-based compensation, loss on the extinguishment of related party convertible notes and warrant re-measurement and a $2.9 million increase in accounts payable and accrued expenses. Net cash used in operating activities for the year ended December 31, 2013 was $2.2 million, primarily the result of the net loss of $5.3 million offset by $3.0 million of non-cash cash charges related to stock-based compensation, loss on the extinguishment of related party convertible notes and charge on collaboration acquisition costs associated with sale of Series A convertible preferred stock.

Net cash used in operating activities was $2.2 million and $1.3 million for 2013 and 2012, respectively. Cash used in operating activities in 2013 increased compared to 2012 primarily due to higher net loss from operations as we increased our research and development expenditures due to increased clinical trial activity during 2013.

Cash Used in Investing Activities

Cash used in investing activities consisted of our investments in property and equipment to facilitate our increased research and development activities and increased headcount.

Cash Provided by Financing Activities

Cash provided by financing activities was $165.4 million for 2014, compared to $2.5 million for 2013. Cash provided for the year ended December 31, 2014 consisted primarily of $116.5 million of net proceeds from our IPO and the concurrent private placement in July and August 2014, $0.6 million of proceeds from exercises of warrants, $50.4 million of proceeds from the sale of Series B convertible preferred stock, net of expenses, in April 2014, and $2.0 million of related-party convertible notes received in January and April 2014, offset by $4.0 million used to repurchase Series A convertible preferred stock in April 2014. Cash provided by financing activities for 2013 consisted of $1.5 million from the borrowing under related-party convertible notes as well as $1.0 million in net proceeds from the issuance of Series A convertible preferred stock in November 2013 to a potential collaborator.

Cash provided by financing activities was $2.5 million for 2013, compared to $0.5 million for 2012. Cash provided by financing activities for 2013 consisted of $1.5 million from the borrowing under related-party convertible notes as well as $1.0 million in net proceeds from the issuance of Series A convertible preferred stock in November 2013 to a potential collaborator. Cash provided by financing activities for 2012 year consisted primarily of net proceeds from the issuance of convertible notes.

Contractual Obligations and Commitments

We have lease obligations consisting of an operating lease for our operating facility that expires in 2020.

The following table summarizes our contractual obligations as of December 31, 2014:

	PAYMENTS DUE BY PERIOD				
(in thousands)	LESS THAN 1 YEAR	1 TO 3 YEARS	4 TO 5 YEARS	AFTER 5 YEARS	TOTAL
Lease obligations	$ 826	$ 2,228	$ 2,359	$ 403	$ 5,816

The lease agreement provides for an escalation of rent payments each year and will expire on May 8, 2020. We may extend the lease term for up to four years.

We are obligated to make future payments to third parties under in-license agreements, including sublicense fees, royalties and payments that become due and payable on the achievement of certain development and commercialization milestones. As the amount and timing of sublicense fees and the achievement and timing of these milestones are not probable and estimable, such commitments have not been included on our balance sheet or in the contractual obligations tables above.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Foreign Currency Exchange Risk

A portion of our operating expenses are incurred outside the United States and are denominated in foreign currencies and are subject to fluctuations due to changes in foreign currency exchange rates, particularly changes in the Australian dollar. Additionally, fluctuations in foreign currency exchange rates may cause us to recognize transaction gains and losses in our statement of operations. To date, foreign currency transaction gains and losses have not been material to our consolidated financial statements, and we have not engaged in any foreign currency hedging transactions. As our international operations grow, we will continue to reassess our approach to managing the risks relating to fluctuations in currency rates.

Interest Rate Risk

We had cash and cash equivalents of $159.4 million and $0.6 million as of December 31, 2014 and 2013, respectively, consisting of bank deposits that are not interest bearing and money market funds. To date, fluctuations in interest income have not been significant.

We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed to, nor do we anticipate being exposed to, material risks due to changes in interest rates. A hypothetical 10% change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

We do not believe that inflation and change in prices had a significant impact on our results of operations for any periods presented in our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data.

The financial statements required by this item are set forth beginning at page F-1 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2014. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. Based on this evaluation, including the remediation of the material weakness identified in our internal control over financial reporting as of December 31, 2014, as described below, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2014 at the reasonable assurance level.

Material Weakness Previously Identified

Our management previously identified deficiencies in our internal control over financial reporting that constituted a material weakness in our internal control over financial reporting as of December 31, 2013 and which related to the design and operation of our control environment. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis. We did not maintain an effective control environment, which is the foundation for effective internal control over financial reporting, as evidenced by: (i) an insufficient number of personnel to perform control monitoring activities, (ii) an insufficient number of personnel with an appropriate level of knowledge of U.S. GAAP to determine that our consolidated financial statements were properly prepared in accordance with U.S. GAAP, (iii) insufficient management involvement to identify and resolve errors in recording transactions and (iv) inadequate processes for the preparation and review of our consolidated financial statements.

Remediation of Material Weakness

Subsequent to the identification of the material weakness, we hired an experienced Chief Financial Officer, Corporate Controller and additional skilled accounting and finance staff members, (b) formalized and implemented our accounting policies and internal controls and the related documentation and (c) strengthened our accounting systems, financial statements review procedures and the supervisory reviews by our management that are performed during the financial close process and which support the accurate and timely preparation of consolidated financial statements that are fairly presented in accordance with US GAAP. These improvements to our internal control infrastructure were implemented during 2014, and were in place in connection with the preparation of our consolidated financial statements for the year ended December 31, 2014. As such, we believe that these initiatives have remediated the material weakness in internal control over financial reporting as of December 31, 2014.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control Over Financial Reporting

Other than the changes disclosed above regarding the remediation of the previous material weakness, there has been no change in our internal control over financial reporting during the quarter ended December 31, 2014, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations of Controls

Management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent or detect all error and all fraud. Controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the controls. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or deterioration in the degree of compliance with the policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Item 9B. Other Information.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2015 Annual Meeting of Stockholders (the Proxy Statement), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2014, under the headings "Executive Officers," "Election of Directors," "Corporate Governance," and " Section 16(a) Beneficial Ownership Reporting Compliance," and is incorporated herein by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the Corporate Governance section of our website, which is located at www.avalanchebiotech.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item will be contained in the Proxy Statement under the headings "Executive Compensation" and "Director Compensation," and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item will be contained in the Proxy Statement under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information," and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item will be contained in the Proxy Statement under the headings "Certain Relationships and Related Party Transactions" and "Corporate Governance," and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be contained in the Proxy Statement under the heading "Ratification of Independent Registered Public Accounting Firm—Principal Accounting Fees and Services" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The financial statements schedules and exhibits filed as part of this Annual Report on Form 10-K are as follows:

(a)(1) Financial Statements

Reference is made to the financial statements included in Item 8 of Part II hereof.

(a)(2) Financial Statement Schedules

All other schedules are omitted because they are not required or the required information is included in the financial statements or notes thereto.

(a)(3) Exhibits

Reference is made to the Exhibit Index accompanying this Annual Report on Form 10-K.

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.

Date: March 5, 2015

AVALANCHE BIOTECHNOLOGIES, INC.

By: /s/ Thomas W. Chalberg, Jr., Ph.D.
Thomas W. Chalberg, Jr., Ph.D.
President and Chief Executive Officer

Power of Attorney

Each person whose individual signature appears below hereby authorizes and appoints Thomas W. Chalberg, Jr., Ph.D. and Linda C. Bain, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this annual report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Thomas W. Chalberg, Jr., Ph.D. Thomas W. Chalberg, Jr., Ph.D.	Director, President and Chief Executive Officer *(Principal Executive Officer)*	March 5, 2015
/s/ Linda C. Bain Linda C. Bain	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 5, 2015
/s/ Mark S. Blumenkranz, M.D. Mark S. Blumenkranz, M.D.	Chairman of the Board	March 5, 2015
/s/ John P. McLaughlin John P. McLaughlin	Director	March 5, 2015
/s/ Steven D. Schwartz, M.D. Steven D. Schwartz, M.D.	Director	March 5, 2015
/s/ Paul D. Wachter Paul D. Wachter	Director	March 5, 2015

AVALANCHE BIOTECHNOLOGIES, INC.
CONSOLIDATED FINANCIAL STATEMENTS
YEARS ENDED DECEMBER 31, 2014, 2013 AND 2012

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Avalanche Biotechnologies, Inc.
Menlo Park, California

We have audited the accompanying consolidated balance sheets of Avalanche Biotechnologies, Inc. and its subsidiary (collectively the "Company") as of December 31, 2014 and 2013, and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements 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 their 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, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Avalanche Biotechnologies, Inc. and its subsidiary as of December 31, 2014 and 2013, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2014, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

San Jose, California
March 5, 2015

AVALANCHE BIOTECHNOLOGIES, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	DECEMBER 31,	
	2014	2013
ASSETS		
Current assets:		
Cash and cash equivalents	$ 159,404	$ 564
Accounts receivable	—	8
Prepaid expenses and other current assets	874	250
Total current assets	160,278	822
Property and equipment, net	1,085	69
Deposit and other long-term assets	543	194
Total assets	$ 161,906	$ 1,085
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 951	$ 769
Accrued expenses and other current liabilities	3,707	393
Deferred revenue	813	—
Total current liabilities	5,471	1,162
Long-term liabilities:		
Common stock warrant liability	—	42
Convertible preferred stock warrant liability	—	91
Deferred rent	306	8
Deferred revenue, net of current portion	6,646	—
Total liabilities	12,423	1,303
Commitments and contingencies (Note 7)		
Convertible preferred stock (Note 9)		
Series A convertible preferred stock, par value $0.0001 per share—no shares and 4,233,295 shares authorized at December 31, 2014 and 2013, respectively; no shares and 3,899,232 shares issued and outstanding at December 31, 2014 and 2013, respectively (liquidation preference of $0 and $5,654 at December 31, 2014 and 2013, respectively)	—	7,992
Stockholders' equity (deficit):		
Preferred stock, par value $0.0001 per share, 5,000,000 shares authorized at December 31, 2014; no shares issued and outstanding	—	—
Common stock, par value $0.0001 per share—300,000,000 and 15,000,000 shares authorized at December 31, 2014 and 2013, respectively; 22,754,037 and 3,672,885 shares issued and outstanding at December 31, 2014 and 2013, respectively	2	—
Additional paid-in capital	186,186	632
Accumulated other comprehensive income	10	27
Accumulated deficit	(36,715)	(8,869)
Total stockholders' equity (deficit)	149,483	(8,210)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 161,906	$ 1,085

See accompanying notes to consolidated financial statements.

AVALANCHE BIOTECHNOLOGIES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except per share data)

	YEARS ENDED DECEMBER 31,		
	2014	2013	2012
Collaboration and license revenue	$ 572	$ —	$ —
Government grant revenue	—	480	30
Total revenue	572	480	30
Operating expenses:			
Research and development	16,976	2,151	1,310
General and administrative	7,998	1,783	536
Total operating expenses	24,974	3,934	1,846
Operating loss	(24,402)	(3,454)	(1,816)
Other (expense) income:			
Interest expense	(18)	(73)	(8)
Other income (expense), net	(21)	(4)	(6)
Change in fair value of embedded derivative	—	18	6
Changes in fair value of warrant liabilities	(759)	(92)	13
Loss on extinguishment of related-party convertible notes	(204)	(1,671)	—
Total other (expense) income, net	(1,002)	(1,822)	5
Net loss	(25,404)	(5,276)	(1,811)
Deemed dividend	(3,230)	—	—
Net loss attributable to common stockholders	(28,634)	(5,276)	(1,811)
Other comprehensive income (loss):			
Foreign currency translation adjustment	(17)	19	8
Comprehensive loss	$ (25,421)	$ (5,257)	$ (1,803)
Net loss per share attributable to common stockholders—basic and diluted	$ (2.46)	$ (1.44)	$ (0.50)
Weighted-average common shares outstanding—basic and diluted	11,651	3,673	3,643

See accompanying notes to consolidated financial statements.

AVALANCHE BIOTECHNOLOGIES, INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands except share and per share data)

	SERIES A CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		SERIES B CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		COMMON STOCK $0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE INCOME	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY (DEFICIT)
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT				
BALANCE—DECEMBER 31, 2011	1,789,618	$ 2,471	—	$ —	3,573,927	$ —	$ 38	$ —	$ (1,782)	$ (1,744)
Vesting of common stock related to purchase of unvested restricted stock	—	—	—	—	98,958	—	—	—	—	—
Issuance of common stock warrants in partial consideration for intellectual property	—	—	—	—	—	—	3	—	—	3
Stock-based compensation expense	—	—	—	—	—	—	76	—	—	76
Foreign currency translation adjustment	—	—	—	—	—	—	—	8	—	8
Net loss	—	—	—	—	—	—	—	—	(1,811)	(1,811)
BALANCE—DECEMBER 31, 2012	1,789,618	2,471	—	—	3,672,885	—	117	8	(3,593)	(3,468)
Conversion of the related-party convertible notes and accrued interest into Series A convertible preferred stock in November 2013	1,419,959	3,730	—	—	—	—	—	—	—	—
Issuance of Series A convertible preferred stock in November 2013 for cash, net of issuance costs of $20	689,655	1,791	—	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	515	—	—	515
Foreign currency translation adjustment	—	—	—	—	—	—	—	19	—	19
Net loss	—	—	—	—	—	—	—	—	(5,276)	(5,276)
BALANCE—DECEMBER 31, 2013	3,899,232	7,992	—	—	3,672,885	—	632	27	(8,869)	(8,210)

AVALANCHE BIOTECHNOLOGIES, INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (continued)

(In thousands except share and per share data)

	SERIES A CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		SERIES B CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		COMMON STOCK $0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE INCOME	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY (DEFICIT)
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT				
BALANCE—DECEMBER 31, 2013	3,899,232	7,992	—	—	3,672,885	—	632	27	(8,869)	(8,210)
Beneficial conversion feature in related-party convertible notes	—	—	—	—	—	—	2,000	—	—	2,000
Repurchase of beneficial conversion feature upon conversion of related-party convertible notes	—	—	—	—	—	—	(2,000)	—	—	(2,000)
Conversion of related-party convertible notes into Series B convertible preferred stock in April 2014	—	—	295,115	2,222	—	—	—	—	—	—
Issuance of Series B convertible preferred stock in April 2014 for cash, net of issuance costs of $2,806	—	—	7,025,888	50,099	—	—	—	—	—	—
Repurchase of Series A convertible preferred stock for cash in April 2014	(531,208)	(770)	—	—	—	—	(788)	—	(2,442)	(3,230)
Issuance of common stock warrants in consideration for services	—	—	—	—	—	—	307	—	—	307
Issuance of Series A convertible preferred stock upon exercises of convertible preferred stock warrants in July 2014	54,716	79	—	—	—	—	851	—	—	851
Conversion of Series A preferred stock to common stock upon initial public offering	(3,422,740)	(7,301)	—	—	3,422,740	—	7,301	—	—	7,301

AVALANCHE BIOTECHNOLOGIES, INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (continued)
(In thousands except share and per share data)

	SERIES A CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		SERIES B CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		COMMON STOCK $0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE INCOME	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY (DEFICIT)
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT				
Conversion of Series B preferred stock to common stock upon initial public offering	—	—	(7,321,003)	(52,321)	7,321,003	1	52,320	—	—	52,321
Issuance of common stock upon exercise of warrants	—	—	—	—	352,415	—	526	—	—	526
Issuance of common stock upon initial public offering, net of issuance costs of $9,776 in July 2014	—	—	—	—	6,000,000	1	92,223	—	—	92,224
Issuance of common stock upon private placement in July 2014	—	—	—	—	588,235	—	10,000	—	—	10,000
Issuance of common stock upon exercise of option by underwriters, net of issuance costs of $1,071 in August 2014	—	—	—	—	900,000	—	14,229	—	—	14,229
Stock-based compensation expense	—	—	—	—	—	—	8,567	—	—	8,567
Common stock issued upon exercise of stock options	—	—	—	—	496,759	—	18	—	—	18
Foreign currency translation adjustment	—	—	—	—	—	—	—	(17)	—	(17)
Net loss	—	—	—	—	—	—	—	—	(25,404)	(25,404)
BALANCE—DECEMBER 31, 2014	—	$ —	—	$ —	22,754,037	$ 2	$ 186,186	$ 10	$ (36,715)	$ 149,483

AVALANCHE BIOTECHNOLOGIES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	YEARS ENDED DECEMBER 31,		
	2014	**2013**	**2012**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (25,404)	$ (5,276)	$ (1,811)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	162	26	1
Stock-based compensation	8,567	515	76
Non-cash research and development expense	—	—	8
Non-cash interest expense	18	53	5
Amortization of debt issuance costs	—	20	3
Change in fair value of embedded derivative liability	—	(18)	(6)
Change in fair value of warrants liabilities	759	92	(13)
Loss on extinguishment of related-party convertible notes	204	1,671	—
Non-cash collaboration acquisition costs associated with sale of Series A convertible preferred stock	—	812	—
Changes in operating assets and liabilities:			
Accounts receivable, net	8	(7)	—
Prepaid expenses and other assets	(624)	(293)	(18)
Deposit	7	(144)	—
Accounts payable	(6)	286	445
Accrued expenses and other liabilities	2,904	80	43
Deferred revenue	7,459	—	—
Deferred rent	298	8	—
Net cash used in operating activities	(5,648)	(2,175)	(1,267)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(943)	(91)	(3)
Net cash used in investing activities	(943)	(91)	(3)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from public offering of common stock, net	106,453	—	—
Proceeds from the sale of common stock to collaborative partner	10,000	—	—
Proceeds from issuance of Series A convertible preferred stock	—	1,000	—
Expenses related to issuance of Series A convertible preferred stock	—	(20)	—
Proceeds from issuance of Series B convertible preferred stock	52,905	—	—
Expenses related to issuance of Series B convertible preferred stock	(2,540)	—	—
Proceeds from issuance of related-party convertible notes	2,000	1,500	500
Repurchase of Series A convertible preferred stock	(4,000)	—	—
Proceeds from exercises of warrants	606	—	—
Proceeds from issuance of common stock pursuant to option exercises	18	—	—
Net cash provided by financing activities	165,442	2,480	500
Effect of foreign exchange rate on cash	(11)	(7)	9
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	158,840	207	(761)
Cash and cash equivalents at beginning of year	564	357	1,118
Cash and cash equivalents at end of year	$ 159,404	$ 564	$ 357
SUPPLEMENTAL DISCLOSURES OF NONCASH INVESTING AND FINANCING INFORMATION			
Conversion of related-party convertible notes and accrued interest to convertible preferred stock	$ 2,000	$ 2,059	$ —
Warrants issued in connection with issuance of Series B convertible preferred stock	$ 266	$ —	$ —
Deferred stock issuance costs	$ 379	$ 50	$ —
Warrants issued in connection with license agreements	$ 42	$ —	$ 3
Fixed assets in accounts payable	$ 235	$ —	$ —

AVALANCHE BIOTECHNOLOGIES, INC.

Notes to Consolidated Financial Statements

1. Description of the business

Nature of Business—Avalanche Biotechnologies, Inc. (the "Company", "we" or "us") was incorporated in Delaware on July 17, 2006, and is headquartered in Menlo Park, California. The Company is a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. Since the Company's inception, it has devoted its efforts principally to performing research and development activities, including early clinical trials, filing patent applications, obtaining regulatory approvals, hiring personnel, and raising capital to support these activities.

The Company has not generated any revenue from the sale of products since its inception. The Company has experienced net losses since its inception and has an accumulated deficit of $36.7 million as of December 31, 2014. The Company expects to incur losses and have negative net cash flows from operating activities as it expands its portfolio and engages in further research and development activities, particularly conducting preclinical studies and clinical trials.

Initial Public and Follow-on Offerings —On August 5, 2014, the Company completed its initial public offering (IPO) of shares of its common stock. As a result, the following transactions were recorded in the Company's consolidated financial statements on August 5, 2014 (the third quarter of 2014):

- the sale of 6,900,000 shares of common stock, including 900,000 from the exercise by the underwriters of their option to purchase additional shares, at an offering price of $17.00 per share, for net proceeds of $106.5 million, after deducting the underwriters' discounts, commissions and offering expenses;
- concurrent with the IPO, the private placement of 588,235 shares of common stock to Regeneron Pharmaceuticals, Inc. (Regeneron), pursuant to the Regeneron agreement signed in May 2014, at the offering price of $17.00 per share for gross proceeds of $10.0 million and no underwriting discounts or commissions;
- immediately prior to the completion of the IPO, all the outstanding shares of the Company's convertible preferred stock were converted into 10,689,027 shares of common stock; and
- immediately prior to the completion of the IPO, all outstanding warrants for convertible preferred stock and common stock were exercised into 407,131 shares of common stock for proceeds of $0.6 million.

In January 2015, the Company completed a public offering of 2,369,375 shares of its common stock (Follow-on Offering), which includes 359,918 shares the Company issued pursuant to the underwriters' exercise of their option to purchase additional shares, and the Company received net proceeds of approximately $130.5 million, after underwriting discounts, commissions and estimated offering expenses.

2. Summary of significant accounting policies and basis of presentation

Use of Estimates—The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of income and expenses during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. On an ongoing basis, the Company evaluates its estimates and assumptions, including those related to clinical trial accruals, stock-based compensation, income taxes and, prior to the IPO, fair value of embedded derivative liability, fair value of convertible preferred stock and fair values of common and convertible preferred stock warrants. The Company's actual results may differ from these estimates under different assumptions or conditions. There have been no significant changes from our original estimates in any periods presented.

Principles of Consolidation—The Company's consolidated financial statements have been prepared in accordance with U.S. GAAP and include the accounts of the Company and its wholly-owned subsidiary in Australia. All intercompany transactions and balances have been eliminated in consolidation.

Reclassifications—The Company has reclassified certain prior period amounts to conform to the current period presentation. The Company reclassified changes in fair value of warrant liabilities from other income (expense), net and presented it as a separate line item on our consolidated statements of operations and comprehensive loss. The reclassification had no impact on the total income (expense), net or net loss.

Foreign Currency Translation—The Company's consolidated financial statements are prepared in U.S. dollars. Its foreign subsidiary uses the Australian dollar as its functional currency and maintains its records in the local currency. Assets and liabilities are re-measured at exchange rates in effect at the end of the reporting period. Equity is measured at historical rates and income and expenses are re-measured at average exchange rates for the reporting period. The resulting foreign currency translation adjustment is recorded in accumulated other comprehensive income (loss) in the consolidated balance sheets and in the consolidated statements of operations and comprehensive loss. Transactions denominated in foreign currency are translated at exchange rates at the date of transaction with foreign currency gains (losses) recorded in other income (expense), net in the consolidated statements of operations and other comprehensive loss.

Cash and Cash Equivalents—As December 31, 2014, cash equivalents were comprised of money market funds. We consider all highly liquid investments purchased with original maturities of three months or less at the date of purchase to be cash equivalents. Cash equivalents are stated at fair value.

Deposit—Deposit in the amount of $0.1 million as of December 31, 2014 and 2013 represents amounts paid in connection with the Company's facility lease agreement and recorded as a long-term asset.

Segment Reporting—The Company operates and manages its business as one reporting and operating segment, which is the business of developing and commercializing gene therapeutics. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance.

Concentrations of Credit Risk and Other Uncertainties—Financial instruments that potentially subject us to significant concentrations of credit risk consists primarily of cash and cash equivalents. As of December 31, 2014, substantially all of the Company's cash and cash equivalents was deposited in accounts at four financial institutions, and amounts may exceed federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial strength of the depository institutions in which the financial instrument are held.

The Company is subject to certain risks and uncertainties, including, but not limited to changes in any of the following areas that the Company believes could have a material adverse effect on future financial position or results of operations: ability to obtain future financing; regulatory approval and market acceptance of, and reimbursement for, the Company's product candidates; performance of third-party clinical research organizations and manufacturers; development of sales channels; protection of the intellectual property; litigation or claims against the Company based on intellectual property, patent, product, regulatory or other factors; and the Company's ability to attract and retain employees necessary to support the growth.

Property and Equipment—Property and equipment are recorded at cost, net of accumulated depreciation and amortization. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are capitalized and amortized over the shorter period, expected life or lease term. Major replacements and improvements are capitalized, while general repairs and maintenance are expensed as incurred.

Impairment of Long-Lived Assets—We evaluate the carrying amount of the Company's long-lived assets whenever events or changes in circumstances indicate that the assets may not be recoverable. An impairment loss would be recognized when estimated future cash flows expected to result from the use of the asset and its eventual disposition is less than the carrying amount of the asset. To date, there have been no such impairment losses.

Deferred Offering Costs—We capitalize deferred offering costs, which primarily consist of direct incremental legal and accounting fees relating to our public offerings. We offset the deferred offering costs against our public offering proceeds upon the consummation of our public offerings. As of December 31, 2014 and 2013, $0.4 million and $50,000 of deferred offering costs were capitalized in deposits and other long-term assets on our consolidated balance sheets, respectively.

Convertible Preferred Stock—The Company recorded issued convertible preferred stock at fair value on the dates of issuance, net of issuance costs. The convertible preferred stock was recorded outside of stockholders' deficit because the shares contain liquidation features that are not solely within the Company's control. All of the outstanding shares of convertible preferred stock were converted into common stock shares immediately prior to the completion of the IPO in July 2014.

Derivative Instruments—The Company has recorded convertible preferred stock warrants issued to investors and note holders as derivative liabilities. The convertible preferred stock warrants are initially recorded at fair value, with gains and losses arising from changes in fair value recognized in other income (expense) in the consolidated statements of operations and comprehensive loss at each period end while such instruments are outstanding and classified as long-term liabilities. In connection with the completion of the Company's IPO in August 2014, all of the outstanding warrants to purchase convertible preferred stock were exercised. As a result of the exercises, the Company recorded a $0.8 million loss related to the change in fair value in our consolidated statements of operations and comprehensive loss and reclassified the fair value of $0.9 million to additional paid-in capital.

The Company has also recorded as a derivative liability the Company's obligation to issue common stock warrants in connection with license agreements as the terms of the warrants were not fixed due to potential adjustments in the exercise price. The derivative liability associated with the common stock warrants was initially recorded at fair value, with gains and losses arising from changes in fair value recognized in the consolidated statements of operations and comprehensive loss at each period end while such instruments are classified as liabilities. In March 2014, the liability terminated upon the issuance of common stock warrant and was recorded to additional paid-in capital.

Both the preferred stock and common stock warrant liabilities were valued using a Black-Scholes valuation model (refer to Note 10).

Immediately prior to the completion of the IPO, all outstanding warrants to purchase preferred stock and common stock were exercised, and the outstanding liability was reversed.

Revenue Recognition—The Company has primarily generated contract revenue through a research and collaboration arrangement with a strategic partner for the development and commercialization of product candidates, and a license agreement related to the licensing of certain of our intellectual property. Additionally, the Company has historically generated grant revenue from research and development grant programs.

The Company recognizes revenue in accordance with Accounting Standards Codification Topic 605, *Revenue Recognition* (ASC 605). Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- Persuasive evidence of an arrangement exists;
- Delivery has occurred or services have been rendered;

- The seller's price to the buyer is fixed or determinable; and
- Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Collaboration and License Revenue

In May 2014, the Company entered into a research collaboration and license agreement with Regeneron to discover, develop and commercialize novel gene therapy products for the treatment of ophthalmologic diseases. The collaboration covers up to eight distinct therapeutic targets (collaboration targets). The Company and Regeneron will collaborate during the initial research period of three years that can be extended by Regeneron for up to an additional five years. During the research period, Regeneron has the option to obtain an exclusive worldwide license for a collaboration target's further development by giving written notice to the Company and paying $2.0 million per target. If Regeneron exercises its option, it will be responsible for all further development and commercialization of the target. The Company is then eligible to receive contingent payments of up to $80.0 million upon achievement of certain development and regulatory milestones for product candidates directed toward each collaboration target, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight collaboration targets, plus a royalty in the low- to mid-single-digits on worldwide net sales of collaboration products.

For any two collaboration targets, the Company has an option to share up to 35% of the worldwide product candidate development costs and profits. If the Company exercises this option, the Company will not be eligible for milestone and royalty payments discussed above but rather the Company will share development costs and profits with Regeneron.

The agreement will expire with respect to each collaboration target upon the earlier of the (a) expiration of the research term if the option right has not been triggered by the end of the research term or (b) expiration of the option right if the option right has not been exercised by Regeneron. If the option right has been exercised, the agreement in connection with each collaboration target will expire upon expiration of all payment obligations by Regeneron. In addition, the agreement, or Regeneron's rights to any target development under the agreement, may terminate early under the following situations:

- Regeneron may terminate the agreement for convenience at any time on a target by target basis or in totality upon a 30-day notice.
- Each party can terminate the agreement if another party commits a material breach or material default in performance of its obligations and such breach or default is not cured within 60 days.
- The agreement is automatically terminated upon initiation of any bankruptcy proceedings, reorganization or dissolution of either party.
- The Company can terminate the agreement upon 30-day notice if Regeneron challenges the validity, scope or enforceability of any Company patent.

In connection with the agreement, Regeneron also acquired a time-limited right of first negotiation for a potential license to develop and commercialize AVA-101, the Company's gene therapy product currently under development and undergoing a Phase 2a clinical trial. If and when such negotiation is successful, the Company and Regeneron will enter into a separate agreement for AVA-101.

Under the terms of the agreement, the Company received initial upfront non-refundable cash payments of $8.0 million that included payment for research license fees, prepaid collaboration research costs and the time-limited right of first negotiation for AVA-101. As the agreement provides for multiple deliverables, the Company accounts for this agreement as a multiple elements revenue arrangement. If deliverables did not appear to have a standalone value, they were combined with other deliverables into a unit of accounting with standalone value. The Company allocated the $8.0 million to the relative fair value of the two units of accounting identified in the arrangement. The Company expects to recognize $6.5 million for the research licenses and related research and development services ratably over the associated period of performance, which is the maximum research period of eight years. As there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, the Company will recognize revenue on a straight-line basis over the eight year performance period. The remaining $1.5 million allocated to the second unit of accounting for the rights of first negotiation for AVA-101 is deferred and will be recognized during the period when Regeneron has exclusive access to the results of the Phase 2a clinical trial.

For the year ended December 31, 2014, the Company recognized $0.5 million of collaboration and license revenue related to the research collaboration license agreement with Regeneron. As of December 31, 2014, we have deferred revenue relating to this collaboration agreement of $7.5 million.

The Company also recorded $30,000 license revenue in 2014 related to the licensing of certain of its intellectual property under a licensing agreement entered into during February 2014.

Government Grants

Government grants provide funds for certain types of expenditures in connection with research and development activities over a contractually defined period. Revenue related to government grants is recognized in the period during which the related costs are incurred and the related services are rendered, provided that the applicable performance obligations under the government grants have been met.

Funds received under government grants are recorded as revenue if we are deemed to be the principal participant in the contract arrangements because the activities under the contracts are part of our development programs. If we are not the principal participant, the funds from government grants are recorded as a reduction to research and development expense. Funds received from government grants are not refundable and are recognized when the related qualified research and development expenses are incurred and when there is reasonable assurance that the funds will be received. Funds received in advance of the performance of the services are recorded as deferred revenue.

For the years ending December 31, 2013 and 2012, the Company recognized $0.5 million and $30,000, respectively, of government grant revenue. No government grant revenue was recorded in 2014 as we completed the work performed under the grant in 2013. We intend to continue to evaluate pursuing additional grant opportunities on a case-by-case basis.

Research and Development Expenses—Research and development expenses are charged to expense as incurred. Research and development expenses include certain payroll, stock compensation and other personnel-related expenses, laboratory supplies, consulting costs, external contract research and development expenses, and allocated overhead, including rent, equipment depreciation and utilities. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

The Company estimates preclinical studies and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on the Company's behalf. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. These

estimates are based on communications with the third party service providers and our estimates of accrued expenses and on information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. There have been no significant changes from our original estimates in any of the periods presented.

The Company received tax credits from the Australian government in connection with certain research costs incurred in conducting research by the Company's Australian subsidiary. These refunds do not depend on the taxable income or tax position of the Company and therefore the Company does not account for them under an income tax accounting model. The Company recognizes such refunds as government grants in the period when qualified expenses are incurred as a reduction of research expenses. The Company has recorded the reimbursement of $0.1 million, $0.8 million and zero from the Australian tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss in the years ended December 31, 2014, 2013 and 2012, respectively.

Fair Value Measurements—Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The carrying amounts of the Company's financial instruments, including cash and cash equivalents, prepaid and other current assets, accounts payable, accrued expenses and other warrant liabilities approximate its fair value due to their short-term maturities. Refer to Note 3 for the methodologies and assumptions used in valuing financial instruments.

Stock-Based Compensation Expense—Stock-based compensation expense related to awards to employees is measured at the grant date based on the fair value of the award. The fair value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period, which is generally the vesting period. The expense recognized for the portion of the award that is expected to vest has been reduced by an estimated forfeiture rate. The forfeiture rate is determined at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

The Company uses the Black-Scholes valuation model as the method for determining the estimated fair value of stock-based awards.

Expected Term—The expected term assumption represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method.

Expected Volatility—Expected volatility is estimated using comparable public companies volatility for similar terms.

Expected Dividend—The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company has never paid dividends and has no plans to pay dividends.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero-coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. The fair value of non-employee stock options is estimated using the Black-Scholes valuation model with assumptions generally consistent with those used for employee stock options, with the exception of the expected term, which is the remaining contractual life at each measurement date. Refer to Note 11 for more information on assumptions used in estimated stock-based compensation expense.

Income Taxes—The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been

included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize its deferred income tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2014 and 2013, the Company has recorded a full valuation allowance on its deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Comprehensive Loss—Comprehensive loss is comprised of net loss, deemed dividend to a preferred stockholder and other comprehensive income or loss. Other comprehensive income or loss consists of foreign currency translation adjustments related to translation of the financial statements of the Australian subsidiary.

Basic and Diluted Net Loss Per Share—Basic net loss per common share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period. Diluted net loss per common share is computed by dividing the net loss by the weighted-average number of common shares and dilutive common share equivalents outstanding during the period. Because the Company has reported a net loss attributable to common stockholders for all periods presented, diluted net loss per common share is the same as basic net loss attributable to common stockholders per common share for those periods. While shares of the convertible preferred stock were outstanding they were considered to be participating securities as they were entitled to participate in undistributed earnings with shares of common stock. Due to net losses in all periods presented, there is no impact on net loss per share calculation in applying the two-class method since the participating securities have no legal requirement to share in any losses.

Recently Issued Accounting Pronouncements—In August 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standard Update (ASU) 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, requiring management to evaluate whether events or conditions could impact an entity's ability to continue as a going concern and to provide disclosures if necessary. Management will be required to perform the evaluation within one year after the date that the financial statements are issued. Disclosures will be required if conditions give rise to substantial doubt and the type of disclosure will be determined based on whether management's plans will be able to alleviate the substantial doubt. The accounting standards update will be effective for the first annual period ending after December 15, 2016, and for annual periods and interim periods thereafter with early application permitted. The adoption of this guidance is not expected to impact the Company's financial position or results of operations.

In June 2014, the FASB issued ASU No. 2014-10, *Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*. The amendments in this update remove the definition of a development stage entity from the Master Glossary of the Accounting Standards Codification, thereby removing the financial reporting distinction between development stage entities and other reporting entities from U.S. GAAP. In addition, the amendments eliminate the requirements for development stage entities to (1) present inception-to-date information, (2) label the financial statements as those of a development stage entity, (3) disclose a description of the development stage activities in which the entity is engaged and (4) disclose in the first year in which the entity is no longer a development stage entity that in prior

years it had been in the development stage. The Company has elected to early adopt this guidance, as permitted, for its consolidated financial statements for the year ended December 31, 2014, and no longer labeled its financial statements as those of a development stage entity or included any inception-to-date information.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in ASC 605*, Revenue Recognition*. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. The ASU's effective date for the Company will be January 1, 2017. The Company is evaluating the application of this ASU, but has not yet determined the potential effects it may have on the Company's consolidated financial statements.

3. Fair Value Measurements and Fair Value of Financial Instruments

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

The fair value of Level 1 assets has been determined using quoted prices in active markets for identical assets. Level 1 securities consist of highly liquid money market funds and recorded as cash and cash equivalents on the consolidated balance sheets.

The Company's financial instruments had consisted of Level 3 liabilities. In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3 within the valuation hierarchy. Level 3 liabilities that are measured at estimated fair value on a recurring basis consist of common and preferred stock warrant liabilities, and change in control provision embedded derivative liability related to the Company's convertible notes.

The estimated fair values of the outstanding common and preferred stock warrant liabilities are measured using the Black-Scholes valuation model. This method of valuation involves using such inputs as the estimated fair value of the underlying stock at the measurement date, the expected term, which is the remaining contractual term of the warrants, risk-free interest rates, expected dividends on stock and expected volatility of the price of the underlying stock (refer to Note 10). Due to the nature of these inputs, the valuation of the warrants is considered a Level 3 measurement. The convertible preferred stock and common stock warrant liabilities will increase or decrease each period based on the fluctuations of the fair value of the underlying security. A significant fluctuation in the common or convertible preferred stock fair value would result in a material change in the fair values of the convertible preferred stock and common stock warrant liabilities.

The estimated fair value of the change in control embedded derivative liability related to the Company's convertible notes was determined using a probability-weighted expected return model. The probability of a change in control occurring was determined to be 5% during fiscal 2013 and 2012. The future cash flows were discounted to their net present value using a discount rate of 21% at each measurement date. The embedded derivative liability increases or decreases each period based on the amount of convertible notes outstanding at each measurement date. This liability ceased in November 2013 upon the conversion of the convertible notes into Series A convertible preferred stock (refer to Note 8).

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at estimated fair value using Level 3 inputs. There were no transfers within the hierarchy during the years ended December 31, 2014, 2013 and 2012.

The following table summarizes, for assets and liabilities recorded at fair value, the respective fair value and the classification by level of input within the fair value hierarchy as described above (in thousands):

	TOTAL CARRYING VALUE	QUOTED PRICES IN ACTIVE MARKETS (LEVEL 1)	SIGNIFICANT OTHER OBSERVABLE INPUTS (LEVEL 2)	SIGNIFICANT UNOBSERVABLE INPUTS (LEVEL 3)
December 31, 2014				
Assets:				
Money market funds	$ 40,000	$ 40,000	$ —	$ —
Total assets	$ 40,000	$ 40,000	$ —	$ —
December 31, 2013				
Liabilities:				
Preferred stock warrant liability	$ 91	$ —	$ —	$ 91
Common stock warrant liability	42	—	—	42
Total liabilities	$ 133	$ —	$ —	$ 133

The following table provides a summary of changes in the estimated fair value of the Company's warrants liabilities and embedded derivative liability measured at estimated fair value using significant Level 3 inputs (in thousands):

	CONVERTIBLE PREFERRED STOCK WARRANT LIABILITY (1)	COMMON STOCK WARRANT LIABILITY (2)	EMBEDDED DERIVATIVE LIABILITY (3)
Balance—January 1, 2012	$ 49	$ —	$ —
Obligation to issue a warrant	—	5	—
Embedded derivative on notes payable issuance	—	—	24
Change in fair value	(13)	—	(6)
Balance—December 31, 2012	36	5	18
De-recognition of embedded derivative upon convertible notes conversion	—	—	(18)
Change in fair value	55	37	—
Balance—December 31, 2013	91	42	—
Issuance of common stock warrant	—	(41)	—
Change in fair value	760	(1)	—
Exercises	(851)	—	—
Balance—December 31, 2014	$ —	$ —	$ —

(1) In July 2014, all of the outstanding warrants to purchase convertible preferred stock and common stock were exercised immediately prior to the completion of the IPO.
(2) In March 2014, the common stock warrant was issued and was recorded to additional paid-in capital.
(3) In November 2013, the liability terminated upon the conversion of the notes into Series A convertible preferred stock.

4. Significant Agreements

University of California—In May 2010, the Company entered into a license agreement, as amended, with the Regents of University of California (Regents) for exclusive rights in the United States to certain patents owned by the Regents. Under the terms of the agreement, the Company paid an up-front license fee of $100,000 and agreed to reimburse the Regents for patent-related expenses. The Company is obligated to pay the Regents royalties on net sales, if any, as well as an annual maintenance fee of $50,000 beginning in the calendar year after the first commercial sale of a licensed product and milestone payments related to the achievement of certain clinical and regulatory goals totaling up to $900,000 for the first indication and $500,000 for each additional indication for up to two additional indications. Through December 31, 2014, none of these goals had been achieved, and no milestones were payable.

5. Property and Equipment, Net

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

	DECEMBER 31,	
	2014	2013
Computer equipment and software	$ 142	$ 10
Laboratory equipment	1,012	87
Furniture and fixtures	73	—
Leasehold improvements	48	—
Total property and equipment	1,275	97
Less accumulated depreciation	(190)	(28)
Property and equipment, net	$ 1,085	$ 69

Depreciation expense related to property and equipment was $162,000, $26,000 and $1,000 for the years ending December 31, 2014, 2013 and 2012, respectively.

6. Accrued Expenses and Other Current Liabilities

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

	DECEMBER 31,	
	2014	2013
Employee compensation	$ 1,509	$ 162
Accrued professional fees	1,236	162
Accrued clinical and process development costs	942	54
Other	20	15
Total accrued expenses and other current liabilities	$ 3,707	$ 393

7. Commitments and Contingencies

Facility Lease Agreement

The Company leases its' office building under a non-cancelable lease agreement, which expires on May 8, 2020. The Company may extend this lease for up to four years. The lease agreement provides for an escalation of rent payments each year. The Company records rent expense on a straight-line basis over the term of the lease.

As of December 31, 2014, future minimum commitments under our facility operating lease were as follows (in thousands):

YEARS ENDED DECEMBER 31,	TOTAL LEASE COMMITMENTS
2015	826
2016	1,099
2017	1,129
2018	1,162
2019	1,197
2020 and thereafter	403
Total minimum lease payments	$ 5,816

Rent expense recognized under the operating lease, including additional rent charges for utilities, parking, maintenance, and real estate taxes was $662,000, $53,000 and $17,000 for the years ended December 31, 2014, 2013 and 2012, respectively.

Collaborations and License Agreements

The Company is party to various agreements, principally relating to licensed technology that requires future payments relating to milestones or royalties on future sales of specified products. Through December 31, 2014, none of the goals had been achieved under the license agreements and no cash milestones were accrued or payable. Because the achievement of these milestones is not fixed and determinable, such commitments have not been included on the Company's consolidated balance sheets. Royalty payment was $0.1 million for the year ended December 31, 2014.

Guarantees and Indemnifications

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for indemnification for certain liabilities. The exposure under these agreements is unknown because it involves claims that may be made against the Company in the future but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations. The Company also has indemnification obligations to its directors and executive officers for specified events or occurrences, subject to some limits, while they are serving at the Company's request in such capacities. There have been no claims to date and the Company believe the fair value of these indemnification agreements is minimal. Accordingly, the Company has not recorded any liabilities for these agreements as of December 31, 2014.

8. Related-Party Convertible Notes

2012 Related-Party Convertible Notes

On August 28, 2012, the Company entered into a convertible note payable agreement with a related party investor for the issuance of up to an aggregate principal amount of $2.0 million of convertible notes (2012 Notes). The 2012 Notes were due to mature on February 28, 2014 and accrue interest at a rate of 5% per year. In November 2012, the Company borrowed $0.5 million of 2012 Notes. During February, April, July and September 2013, the Company borrowed the remaining aggregate principal amount of $1.5 million of 2012 Notes.

Upon occurrence of a change of control transaction prior to the maturity date, 130% of $2.0 million minus the outstanding principal balance would be payable to the investor. The change of control provision met the accounting definition of an embedded derivative and required bifurcation. The Company valued this embedded

derivative on the 2012 Notes using a probability-weighted model which included significant estimates regarding the expected time to a change of control event, and a discount rate. The estimated fair value of this embedded derivative on the date of issuance was determined to be approximately $24,000, and was recorded as a discount to the 2012 Notes. This discount was amortized to interest expense through the maturity date of the 2012 Notes. The embedded derivative was re-measured each period end with changes in fair value recorded in the consolidated statements of operations and comprehensive loss. In November 2013, the derivative terminated upon the conversion of the 2012 Notes into Series A convertible preferred stock.

In November 2013, the Company amended the 2012 Notes agreement to provide for the acceleration of the conversion of the 2012 Notes into shares of Series A convertible preferred stock. The outstanding principal and accrued and unpaid interest of $2.1 million was converted into 1,419,959 shares of Series A convertible preferred stock at $1.45 per share. The 2012 Notes modification was recorded as a $1.7 million loss on extinguishment of related-party convertible notes in the consolidated statement of operations and comprehensive loss (refer to Note 9).

2013 Related-Party Convertible Notes

On October 22, 2013, the Company entered into a convertible note purchase agreement with a related party investor for the issuance and sale of up to an aggregate principal amount of $5.0 million of convertible notes (2013 Notes). In each of January 2014 and April 2014, the Company borrowed an aggregate principal amount of $1.0 million of 2013 Notes.

The 2013 Notes had a stated maturity date of December 31, 2016 and accrued interest at a rate of 5% per year. The 2013 Notes and any accrued and unpaid interest were automatically convertible into equity securities sold in the next qualified round of financing occurring prior to the maturity date, at a conversion price equal to 90% of the original issuance price of such equity securities sold in such next round of financing.

The difference between the fair value of the securities into which the debt was convertible and the effective conversion price on the borrowing date represents a beneficial conversion feature. In connection with the January 2014 and April 2014 borrowings, the Company recorded the fair value of the beneficial conversion feature of $1.0 million and $1.0 million, respectively, by allocating a portion of the proceeds to additional paid-in capital, resulting in a discount on the convertible instrument, to be amortized over the repayment period using the effective interest method.

In April 2014, the Company completed a Series B convertible preferred stock financing (refer to Note 9), pursuant to which the outstanding principal amount on the 2013 Notes converted into 295,115 shares of Series B convertible preferred stock at a conversion price of $6.78, which is equal to 90% of the original issuance price of $7.53 per share. At the time of the conversion, the Company recorded a $0.2 million loss on extinguishment of related-party convertible notes in the consolidated statements of operations and comprehensive loss and a repurchase of beneficial conversion feature of $2.0 million as credit to additional paid-in capital.

As of December 31, 2014, there are no outstanding convertible notes recorded in the Company's consolidated balance sheet.

9. Convertible Preferred Stock

In November 2013, the Company issued 1,419,959 shares of Series A convertible preferred stock upon the conversion of the 2012 Notes (refer to Note 8) and issued 689,655 shares to a potential collaborator for cash at $1.45 per share. The estimated fair value of Series A convertible preferred stock was $2.63 per share on the issuance date. The fair value of the Series A convertible preferred stock was determined using a PWERM model, a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering several possible outcomes for the Company in the future, as well

as the economic and control rights of each share class. In the November 2013 valuation, the Company considered the estimated fair value of the Series A preferred stock under three potential scenarios, including an initial public offering, a collaborative partnering agreement model, and a corporate failure. The Company recorded the difference between the effective conversion price and the fair value of the securities into which the debt was converted, resulting in a $1.7 million loss on extinguishment for the 2012 Notes (refer to Note 8). The Company also recorded a charge of $0.8 million associated with the intrinsic value of the convertible preferred Series A shares issued to a potential collaborator, which is recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2013.

At December 31, 2013, the Series A convertible preferred stock rights, privileges and preferences were as follows:

Conversion Rights—Each share of Series A convertible preferred stock was convertible at an option of the holder into one share of common stock (subject to adjustment for certain events, including dilutive issuances, stock splits, and reclassifications). The Series A convertible preferred stock converted automatically into shares of common stock in the IPO.

Dividends—Each holder was entitled to 8% noncumulative dividends per share, if and when declared by the board of directors. The 8% noncumulative dividends were to be paid in advance of any distributions to common stock holders. Each holder was also entitled to participate in dividends on an as-converted pari passu basis together with common stock after distribution of 8% noncumulative dividends. No dividends were declared on the Series A convertible preferred stock .

Voting—Each holder had the right to one vote for each share of common stock into which such Series A convertible preferred stock could have been converted. Certain financing, acquisition, disposition, and recapitalization transactions required the vote of the majority of the shares of outstanding Series A convertible preferred stock, provided that at least 1,000,000 shares of convertible preferred stock were issued and outstanding.

Liquidation Preference—In the event of any liquidation, dissolution, or winding-up of the Company, including a merger, acquisition, or sale of assets, as defined, each Series A convertible preferred stock holder would have been entitled to receive the greater of (1) an amount of $1.45 per share for each share of Series A convertible preferred stock held (as adjusted for recapitalizations, stock combinations, stock dividends, stock splits, and reclassifications), plus any declared but unpaid dividends prior to and in preference to any distribution to the holders of common stock or (2) an amount of cash, securities or other property per share on as-converted to common stock basis. If the assets of the Company had been insufficient to make payment in full to all Series A convertible preferred stock holders than the assets or consideration would have been distributed ratably among such holders.

Any remaining assets would then have been distributed among the holders of the common stock on a pro rata basis based on the number of shares of common stock held by them.

Election of Board of Directors—The holders of Series A convertible preferred stock, voting as a separate class, were entitled to elect one member of the board of directors.

In April 2014, the Company repurchased 531,208 shares of Series A convertible preferred stock for $4.0 million. The difference between the repurchase price of $7.53 and original issuance price of $1.45 was recorded as a deemed dividend of $3.2 million to a preferred stockholder and effected the calculation of net loss attributable to common stockholders and net loss per share for the year ended December 31, 2014.

In April 2014, the Company issued 7,025,888 shares of Series B convertible preferred stock to investors for cash for an aggregate of $52.9 million at $7.53 per share. The Company also converted the $2.0 million outstanding balance under its related-party convertible notes into 295,115 shares of Series B convertible preferred stock.

In connection with the completion of the IPO in August 2014, all outstanding shares of Series A and Series B convertible preferred stock were converted into 10,689,027 shares of common stock on a one-for-one basis.

10. Warrants

As of December 31, 2013, the following warrants and obligations to issue warrants to purchase shares of common stock and convertible preferred stock were outstanding and exercisable:

WARRANT HOLDER	ISSUE DATE	ISSUED IN CONNECTION WITH	WARRANT TO PURCHASE	EXERCISABLE INTO	EXERCISE PRICE	EXPIRATION DATE
LEI	08/20/2010	License Agreement	125,000	Common	$ 0.001	08/20/2015
LEI	02/24/2012	License Agreement	80,000	Common	$ 0.19	02/24/2017
Investors	09/07/2010	Conversion of Notes Payable	59,000	Common	$ 0.15	09/07/2015
Investors	09/07/2010	Conversion of Notes Payable	54,716	Series A	$ 1.45	09/07/2015

The fair value of each warrant recorded as liability was estimated as of December 31, 2013 using the Black-Scholes valuation model with the following assumptions:

		DECEMBER 31, 2013				
WARRANT ISSUE DATE	CLASS	EXPECTED TERM (IN YEARS)	EXPECTED VOLATILITY	RISK-FREE INTEREST RATE	DIVIDEND YIELD	FAIR VALUE OF UNDERLYING SHARES
September 2010	Series A preferred stock	1.68	59%	0.3%	—	$ 2.96
August 2012 (obligation)	Common stock	5.00	75%	1.6%	—	$ 2.75

In connection with an amendment to the LEI license agreement in August 2012 the Company agreed to issue to LEI a warrant to purchase 25,000 shares of common stock. The Company estimated the fair value of the obligation to issue this warrant to be approximately $5,000, which was recorded as research and development expense and common stock warrant liability. The fair value of the obligation was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of $0.30 per share, contractual term of the warrants of 5 years, a risk-free interest rate of 0.7%, an expected volatility of 86% and a 0% expected dividend yield. Until the Company issued the warrant, it classified it as a common stock warrant liability and re-measured the fair value at the end of each reporting period. The fair value of this liability was $42,000 as of December 31, 2013. In March 2014, the Company issued the common stock warrant to LEI with an exercise price of $2.75 per share, at which time the issued common stock warrant was reclassified to additional paid-in capital.

In May 2014, the Company issued a warrant to purchase 63,415 shares of common stock with an exercise price of $6.83 to a financial services firm in connection with the Series B convertible preferred stock financing completed in April 2014. This warrant was exercisable immediately and expired on the earlier of the Company's IPO or May 15, 2019. The Company estimated the fair value of this warrant to be approximately $0.3 million which was recorded as expenses related to issuance of Series B convertible preferred stock. The fair value of the warrant was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of $6.83 per share, contractual term of the warrant of 5 years, a risk-free interest rate of 1.55%, an expected volatility of 75% and a 0% expected dividend yield.

All of the warrants to purchase common stock and preferred stock were exercised for cash in connection with the completion of the IPO in August 2014, resulting in the issuance of an aggregate of 407,131 shares of common stock in exchange for proceeds of $0.6 million. As a result of the exercises of the warrants to purchase preferred

stock, the Company recorded a $0.8 million loss related to the change in fair value in our consolidated statements of operations and comprehensive loss and reclassified the fair value of $0.9 million to permanent equity. The fair value of the warrants to purchase preferred stock was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of $17.00 per share, contractual term of the warrants of 1.1 years, a risk-free interest rate of 0.1%, an expected volatility of 70% and a 0% expected dividend yield.

11. STOCK OPTION PLAN

On December 26, 2006, the Company adopted the 2006 Equity Incentive Plan, which was amended by the board of directors on November 15, 2012 (2006 Plan). The 2006 Plan allowed for the granting of ISOs and NSOs to the employees, members of the board of directors and consultants of the Company. ISOs were granted only to the Company's employees, including officers and directors who are also employees. NSOs were granted to the employees and consultants. In July 2014, the Company's board of directors and its stockholders approved the establishment of the 2014 Equity Incentive Award Plan (2014 Plan), effective upon the date upon which the registration statement for the IPO was declared effective, which was July 30, 2014. As of the date of the IPO, the Company reserved for issuance under the 2014 Plan a total of 2,088,332 shares of its common stock, plus any additional shares that would otherwise return to the 2006 Plan as a result of forfeiture, termination or expiration of awards previously granted under the 2006 Plan. Options may no longer be issued under the 2006 Plan after July 30, 2014, the effective date of the 2014 Plan. In addition, the 2014 Plan provides for annual increases in the number of shares available for issuance thereunder on the first business day of each fiscal year, beginning with 2015, equal to four percent (4%) of the number of shares of the Company's common stock outstanding as of such date or a lesser number of shares as determined by the Company's board of directors.

As of December 31, 2014, a total of 7,544,207 shares of common stock were authorized for issuance and 2,043,715 shares were available for future grants under the 2014 Plan.

Options under the 2006 Plan and 2014 Plan may be granted for periods of up to 10 years and at prices no less than 100% of the estimated fair value of the shares on the date of grant as determined by the board of directors, provided, however, that the exercise price of an ISO and NSO granted to a 10% shareholder may not be less than 110% of the estimated fair value of the shares on the date of grant. Options granted to employees and non-employees generally vest ratably over four years.

In July 2014, the Company's board of directors and its stockholders approved the establishment of the 2014 Employee Stock Purchase Plan (2014 ESPP). The Company reserved for issuance 208,833 shares of its common stock and provided for annual increases in the number of shares available for issuance on the first business day of each fiscal year, beginning in 2015, equal to the lesser of one percent (1%) of the number of shares of the Company's common stock outstanding as of such date or a number of shares as determined by the Company's board of directors.

The following table summarizes option activity under our stock plans and related information:

	NUMBER OF SHARES	WEIGHTED-AVERAGE EXERCISE PRICE	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	AGGREGATE INTRINSIC VALUE (a) (IN THOUSANDS)
Balances, January 1, 2012	705,000	$ 0.05		
Options granted	2,890,000	$ 0.19		
Options exercised	—	—		
Options cancelled	—	—		
Balances, December 31, 2012	3,595,000	$ 0.16	9.3	$ 495
Options granted	45,000	$ 0.34		
Options exercised	—	—		
Options cancelled	—	—		
Balances, December 31, 2013	3,640,000	$ 0.16	8.3	$ 9,411
Options granted	1,870,700	$ 14.58		
Options exercised	(496,759)	$ 0.04		
Options cancelled	(82,083)	$ 1.91		
Balances, December 31, 2014	4,931,858	$ 5.61	8.2	$ 238,653
Vested and expected to vest as of December 31, 2014	4,831,195	$ 5.09	8.2	$ 236,275
Exercisable as of December 31, 2014	1,885,366	$ 0.39	7.4	$ 101,080

(a) The aggregate intrinsic value is calculated as the difference between the options exercise price and the estimated fair value of the underlying common stock at December 31, 2012, 2013 and 2014, respectively.

The weighted-average fair values of options granted during fiscal years 2014, 2013 and 2012 were $9.56, $0.37 and $0.21, respectively. The total intrinsic value of options exercised during the year ended December 31, 2014 was $15.7 million. There were no options exercised in 2013 and 2012.

The following table summarizes information with respect to stock options outstanding and currently exercisable and vested.

As of December 31, 2014:

	OPTIONS OUTSTANDING		OPTIONS EXERCISABLE AND VESTED	
RANGE OF EXERCISE PRICES	NUMBER OUTSTANDING	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	NUMBER OUTSTANDING	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)
$ .0001 – $0.27	3,071,158	7.5	1,789,700	7.3
$ 0.28 – $ 2.95	484,200	9.1	91,500	9.0
$ 2.96 – $ 9.16	265,000	9.3	—	—
$ 9.17 – $11.50	278,400	9.5	—	—
$11.51 – $35.00	743,850	9.7	—	—
$35.01 – $50.49	89,250	9.9	4,166	9.9

The Company has recorded aggregate stock-based compensation expense related to the issuance of stock option awards to employees and nonemployees in the consolidated statement of operations and comprehensive loss as follows:

(in thousands)	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Research and development	$ 7,331	$ 362	$ 54
General and administrative	1,236	153	22
Total	$ 8,567	$ 515	$ 76

Stock Options Granted to Employees

For the years ended December 31, 2014, 2013 and 2012, the Company recorded $1,672,000, $136,000 and $20,000, respectively, of stock-based compensation expense related to employees options. The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Expected volatility	79%	80%	82%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	1.9%	1.0%	0.9%
Expected dividend yield	0.0%	0.0%	0.0%

As of December 31, 2014, there was $15.1 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 3.5 years.

Stock Options Granted to Non-Employees

Stock-based compensation expense related to stock options granted to nonemployees is recognized as the stock options are earned. The Company believes that the estimated fair value of the stock options is more readily measurable than the fair value of the services rendered. For the years ended December 31, 2014, 2013 and 2012, the Company recorded $6,895,000, $379,000 and $56,000, respectively, of stock-based compensation expense related to non-employees options.

We used the following weighted-average assumptions in estimating non-employees stock-based compensation expense:

	YEARS ENDED DECEMBER 31		
	2014	2013	2012
Expected volatility	79%	79%	78%
Expected term (in years)	7.5	7.9	9.0
Risk-free interest rate	2.2%	1.8%	1.6%
Expected dividend yield	0.0%	0.0%	0.0%

As of December 31, 2014, there was $3.4 million of unrecognized stock-based compensation expense related to non-employees' awards that is expected to be recognized over a weighted-average period of 2.9 years.

Fair Value of Common Stock

In determining the exercise prices for options granted, the Company's board of directors has considered the fair value of the common stock as of each grant date. Prior to the IPO, the fair value of the

common stock underlying the stock options was determined by the board of directors at each award grant date based upon a variety of factors, including the results obtained from an independent third party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the current management team, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred shareholders and the prospects of a liquidity event, among others. After the completion of the Company's IPO in August 2014, the fair value of the common stock is based on the closing price of the common stock on the date of grant.

12. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Code. The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. The amount of contributions that the Company made to the 401(k) Plan during the year ended December 31, 2014 was $25,000 and no contributions were made during the year ended December 31, 2013.

13. Income Taxes

No income tax benefit or expense was recorded for the years ended December 31, 2014, 2013 and 2012.

The following table presents domestic and foreign components of loss before provision for income taxes (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		
	2014	2013	2012
U.S.	$ (25,006)	$ (5,031)	$ (1,051)
Foreign	(398)	(245)	(760)
loss before income taxes	$ (25,404)	$ (5,276)	$ (1,811)

A reconciliation of income tax expense computed at the statutory federal income tax rate of 34% to income taxes as reflected in the financial statements is as follows (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		
	2014	2013	2012
Federal income tax expense at statutory rate	$ (8,637)	$ (1,794)	$ (616)
Loss on extinguishment of related-party convertible notes	69	568	—
Non-deductible foreign research expenses	85	26	222
Non-deductible expenses	446	74	5
Research and development tax credits	(304)	(93)	—
Change in valuation allowance	8,349	1,209	359
Foreign rate differential	(8)	10	30
Total tax expense (benefit)	$ —	$ —	$ —

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The following table presents significant components of the Company's deferred tax assets (in thousands):

	AS OF DECEMBER 31,		
	2014	2013	2012
Deferred tax assets:			
Net operating loss carryforwards	$ 8,526	$ 1,876	$ 827
Accruals, reserve and other	222	109	88
Stock-based compensation	3,032	183	32
Tax credit carryforwards	659	145	13
Property and equipment	—	2	—
Intangibles	24	223	130
Other	24	(1)	1
Total deferred tax assets before valuation allowance	12,487	2,537	1,091
Valuation allowance	(12,457)	(2,537)	(1,091)
Total deferred tax assets	30	—	—
Deferred tax liabilities:			
Property and equipment	(30)	—	—
Total deferred tax liabilities	(30)	—	—
Net deferred tax assets	$ —	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2014, 2013 and 2012. The valuation allowance increased approximately $9.9 million, $1.4 million and $0.4 million during the years ended December 31, 2014, 2013 and 2012, respectively, due to net operating losses.

As of December 31, 2014, the Company had U.S. federal NOL carryforwards of approximately $39.6 million to offset future federal income. NOLs expire at various years beginning with 2026. As of December 31, 2014, the Company also had U.S. state NOL carryforwards of approximately $41.0 million to offset future state income. U.S. State NOLs expire at various years beginning with 2016. At December 31, 2014, the Company also had approximately $0.2 million of foreign net operating loss carryforwards which may be available to offset future foreign income; these carryforwards do not expire.

As a result of certain realization requirements of Accounting Standard Codification Topic 718, *Compensation – Stock Compensation* (ASC 718), the table of deferred tax assets and liabilities does not include certain deferred tax assets as of December 31, 2014 that arose directly from tax deductions related to equity compensation that are greater than the compensation recognized for financial reporting. Equity will be increased by $7.4 million if and when such deferred tax assets are ultimately realized. We use ASC 740 ordering when determining when excess tax benefits have been realized.

As of December 31, 2014, the Company had federal research and development tax credit carryforwards of approximately $0.5 million available to reduce future tax liabilities which expire at various years beginning with 2032. As of December 31, 2014, the Company had state credit carryforwards of approximately $0.5 million available to reduce future tax liabilities which do not expire.

Under Section 382 of the Internal Revenue Code of 1986, as amended (Code), our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we have

experienced an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. We believe that we have experienced at least two ownership changes under Section 382, which will result in limitations in our ability to utilize net operating losses and credits. In addition, we may experience ownership changes as a result of our initial public offering in August 2014, future offerings or other changes in the ownership of our stock. As a result, the amount of the NOLs and research and credit carryforwards presented in our financial statements could be limited and may expire unutilized.

The Company files income tax returns in the United States, and state and foreign jurisdictions. The federal, state and foreign income tax returns are open under the statute of limitations subject to tax examinations for the tax years ended December 31, 2010 through December 31, 2014. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service, state or foreign tax authorities to the extent utilized in a future period.

The Company has total unrecognized tax benefits as of December 31, 2014, 2013 and 2012 of approximately $471,000, $43,000 and $5,000 respectively. No amount of the unrecognized tax benefits, if recognized, would reduce the Company's annual effective tax rate because the benefits are in the form of deferred tax assets for which a full valuation allowance has been recorded. The Company does not anticipate a significant change to its unrecognized tax benefits over the next twelve months. A reconciliation of the unrecognized tax benefits is as follows (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		
	2014	2013	2012
Unrecognized tax benefits as of the beginning of the year	$ 43	$ 5	$ —
Increase related to prior year tax provisions	272	7	—
Increase related to current year tax provisions	156	31	5
Unrecognized tax benefits as of the end of the year	$ 471	$ 43	$ 5

The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2014 and 2013, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive loss. There are no ongoing examinations by taxing authorities at this time.

14. Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share for the years ended December 31, 2014, 2013 and 2012 (in thousands, except per share data):

	FOR THE YEARS ENDED DECEMBER 31,		
	2014	2013	2012
Net loss	$ (25,404)	$ (5,276)	$ (1,811)
Deemed dividend	(3,230)	—	—
Net loss attributable to common stockholders	(28,634)	(5,276)	(1,811)
Weighted-average common shares outstanding used to calculate basic and diluted net loss per common share:			
Shares issued	11,651	3,673	3,673
Less: restricted stock subject to repurchase	—	—	(30)
Net shares outstanding	11,651	3,673	3,643
Basic and diluted net loss per common share	$ (2.46)	$ (1.44)	$ (0.50)

The following common stock equivalents outstanding at the end of the periods presented were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

(Shares in thousands)	AS OF DECEMBER 31,		
	2014	2013	2012
Options to purchase common stock	4,932	3,640	3,595
Warrants to purchase common stock	—	264	264
Series A preferred stock	—	3,899	1,789
Warrants to purchase preferred stock	—	55	55
	4,932	7,858	5,703

15. Selected Quarterly Financial Information (Unaudited)

The following amounts are in thousands, except per share amounts:

Quarterly Results of Operations	Quarter Ended			
	March 31, 2014	June 30, 2014	September 30, 2014	December 31, 2014
	(In thousands, except per share amounts)			
Revenue	$ 30	$ 135	$ 204	$ 203
Total operating expenses	$ (1,636)	$(4,588)	$ (8,144)	$ (10,606)
Net loss	$ (1,663)	$(5,094)	$ (8,256)	$ (10,391)
Deemed dividend (1)	$ —	$(3,230)	$ —	$ —
Net loss attributable to common stockholders	$ (1,663)	$(8,324)	$ (8,256)	$ (10,391)
Basic and diluted net loss per share	$ (0.45)	$ (2.27)	$ (0.50)	$ (0.46)

Quarterly Results of Operations	Quarter Ended			
	March 31, 2013	June 30, 2013	September 30, 2013	December 31, 2013
	(In thousands, except per share amounts)			
Revenue	$ 300	$ 150	$ 30	$ —
Total operating expenses	$ (342)	$ (855)	$ (808)	$ (1,929)
Net loss	$ (49)	$ (721)	$ (813)	$ (3,693)
Basic and diluted net loss per share	$ (0.01)	$ (0.20)	$ (0.22)	$ (1.01)

(1) In April 2014, we repurchased 531,208 shares of Series A convertible preferred stock for $4.0 million. The difference between the repurchase price of $7.53 per share and original issuance price of $1.45 per share was recorded as a deemed dividend of $3.2 million to a preferred stockholder and effected the calculation of net loss attributable to common stockholders and net loss per share for the year ended December 31, 2014.

Basic and diluted net loss per share is computed independently for each of the quarters presented. Therefore, the sum of quarterly basic and diluted per share amounts may not equal annual basic and diluted net loss per share amounts.

16. Subsequent Event

In January 2015, the Company completed a public offering of 2,369,375 shares of its common stock (Follow-on Offering), which includes 359,918 shares the Company issued pursuant to the underwriters' exercise of their option to purchase additional shares, and the Company received net proceeds of approximately $130.5 million, after underwriting discounts, commissions and estimated offering expenses.

EXHIBIT INDEX

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE			PROVIDED HEREWITH
		FORM	DATE	EXHIBIT NUMBER	
3.1	Amended and Restated Certificate of Incorporation.	8-K	August 6, 2014	3.1	
3.2	Amended and Restated Bylaws.	8-K	August 6, 2014	3.2	
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	Form of Common Stock Certificate.	S-1/A	July 25, 2014	4.1	
4.3	Amended and Restated Investor Rights Agreement, dated as of April 16, 2014, by and between Avalanche Biotechnologies, Inc. and certain of its stockholders.	S-1/A	July 18, 2014	4.5	
10.1†	Exclusive License for Use of Recombinant Gene Delivery Vectors for Treating or Preventing Diseases of the Eye, dated as of May 27, 2010, by and between Avalanche Biotechnologies, Inc. and The Regents of the University of California.	S-1/A	July 28, 2014	10.1	
10.2†	Amendment #1 to: Exclusive License for Use of Recombinant Gene Delivery Vectors for Treating or Preventing Diseases of the Eye, effective as of September 17, 2013, by and between Avalanche Biotechnologies, Inc. and The Regents of the University of California.	S-1	June 30, 2014	10.2	
10.3†	Research Collaboration and License Agreement, dated as of May 1, 2014, by and between Avalanche Biotechnologies, Inc. and Regeneron Pharmaceuticals, Inc.	S-1/A	July 28, 2014	10.3	
10.4(#)	Avalanche Biotechnologies, Inc. Amended and Restated 2006 Equity Incentive Plan.	S-1	June 30, 2014	10.4	
10.5(#)	Form of Stock Option Grant Notice and Stock Option Agreement under the Amended and Restated 2006 Equity Incentive Plan.	S-1/A	July 25, 2014	10.16	
10.6(#)	Avalanche Biotechnologies, Inc. 2014 Equity Incentive Award Plan.	S-1/A	July 25, 2014	10.5	
10.7(#)	Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan.	S-1/A	July 25, 2014	10.17	
10.8(#)	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2014 Equity Incentive Award Plan.	S-1/A	July 25, 2014	10.18	

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE			PROVIDED HEREWITH
		FORM	DATE	EXHIBIT NUMBER	
10.9(#)	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2014 Equity Incentive Award Plan.	S-1/A	July 25, 2014	10.19	
10.10(#)	Avalanche Biotechnologies, Inc. 2014 Employee Stock Purchase Plan.	S-1/A	July 25, 2014	10.6	
10.11(#)	Letter Agreement, dated as of September 18, 2010, by and between Avalanche Biotechnologies, Inc. and Thomas W. Chalberg, Jr., Ph.D.	S-1	June 30, 2014	10.7	
10.12(#)	Letter Agreement, dated as of April 2, 2014, by and between Avalanche Biotechnologies, Inc. and Linda C. Bain.	S-1	June 30, 2014	10.8	
10.13(#)	Letter Agreement, dated as of July 15, 2012, by and between Avalanche Biotechnologies, Inc. and Hans P. Hull.	S-1	June 30, 2014	10.9	
10.14(#)	Letter Agreement, dated as of June 3, 2013, by and between Avalanche Biotechnologies, Inc. and Mehdi Gasmi.	S-1	June 30, 2014	10.10	
10.15(#)	Letter Agreement, dated as of June 13, 2014, by and between Avalanche Biotechnologies, Inc. and Samuel Barone.	S-1	December [18], 2014	10.15	
10.16(#)	Letter Agreement, dated as of August 28, 2014, by and between Avalanche Biotechnologies, Inc. and Roman Rubio.	S-1	December [18], 2014	10.16	
10.17	Lease Agreement, dated as of December 20, 2013, by and between Avalanche Biotechnologies, Inc. and O'Brien Drive Portfolio, LLC.	S-1	June 30, 2014	10.11	
10.18	First Amendment to Lease, dated August 1, 2014, by and between O'Brien Drive Portfolio, LLC and Avalanche Biotechnologies, Inc.	8-K	September 12, 2014	10.1	
10.19	Second Amendment to Lease, dated October 30, 2014, by and between O'Brien Drive Portfolio, LLC and Avalanche Biotechnologies, Inc.	8-K	November 4, 2014	10.1	
10.19(#)	Form of Indemnification Agreement for directors and executive officers.	S-1/A	July 18, 2014	10.12	
10.20(#)	2012 Change in Control Benefit Plan.	S-1/A	July 18, 2014	10.13	
10.21(#)	Form of Change in Control Severance Agreement.	S-1/A	July 25, 2014	10.14	
10.22(#)	Form of Chief Executive Officer Change in Control Severance Agreement.	S-1/A	July 25, 2014	10.15	

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE			PROVIDED HEREWITH
		FORM	DATE	EXHIBIT NUMBER	
21.1	List of Subsidiaries.				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
24.1	Power of Attorney (included on signature page hereto)				X
31.1	Certification of Chief Executive Officer, as required by Rule 13a-14(a) or Rule 15d-14(a).				X
31.2	Certification of Chief Financial Officer, as required by Rule 13a-14(a) or Rule 15d-14(a).				X
32.1*	Certification by the Chief Executive Officer and Chief Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 36 of Title 18 of the United States Code (18 U.S.C. §1350).				X
101.INS	XBRL Instance Document.				X
101.SCH	XBRL Taxonomy Extension Schema Document.				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.				X

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

# Indicates management contract or compensatory plan.

* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Avalanche Biotechnologies, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

Exhibit 21.1

SUBSIDIARY OF AVALANCHE BIOTECHNOLOGIES, INC.

Name of Subsidiary	**Country of Incorporation**
Avalanche Australia PTY LTD	Australia

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-199296 on Form S-8 of our report dated March 5, 2015, relating to the consolidated financial statements of Avalanche Biotechnologies, Inc. and its subsidiary (the "Company"), appearing in this Annual Report on Form 10-K of the Company for the year ended December 31, 2014.

/s/ *DELOITTE & TOUCHE LLP*

San Jose, California
March 5, 2015

Exhibit 31.1

Certification of Chief Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Thomas W. Chalberg, Jr., Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Avalanche Biotechnologies, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined by Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

   a. All significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting, which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls over financial reporting.

Date: March 5, 2015

By: /s/ Thomas W. Chalberg, Jr., Ph.D.
Name: Thomas W. Chalberg, Jr., Ph.D.

Title: *President and Chief Executive Officer*

Exhibit 31.2

Certification of Chief Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Linda C. Bain, certify that:

1. I have reviewed this Annual Report on Form 10-K of Avalanche Biotechnologies, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined by Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

   a. All significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting, which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls over financial reporting.

Date: March 5, 2015

By: /s/ Linda C. Bain
Name: Linda C. Bain

Title: *Chief Financial Officer*

Exhibit 32.1

Certification Pursuant to
18 U.S.C. Section 1350,
as Adopted Pursuant to
Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report of Avalanche Biotechnologies, Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2014, as filed with the Securities and Exchange Commission (the "Report"), Thomas W. Chalberg, Jr., Ph.D., President and Chief Executive Officer of the Company and Linda C. Bain, Chief Financial Officer of the Company, respectively, do each hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- The information in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 5, 2015

By: /s/ Thomas W. Chalberg, Jr., Ph.D.
Name: Thomas W. Chalberg, Jr., Ph.D.

Title: *President and Chief Executive Officer*

By: /s/ Linda C. Bain
Name: Linda C. Bain

Title: *Chief Financial Officer*