ELEVEN BIOTHERAPEUTICS, INC.

FORM 10-K
(Annual Report)

Filed 03/25/16 for the Period Ending 12/31/15

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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2015
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 No. 001-36296

Eleven Biotherapeutics, Inc.
(Exact name of registrant as specified in its charter)

DELAWARE	**26-2025616**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
215 First Street, Suite 400 Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip code)**

Registrant's telephone number, including area code: (781) 461-1000

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 $0.001 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 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.

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 Exchange Act.): ☐ Yes ☒ No

As of June 30, 2015, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $12.1 million, based on the closing price of the registrant's common stock on June 30, 2015.

Number of outstanding shares of Common Stock as March 15, 2016 : 19,684,875

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2016 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future product research or development, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "goals," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our plans to research and develop our product candidates;
- the initiation and conduct of clinical trials, including the timing, cost, conduct and outcome of our clinical trials of EBI-031 for the treatment of diabetic macular edema and uveitis, including statements regarding the timing of the availability of, and the costs to obtain, top-line data from such trials, the timing of completion of and outcomes of such trials, and the timing of regulatory filings, including our planned investigational new drug application for EBI-031;
- our ability to successfully develop our product candidates and complete our planned clinical programs;
- results of early clinical studies or preclinical trials and whether they will be indicative of the results of future studies;
- expectations regarding regulatory approvals, including the requirements for marketing approval of EBI-031, the nature and timing of our future interactions with regulatory authorities and our ability to design, implement and complete registration trials acceptable to such regulatory authorities and sufficient to support applications for regulatory approvals;
- the timing of and our ability to obtain marketing approval of EBI-031 and our other product candidates, and the ability of EBI-031 and our other product candidates to meet existing or future regulatory standards;
- the potential advantages of EBI-031;
- our estimates regarding the potential market opportunity for EBI-031 and our other product candidates;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacture of EBI-031 and our other product candidates;
- our ability to enter into and successfully complete collaborations or in-license or acquire rights to other products, product candidates or technologies;
- our ability to obtain, maintain and protect our intellectual property for our technology and products;
- the rate and degree of market acceptance and clinical utility of our products;
- our estimates regarding expenses, future revenues, capital requirements and need for additional financing;
- the impact of governmental laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and our stockholders should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual

Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

PART I

Item 1. Business.

Overview

We are a preclinical stage biopharmaceutical company with a proprietary protein engineering platform, called AMP-Rx, that we apply to the discovery and development of protein therapeutics to treat diseases of the eye. Our therapeutic approach is based on the role of cytokines in diseases of the eye, our understanding of the structural biology of cytokines and our ability to rationally design and engineer proteins to modulate the effects of cytokines. Cytokines are cell signaling molecules found in the body that can have important inflammatory effects. Our most advanced product candidate, which is still in preclinical development, is EBI-031, which we designed, engineered and generated using our AMP-Rx platform and are developing as an intravitreal injection for diabetic macular edema, or DME, and uveitis. In 2015, we initiated the necessary chemistry, manufacturing and control, or CMC, development work and nonclinical safety studies of EBI-031 to support the submission of an investigational new drug application, or IND, to the United States Food and Drug Administration, or FDA. If the results of these efforts and our additional preclinical studies of EBI-031 are favorable, we intend to submit an IND for EBI-031 for the treatment of DME to the FDA in the first half of 2016 for the purpose of conducting clinical trials. We hold worldwide commercialization rights to EBI-031.

We believe cytokines play a major role in the pathology underlying many eye diseases and that protein therapeutics are an effective means of modulating the effects of cytokines in diseases of the eye. We have used our AMP-Rx platform to rationally design, engineer and generate a pipeline of innovative protein therapeutic candidates that target cytokines we believe are central to diseases of the eye. We are conducting research and development programs directed at ocular diseases, with a current focus on diseases of the back of the eye, such as DME and uveitis. Our EBI-031 program is based on the role that elevated levels of the inflammatory cytokine interleukin-6, or IL-6, plays in the initiation and maintenance of the inflammation and pain associated with DME and uveitis.

DME is characterized by an abnormal accumulation of fluid in the macula, the portion of the retina that provides the clearest and most detailed vision, due to leakage from blood vessels in the retina. According to the American Diabetes Association, DME is one of the most common causes of vision loss in the United States. In studies published in the peer reviewed journal *Ophthalmology* , IL-6 levels in the eye positively correlated with the severity of DME. According to a presentation at The Association for Research in Vision and Ophthalmology 2012 Annual Meeting, IL-6 levels in the eye positively correlated with resistance to therapies that target a protein called vascular endothelial growth factor, or VEGF. Anti-VEGF therapies are among the current standard of care for the treatment of DME.

We previously invested a significant portion of our efforts and financial resources in the development of our product candidate isunakinra (EBI-005) for the treatment of patients with dry eye disease and allergic conjunctivitis. Notwithstanding this significant investment, based on the negative results from our completed Phase 3 clinical trials in dry eye disease and allergic conjunctivitis, we do not plan to pursue further development of isunakinra.

Background

Until recently, ocular therapies generally have been developed based on a limited understanding of the biology underlying the initiation and maintenance of the disease state. As a result, many of the therapies for diseases of the eye were not the result of rational drug design, but instead were ophthalmic formulations of pharmaceuticals, that were originally developed and approved for non-ocular diseases, such as steroids and antihistamines. We believe this limited understanding of the biology of eye diseases impeded the discovery and development of innovative ophthalmic therapeutics.

Over the past 15 years, researchers have been developing a greater understanding of the key proteins and pathways involved in ocular disease. For instance, the understanding of the protein pathways involved in the retinal disease wet age-related macular degeneration, or wet AMD, has greatly expanded. Wet AMD is characterized by abnormal new blood vessel growth in the back of the eye. By studying the biological processes associated with this abnormal growth, researchers identified the key role that VEGF plays in the initiation and maintenance of wet AMD. This understanding then led to the successful development of VEGF-blockers, such as Lucentis® and Eylea®, as new treatments for wet AMD that have dramatically improved outcomes for many patients. The developers of these VEGF-blockers have created a multi-billion dollar ophthalmic drug market where none existed 10 years ago. We believe that we can apply similar advances in the understanding of other protein pathways involved in eye diseases to the discovery and development of new treatments for these diseases.

Our Approach

We apply a rational, biology-based approach to the discovery and development of novel protein therapeutics for patients suffering from eye diseases. Our therapeutic approach is based on the role of cytokines in diseases of the eye, our understanding of the structural biology of cytokines and our ability to rationally design and engineer proteins to modulate the effects of cytokines.

AMP-Rx is our proprietary platform that we use to design, engineer and generate novel protein therapies that modulate key molecular targets we believe are responsible for the initiation or maintenance of an ocular disease. We begin by analyzing the target and identifying the protein-based approaches we may use to modulate the target. We then generate protein candidates and model protein/target interactions to inform an iterative protein optimization technique. We use this process to modify protein drugs to meet design specifications for improved biological and drug-like properties. We believe that key advantages of the AMP-Rx platform are:

- *Broad applicability* . We can apply the AMP-Rx platform to select among most forms of protein therapeutics, including antibodies, enzymes, soluble receptors and signaling proteins, for the optimal approach to treatment.
- *Efficiency* . We use the AMP-Rx platform to optimize multiple properties of drug candidates simultaneously. We generally avoid the time-consuming approach of traditional protein drug discovery that involves sequential screening and selection of product characteristics.
- *Customized drug design* . We use the AMP-Rx platform to design and engineer therapeutics that incorporate a range of key pharmaceutical properties, such as rapid onset of effect, increased half-life and improved ocular surface retention.
- *Manufacturability of drug candidates* . We use the AMP-Rx platform to generate drug candidates that have favorable manufacturing characteristics, such as high production yield, improved solubility and thermal stability. We believe these characteristics will allow us to minimize costly or difficult production and purification processes.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing novel protein therapeutics to treat diseases of the eye. The key elements of our strategy in support of this goal are to:

- *Advance EBI-031 for the treatment of diabetic macular edema.* Our most advanced product candidate, which is still in preclinical development, is EBI-031, an optimized version of an anti-IL-6 antibody, for the treatment of DME. We are undertaking the necessary CMC development work and nonclinical safety studies to support the submission of an IND to the FDA. If the results of these efforts and our additional preclinical studies of EBI-031 are favorable, we intend to submit an IND in the first half of 2016 for the purpose of conducting clinical trials of EBI-031 for the treatment of DME.
- *Apply AMP-Rx platform to build a pipeline of product candidates for the treatment of eye diseases.* We use our AMP-Rx platform to rationally design, engineer and generate a pipeline of innovative protein therapeutic candidates that target cytokines that we believe are central to diseases of the eye. We have designed, engineered and generated EBI-031 and our other preclinical product candidate using our AMP-Rx platform. We plan to continue to apply our platform to expand our product pipeline.
- *Pursue collaborative and other strategic opportunities.* We have established a collaboration with ThromboGenics N.V., or ThromboGenics, a European based, publicly held biopharmaceutical company focused on developing and commercializing innovative ophthalmic medicines. In this collaboration, we applied our proprietary AMP-Rx platform to design, engineer and generate protein therapeutics that can modulate a specific novel pathway in retinal disease and that may have key pharmaceutical attributes. This collaboration provided us with funding for the specific program that was the subject of the collaboration and allowed us to apply our AMP-Rx platform to a product discovery effort we might not otherwise have pursued. We plan to evaluate opportunities to enter into other collaborations that may contribute to our ability to advance our product candidates and to progress concurrently a range of discovery and development programs. We also plan to evaluate opportunities to in-license or acquire the rights to other products, product candidates or technologies for the treatment of eye diseases.

Review of Strategic Alternatives

We are in the process of reviewing a range of strategic alternatives that could result in potential changes to our current business strategy and future operations. As part of this process, we are reviewing strategic alternatives with a goal to maximize shareholder value. We have engaged an investment bank to advise us in this process. As a result of this process, we could determine to:

- engage in one or more potential transactions, such as the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies; or
- continue to operate our business in accordance with our existing business strategy.

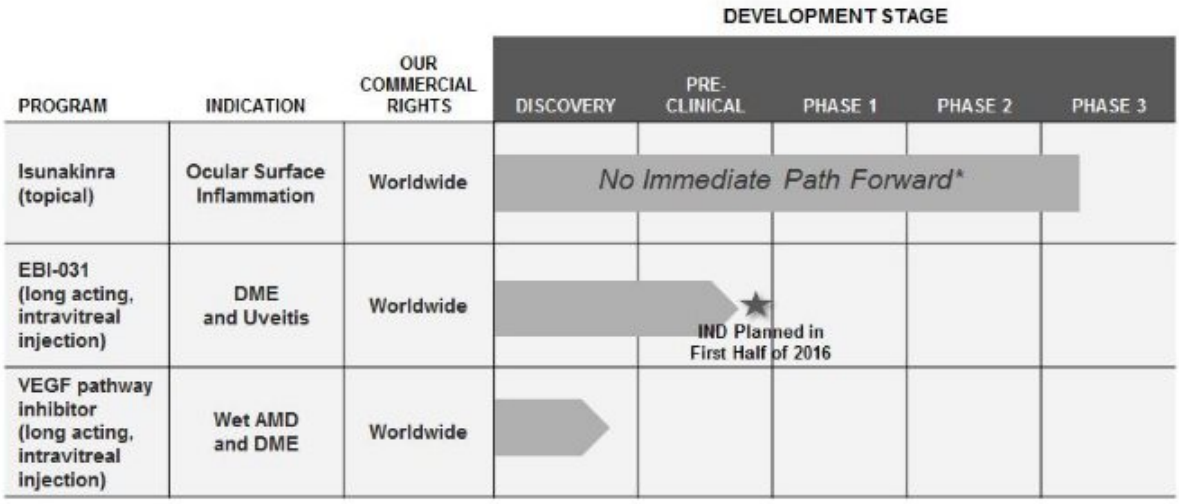
Pending any decision to change strategic direction, we are continuing our research and development activities in accordance with our existing business strategy while managing our cash position. We cannot provide any commitment regarding when or if this strategic review process will result in any type of transaction and no assurance can be given that we will determine to pursue a potential sale, strategic partnership or licensing arrangement.

Our Product Development Programs

We apply our proprietary AMP-Rx platform to the discovery and development of protein therapeutics to treat diseases of the eye. Our therapeutic approach is based on the role of cytokines in diseases of the eye, our understanding of the structural biology of cytokines and our ability to rationally design and engineer proteins to modulate the effects of cytokines. We have generated a product pipeline of innovative protein therapeutic candidates that address ocular diseases that are not well served by current therapies.

The following table summarizes key information about our product development programs.

Our Product Candidates



*Isunakinra (EBI-005) is a topically administered IL-1 receptor blocker which was in development for ocular surface inflammatory diseases but did not meet endpoints in two Phase 3 clinical trials.

EBI-031 – a Novel Inhibitor of the Cytokine IL-6

Our most advanced product candidate, which is still in preclinical development, is EBI-031. We designed and engineered EBI-031using our AMP-Rx platform to block two forms of IL-6: free IL-6 and IL-6 bound to soluble IL-6 receptor, or IL-6R. We believe the ability of EBI-031 to block these two forms of IL-6 will result in more effective inhibition of IL-6 activity

compared to other antibodies that block only one of these two forms of IL-6. We are developing EBI-031 as an intravitreal injection for DME and uveitis.

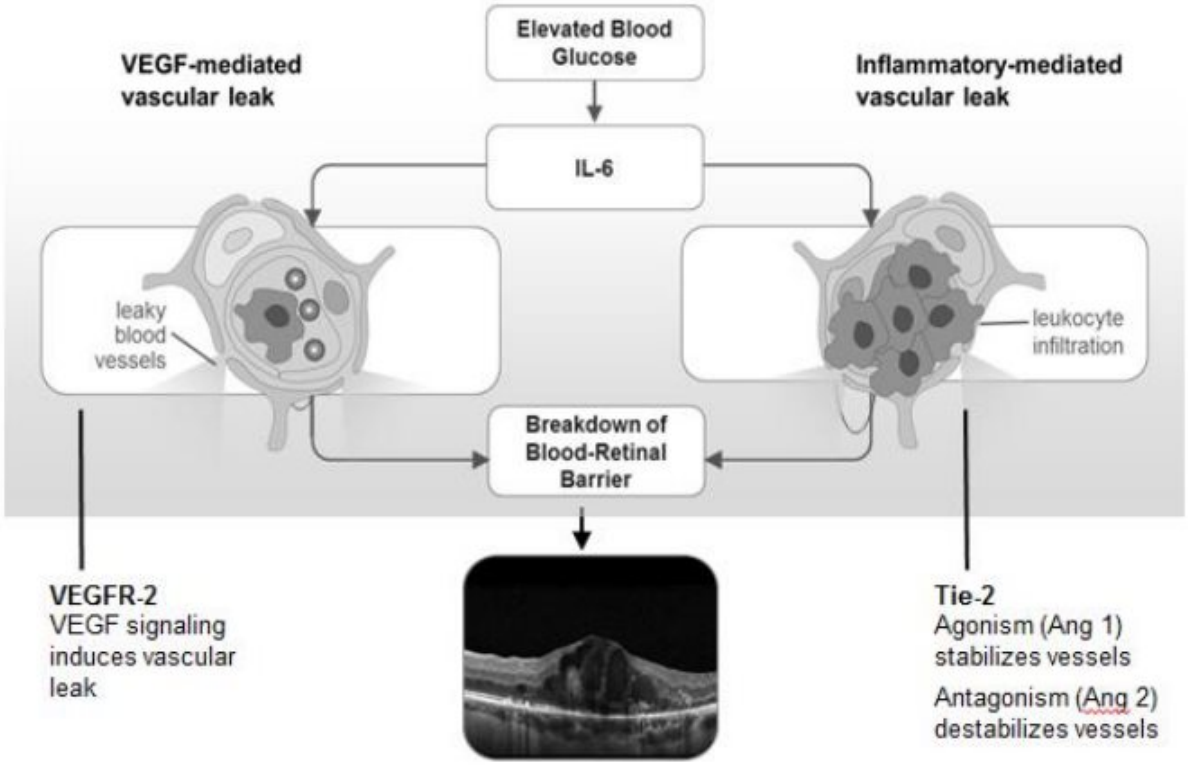
Diabetic Macular Edema

DME is characterized by an abnormal accumulation of fluid, in the macula, the portion of the retina that provides the clearest and most detailed vision, due to leakage from blood vessels in the retina. According to the American Diabetes Association, DME is one of the most common causes of vision loss in the United States. In studies published in the peer reviewed journal *Ophthalmology* , IL-6 levels in the eye positively correlated with the severity of DME. According to a presentation at The Association for Research in Vision and Ophthalmology 2012 Annual Meeting, IL-6 levels in the eye positively correlated with resistance to anti-VEGF therapies, which are among the current standard of care for the treatment of DME.

While the pathogenesis of DME is not completely understood, there is evidence that the blood vessel leakage, or vascular leak, associated with DME involves components of both angiogenesis, the physiological process through which new blood vessels form from pre-existing blood vessels, and inflammation. VEGF is likely a primary mediator of the “angiogenic” vascular leak as VEGF levels are significantly elevated in DME patients, and the disease is often successfully treated by VEGF blockade. There is also evidence that inflammation is a significant driver of DME as leukocyte infiltration, the abnormal intravascular aggregation and clumping of white blood cells, was observed in animal models and human subjects, and corticosteroids successfully reduce edema in many cases.

Several lines of evidence suggest that IL-6 is a key mediator of both VEGF-mediated and inflammatory vascular leak in DME, through either direct or indirect effects on the internal lining of blood vessels. First, IL-6 is significantly upregulated in the eyes of patients with DME and diabetic retinopathy and its concentration correlates with disease severity. Second, IL-6 promotes leukocyte infiltration in animal models by directly upregulating intercellular adhesion molecule 1, or ICAM-1, and monocyte chemotactic protein 1, or MCP-1, known pathways involved in inflamation. Third, IL-6 blockade reduces cystoid macular edema, an inflammatory edema in patients with uveitis that is often refractory to anti-VEGF therapy. Fourth, IL-6 directly upregulates VEGF *in vitro* and *in vivo* and blocking IL-6 signaling with tocilizumab, an anti-IL-6 receptor antibody, in rheumatoid arthritis patients reduces circulating VEGF levels to baseline. Fifth, systemic IL-6 blockade is efficacious in animal models of retinal inflammation and angiogenesis.

The figure below depicts the mechanisms by which IL-6 may play a central role in both directly and indirectly driving the macular edema associated with inflammatory eye diseases such as DME and uveitis. In diabetes, elevated glucose levels serve as a signal which results in the increased production of pro-inflammatory molecules, including IL-6. As described above, increased local and systemic levels of IL-6 can result in an increase in the levels of VEGF, which directly drives vascular leak by signaling through the VEGFR-2 receptor leading to macular edema, as is shown on the left side of the figure. The right side of the figure shows the pro-inflammatory activity of IL-6 and the potential effect on vascular leak, both through the direct mechanism of recruiting inflammatory cells that can destabilize vessel walls leading to edema, as well as destabilizing vessel walls by increasing the activity of a molecule known as angiopoeitin-2, or Ang 2, which antagonizes the receptor Tie-2's signaling through the stabilizing molecule angiopoeitin-1, or Ang 1.

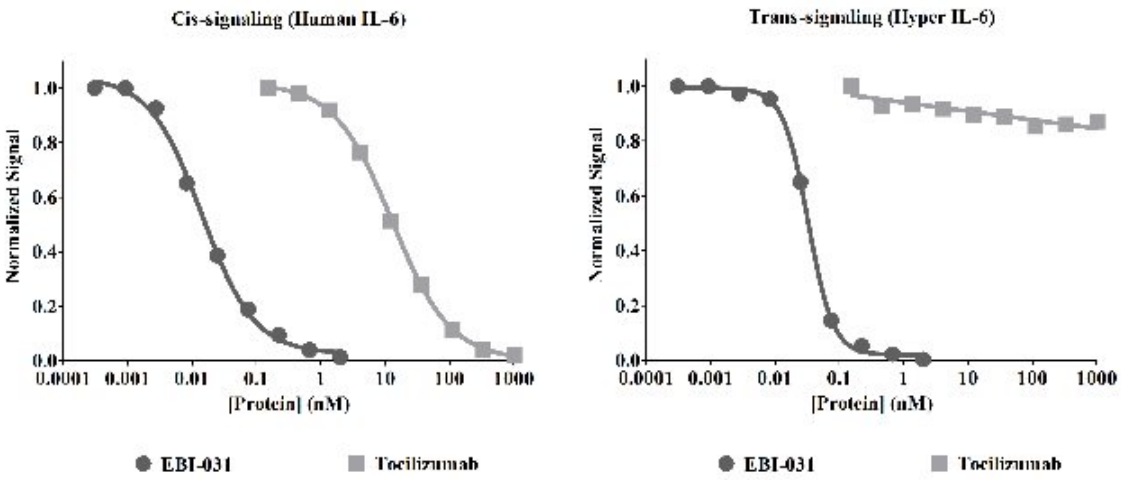


Uveitis

Uveitis is a heterogeneous group of ocular conditions that are characterized by inflammation of the middle layer of the eye known as the uvea. Based on prevalence data published in the peer reviewed journal *American Journal of Ophthalmology* and 2010 United States census data, we estimate that approximately 215,000 to 315,000 individuals in the United States suffer from some form of uveitis. According to the peer reviewed journal *British Journal of Ophthalmology* , uveitis also accounts for approximately 10% to 15% of cases of blindness in the United States. According to a poster presented by a group from Barcelona, Spain at the Association for Research in Vision and Ophthalmology 2015 Annual Meeting, the IL-6 receptor inhibitor, tocilizumab, administered systemically led to suppression of uveitis and macular edema in the back of the eye of patients whose disease had been refractory to previous treatments. We believe that IL-6 inhibition could be an effective target for treating uveitis and its associated macular edema.

Preclinical Studies

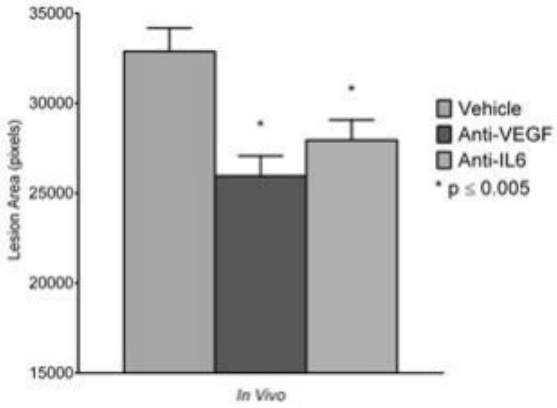
The graphs below illustrate the blocking of IL-6 signaling in an *in vitro* cell-based assay by increasing concentrations of EBI-031 that blocked IL-6 and of a reference anti-IL-6R antibody, tocilizumab, that it also blocked IL-6 signaling. In contrast, tocilizumab blocked signaling of free IL-6 (referred to as cis-signaling, left panel) but did not block signaling of IL-6 bound to soluble IL-6R (referred to as trans signaling, right panel).



In order to test the effects of an anti-IL-6 antibody in an animal model, we used a rat model of choroidal neovascularization, or CNV. CNV is abnormal new blood vessel formation and growth in the layer of tissue beneath the retina called the choroid. This CNV model uses a laser beam to damage part of the eye near the retina, resulting in an inflammatory and vascular response that we believe is useful for studying the retinal inflammation that occurs in association with DME. CNV is measured by the size of an area of increased blood vessel growth, or an angiogenic area, at 22 days after laser, or day 22. An active treatment in the CNV model reduces the size of the angiogenic area.

We are unable to test EBI-031 directly in this rat model because EBI-031 only blocks human and non-human primate IL-6. In the rat model of CNV, we used a commercially available goat anti-IL-6 antibody that blocks rat IL-6 as a surrogate for EBI-031. This study compared the goat anti-IL-6 antibody to a goat anti-VEGF antibody that blocks rat VEGF. In this study, we observed a significant reduction in the angiogenic area at day 22 in animals treated with the goat anti-IL-6 antibody compared to animals that received no treatment. The reduction in the angiogenic area at day 22 in rats treated with the goat anti-IL-6 antibody was comparable to the reduction in angiogenic area observed in rats treated with the goat anti-VEGF antibody.

The figure below presents the reduction in angiogenic area observed at day 22 in rats treated with vehicle, goat anti-VEGF antibody and goat anti-IL-6 antibody. The difference in angiogenic area between rats treated with goat anti-VEGF antibody and vehicle was statistically significant (p=0.0003). The difference in angiogenic area between rats treated with the goat anti-IL-6 antibody and vehicle also was statistically significant (p=0.0005). As the CNV model is a model for inflammation, we believe that this model suggests IL-6 inhibition may reduce the inflammation associated with DME.



We believe that a significant shortcoming of current treatments of DME is the need for frequent injections of the therapeutic agent, typically anti-VEGF therapy, into the eye. We compared the half-life of EBI-031 to aflibercept, marketed under the

trademark Eylea, and tocilizumab, marketed under the trademark Actemra, in a standard rabbit model of pharmacokinetics of intravitreal agents. Aflibercept is an anti-VEGF agent approved for the treatment of DME. Anti-VEGF therapies are the standard of care for the treatment of DME.

The table below shows that EBI-031 remained in the vitreous, the gel-filled center of the eye, nearly twice as long as aflibercept and twice as long as tocilizumab. We believe that the longer half-life, or $T_{1/2}$, of EBI-031 in the vitreous compared to aflibercept may lead to less frequent injections of EBI-031 than current treatment regimens with aflibercept.

Agent	$T_{1/2}$ (days)
EBI-031	10
aflibercept	6
tocilizumab	5

We have also demonstrated the half-life of EBI-031 in the vitreous in a non-human primate study to be approximately 5 days. This compares with historical studies which demonstrated vitreous half-life of anti-VEGF agents to be approximately 2-4 days.

We have also engineered EBI-031 to be cleared more rapidly from systemic circulation than most antibodies approved for systemic administration in humans. We believe that more rapid clearance from the systemic circulation of an antibody that transits from the eye lowers systemic exposure, which could reduce the risk of side-effects.

Our Other Product Candidate

In addition to EBI-031, we have another proprietary product candidate in early preclinical development which is designed to block VEGF. We are developing this product candidate as an intravitreal injection for the treatment of certain retinal diseases, such as wet AMD. We have engineered a series of recombinant VEGF blockers in a manner that we believe could result in longer intravitreal retention. We are initiating animal studies to evaluate the pharmacology of these candidate VEGF blockers.

We believe there is substantial unmet medical need to reduce the frequency of intravitreal injections of VEGF inhibitors in the treatment of wet AMD, DME, and other posterior eye vascular disorders. Currently, treatments for wet AMD frequently require monthly intravitreal administration, and even when administered as needed, a patient may require an average of seven to eight injections per year. Our goal is to develop a long-acting VEGF pathway blocker that requires four or fewer intravitreal injections per year once the required initial doses are given to address the disease.

In part leveraging the increasing understanding of the long intravitreal half-life of EBI-031 in rabbit studies, we believe we can utilize similar approaches to create long-lasting VEGF pathway blockers.

In addition to this product candidate and EBI-031, we are continuing to apply our AMP-Rx platform to generate new product candidates.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our candidate products, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other things, filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of March 15, 2016 , we owned or exclusively in-licensed a total of 14 families of patent applications. As of March 15, 2016 , our patent portfolio includes the following patents and applications that we own or, where noted below, license:

- a Patent Cooperation Treaty, or PCT, patent application covering the IL-6 antibody EBI-031, which, if granted, is expected to expire in 2035;
- a United States provisional application covering the IL-6 antibody EBI-031 formulation, which, if converted to a nonprovisional application and if granted, is expected to expire in 2036;

- a United States, a New Zealand, and a South Africa composition-of-matter patent covering isunakinra which expires in 2031;
- composition-of-matter patent applications covering isunakinra in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Korea, Mexico, Russia, Singapore, and Taiwan, which, if granted, are expected to expire in 2031;
- patent applications covering the formulation of isunakinra filed in the United States, Australia, Brazil, Canada, China, Europe, India, Japan, Mexico, New Zealand, Russia, Singapore, and South Africa, which, if granted, are expected to expire in 2034;
- patent applications covering methods of manufacturing isunakinra filed in the United States, Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Russia and Singapore, which, if granted are expected to expire in 2032;
- a European patent and pending applications licensed from The Schepens Eye Research Institute, Inc., or Schepens, pursuant to a license that terminates effective April 12, 2016; the Schepens applications are pending in the United States, Australia, Canada and Japan, and, if granted, are expected to expire in 2030; the Schepens applications cover the use of IL-1 inhibitors to treat certain ocular diseases;
- patent applications covering IL-6 antibody EBI-029, a precursor of EBI-031, filed in the United States, Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Korean, Mexico, New Zealand, Russia, Singapore, and South Africa, which, if granted, are expected to expire in 2033; and
- a PCT patent application covering methods and compositions for increasing the retention of therapeutic agents in the eye which, if granted, is expected to expire in 2035.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates, including EBI-031, receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. The expiration dates referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by 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.

Collaboration and License Agreement with ThromboGenics, N.V.

In May 2013, we entered into a collaboration and license agreement with ThromboGenics. Under the agreement, we and ThromboGenics are collaborating to identify protein or peptide therapeutics that directly modulate any of a specified set of targets in a novel pathway in retinal disease. We call the therapeutics that are identified, and whose modulation of one of the targets is confirmed, in the course of the collaboration, collaboration products.

During the term of the agreement, neither we nor ThromboGenics, nor our respective affiliates other than any entities which become affiliates as a result of an acquisition of us or ThromboGenics, are permitted to research, develop, manufacture or commercialize any protein or peptide therapeutic that directly modulates one of the specified targets, except as otherwise provided in the agreement.

Research and Development Obligations . The initial research term is for a specified number of months from the date we entered into the agreement, but may be extended on mutual agreement. The research is conducted in accordance with a mutually agreed plan and budget. We are responsible for specified non-clinical activities during the research term. ThromboGenics is responsible for all development, manufacturing and commercialization activities with respect to the collaboration products. ThromboGenics is obligated to use commercially reasonable efforts to research, develop and obtain all necessary regulatory approvals for the collaboration products and, upon receipt of the applicable marketing approval, to commercialize the collaboration products. The initial research term concluded in November 2015. However the parties have agreed to continue the existing Collaboration and License Agreement to provide us the time required to complete additional research activities for no additional consideration. We expect the relevant data to become available in the second quarter of 2016. To date, no collaboration products have been identified.

Intellectual Property . We and ThromboGenics jointly own any know-how made by or on behalf of either of us in the course of the research and any patent rights claiming such know-how. We call these patent rights and know-how collaboration intellectual property. We have granted ThromboGenics an exclusive, sublicenseable, royalty-bearing license under our rights in these patent rights and know-how, as well as under any other patent rights and know-how that we control during the research term that are necessary for ThromboGenics to perform its obligations to research, develop, manufacture and commercialize collaboration products.

Financial Terms . In connection with the agreement, ThromboGenics paid us a technology licensing fee of $1,750,000 and is obligated to pay us to perform our activities under the agreement at a set rate per full-time equivalent person working on the collaboration. ThromboGenics also is obligated to make future payments to us of up to an aggregate of $10,000,000 if ThromboGenics achieves specified preclinical and clinical milestones with respect to collaboration products and up to an aggregate of $15,000,000 if ThromboGenics achieves specified regulatory milestones with respect to collaboration products. ThromboGenics is obligated to pay us a low single digit royalty on sales of collaboration products by ThromboGenics, its affiliates or sublicensees. These royalties may be reduced in specified circumstances. ThromboGenics' obligation to pay us royalties will expire on a collaboration product-by-collaboration product and country-by-country basis on the latest of ten years after the first commercial sale of such compound in such country, the expiration of the patent rights we licensed to ThromboGenics that cover such compound in such country, and the expiration of any data or other regulatory exclusivity for such compound in such country, after which the licenses granted to ThromboGenics will become perpetual and fully paid-up.

Term and Termination . The agreement expires when all of ThromboGenics' payment obligations expire. The agreement provides that either party may terminate the agreement in the event of the other party's insolvency, bankruptcy or comparable proceedings, or if the other party materially breaches the agreement and does not cure such breach during a specified cure period. We may terminate the agreement if ThromboGenics or any of its affiliates or licensees challenges the patent rights that we licensed to ThromboGenics. The agreement may be terminated by ThromboGenics for convenience by giving us a specified period of notice following the end of the research term. If ThromboGenics terminates the agreement for our breach or bankruptcy, ThromboGenics' diligence obligations will terminate, the licenses we granted to ThromboGenics will remain in effect on a perpetual basis, and all milestone and royalty obligations of ThromboGenics will be reduced by a specified percentage.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical quantities of EBI-031 or any other of our product candidates. We currently rely, and expect to continue to rely, on third parties for the manufacture of EBI-031 and our other product candidates. We have personnel with the experience to manage the third-party contract manufacturers producing EBI-031 and other products that we may develop in the future. The process for manufacturing EBI-031 has two main stages: drug substance manufacturing and drug product manufacturing, which results in our finished drug product. We currently engage a single third-party manufacturer to provide drug substance of EBI-031 and a second single third-party manufacturer to provide drug product of EBI-031. We obtain these supplies and services on a purchase order basis. The drug substance manufacturing process utilizes a well-established expression system for recombinant protein therapeutics and includes downstream purification steps using readily available materials. The drug product manufacturing process utilizes our proprietary formulation, is conducted with materials that have been utilized in other approved ophthalmic products, and is configured in a single-use glass vial that has also been used for other intravitreal ocular therapeutic products. The manufacturing process and drug product formulation are proprietary to us and were transferred to third-party vendors for the execution of manufacturing.

Commercialization

In light of our stage of development, we have not yet established a commercial organization or distribution capabilities. We generally expect to retain commercial rights in the United States for our product candidates for which we may receive marketing approvals and which we believe we can commercialize through a focused, specialty sales force. We expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize EBI-031 and any other products that we develop in markets outside the United States.

We hold worldwide commercialization rights to EBI-031. We believe that specialists in the United States who treat most of DME patients are sufficiently concentrated that if EBI-031 receives marketing approval in the United States we could effectively promote EBI-031 to these specialists with a specialty sales and marketing group. Therefore, we may decide to build our own focused, specialty sales force in order to commercialize EBI-031 in the United States. We intend to enter into strategic collaborations for the development and commercialization of EBI-031 outside of the United States.

We also plan to build key capabilities, such as marketing, market access, sales management and medical affairs, to implement marketing and medical strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with thought leaders in relevant fields of medicine.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our potential competitors include large pharmaceutical and biotechnology companies, and specialty pharmaceutical and generic drug companies. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of each of our product candidates, if approved for marketing, are likely to be its efficacy, safety, method of administration, convenience, price, the level of generic competition and the availability of coverage and adequate reimbursement from government and other third-party payors.

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, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. Generic products are currently being used for the indications that we may pursue, and additional products are expected to become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state, and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Licensure of Biologics in the United States

In the United States, the FDA regulates biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug, and Cosmetic Act, or FDCA, and regulations and guidances implementing these laws. The failure to comply with the PHSA, FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other federal and state governmental entities.

An applicant seeking approval to market and distribute a new biologic product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed product for each indication;
- preparation and submission of a BLA to the FDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable; satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the BLA and licensure of the new biologic product; and
- compliance with any post-approval requirements, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and any post-approval studies required by the FDA.

Preclinical Studies and an IND

Preclinical studies include laboratory evaluation of the purity and stability of the biologic product, as well as *in vitro* and animal studies to assess the safety and activity of the product for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive toxicology and carcinogenicity, may continue after the IND is submitted.

Human Clinical Studies in Support of a BLA

Clinical trials involve the administration of the investigational biologic product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, and the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new biologic that is not the subject of an approved BLA. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA

raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

In addition to the foregoing requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with the FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institute of Health for public dissemination on their ClinicalTrials.gov website. These requirements are subject to specific timelines and apply to most controlled clinical trials of FDA-regulated products.

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

Phase 1:	The biologic product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
Phase 2:	The biologic product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
Phase 3:	The biologic product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Post-approval studies may also be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the biologic; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biologic has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted in a BLA.

Submission of a BLA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of a BLA requesting licensure of the biologic product for one or more indications. Under federal law, the submission of most BLAs is additionally subject to an application user fee, currently exceeding $2.3 million, and the sponsor of an approved BLA is also subject to annual product and establishment user fees, currently exceeding $114,000 per product and $585,000 per establishment. These fees are typically increased annually. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for biologics with orphan designation and a waiver for certain small businesses, and an exception from the establishment fee when the establishment does not engage in manufacturing during a particular fiscal year.

The FDA conducts a preliminary review of a BLA within 60 days of its receipt and informs the sponsor by the 74 th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept a BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for

filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of BLAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

The FDA may also refer an application for a biologic product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Compliance with cGMP Requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

Manufacturers and others involved in the manufacture and distribution of biologic products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a biologic being deemed to be adulterated.

FDA's Decision on a BLA

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure and potent.

On the basis of the FDA's evaluation of the BLA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the biologic product with detailed prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a new biologic product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the biologic outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and

distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

A biologic product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of biological products.

In addition, manufacturers and other entities involved in the manufacture and distribution of approved biologics are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA may withdraw the license for a biologic if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with the manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending BLAs or supplements to approved BLAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. That Act established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, one biosimilar product has been approved by the FDA for use in the United States. No interchangeable biosimilars have been licensed under the BPCIA. The FDA has issued several draft guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by FDA in the near term.

Under the Act, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a biologic product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biologic product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting a BLA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product will be entitled to orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the date of review of any application for marketing approval of the product. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is an additional type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan product exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve a biosimilar application.

Patent Term Restoration and Extension

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of a BLA, plus the time between the submission date of a BLA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Biologics in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the European Union

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, or GCP, an applicant must obtain approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than May 28, 2016. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization in the European Union

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active

substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic, or abbreviated, application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company can complete a full MAA with a complete database of pharmaceutical test, preclinical tests and clinical trials and obtain marketing approval of its product.

Orphan Drug Designation and Exclusivity in the European Union

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of: (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the product is safer, more effective or otherwise clinically superior to the original orphan medicinal

product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e.,

arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment

centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, ficticious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully for executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Business Segment and Geographical Information

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

Employees

At December 31, 2015 , we had 19 full-time employees and one part-time employee, including a total of 12 with M.D. or Ph.D. degrees. Of these employees, 13 employees are engaged in research and development activities and seven employees are engaged in finance, business development, legal, human resources, facilities and general management. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relations with our employees to be good.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2008. We were formerly known as Denovo Therapeutics, Inc. and Newco LS14, Inc. before changing our name to Eleven Biotherapeutics, Inc. Our principal executive offices are located at 215 First Street, Suite 400, Cambridge, Massachusetts 02142, and our telephone number is (617) 871-9911.

Available Information

We maintain an internet website at www.elevenbio.com and make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. You can find, copy and inspect information we file at the SEC’s public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC’s public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC’s web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only.

Item 1A. Risk Factors

Risks Related to Our Financial Position and Need For Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $33.5 million for the year ended December 31, 2015 , $34.2 million for the year ended December 31, 2014 and $18.0 million for the year ended December 31, 2013. As of December 31, 2015 , we had an accumulated deficit of $125.2 million . To date, we have financed our operations primarily through private placements of our common stock and preferred stock and convertible bridge notes, venture debt borrowings and our initial public offering, or IPO, sales effected in an "at the market" offering through our agent, Cowen and Company, LLC, and, to a lesser extent, from a collaboration. All of our revenue to date has been collaboration revenue, which we first began to generate in 2013. We have devoted substantially all of our financial resources and efforts to research and development activities. We are still in the early stages of development of our product candidates, and we have not completed development of any drugs. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year.

We anticipate that we will continue to incur substantial expenses in connection with the advancement of our preclinical product candidate, EBI-031, including the expenses associated with our planned submission of an investigational new drug application, or IND, for EBI-031 for the treatment of diabetic macular edema, or DME, in the first half of 2016 and our planned initiation of clinical trials of EBI-031 for the treatment of DME.

We will also incur substantial expenses if and as we:

- pursue the development of EBI-031 for additional indications, such as uveitis, or for use in other patient populations or, if it is approved, seek to broaden the label for EBI-031;
- continue the research and development of our other preclinical product candidates;
- seek to discover and develop additional product candidates;
- in-license or acquire the rights to other products, product candidates or technologies for the treatment of ophthalmic diseases;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish sales, marketing and distribution capabilities and scale up and validate external manufacturing capabilities to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific and management personnel;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and planned future commercialization efforts and our operations as a public company; and
- increase our insurance coverage as we commence clinical trials and potentially commercialize EBI-031.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase substantially if:

- we are required by the United States Food and Drug Administration, or FDA, or the European Medicine Agency, or EMA, to perform studies in addition to those currently expected; or
- if there are any delays in enrollment of patients in, or completing our clinical trials or the development of EBI-031 or any other product candidates that we may develop.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, EBI-031. This will require us to be successful in a range of challenging activities, including:

- submitting an IND and commencing clinical development for EBI-031;

- completing clinical development of EBI-031 in patients with DME, uveitis, or other indications;
- subject to obtaining favorable results from clinical trials, applying for and obtaining marketing approvals for EBI-031;
- establishing sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties, to effectively market and sell EBI-031;
- achieving an adequate level of market acceptance of EBI-031;
- protecting our rights to our intellectual property portfolio related to EBI-031; and
- ensuring the manufacture of commercial quantities of EBI-031.

We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

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

We expect to devote substantial financial resources to our ongoing and planned activities, particularly initiating and completing clinical development of EBI-031 for the treatment of DME, uveitis or other indications and, if successful, seeking marketing approval for EBI-031. We also expect to devote additional financial resources to functions associated with operating as a public company. We also may devote additional financial resources to conducting research and development, if we determine to proceed into clinical development, initiating clinical trials of, and seeking regulatory approval for, our other product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we would need to devote substantial financial resources to commercialization efforts, including product manufacturing, marketing, sales and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

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

- the progress, costs and outcome of clinical development of EBI-031 for the treatment of DME and uveitis;
- the costs and timing of process development and manufacturing scale up and validation activities associated with EBI-031;
- the costs, timing and outcome of regulatory review of EBI-031 in the United States, the European Union and in other jurisdictions;
- the costs and timing of commercialization activities for EBI-031 if we receive, or expect to receive, marketing approval, including the costs and timing of establishing product sales, marketing, distribution and outsourced manufacturing capabilities;
- subject to receipt of marketing approval, the amount of revenue received from commercial sales of EBI-031;
- the progress, costs and outcome of developing EBI-031 for the treatment of additional indications or for use in other patient populations;
- our ability to establish collaborations on favorable terms, if at all, particularly manufacturing, marketing and distribution arrangements for our product candidates;
- the scope, progress, results and costs of preclinical development, laboratory testing and, if we determine to proceed into clinical development, clinical trials of our other product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we in-license or acquire rights to other products, product candidates or technologies for the treatment of ophthalmic diseases.

As of December 31, 2015 , we had cash and cash equivalents of $36.1 million . In March 2016, we prepaid all outstanding amounts and fees under a loan and security agreement with Silicon Valley Bank, in an amount equal to approximately $14.9 million. We believe that our current cash and cash equivalents will be sufficient to fund our operating expenses into the fourth quarter of 2016. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. We are planning to spend significant funds to advance our preclinical development of EBI-031, including costs associated with the submission of an IND and the initiation of clinical trials of EBI-031 for the treatment of DME. At this time we cannot reasonably estimate the remaining costs necessary to complete clinical development to evaluate the safety and efficacy of EBI-031 for the treatment of DME, uveitis or any other indication or to complete the development of any other product candidate.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. Our commercial revenues, if any, will be derived from sales of EBI-031 or any other products that we successfully develop, none of which we expect to be commercially available for many years, if at all. In addition, if approved, EBI-031 or any other product candidate that we develop or any product that we in-license may not achieve commercial success. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in this Annual Report on Form 10-K.

Our report from our independent registered public accounting firm for the year ended December 31, 2015 includes an explanatory paragraph stating that our losses from operations and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding, collaborations, strategic alliances, licensing arrangements and marketing and distribution arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as holders of our common stock. For example, in December 2014, we issued and sold in a private placement an aggregate of 1,743,680 shares of our common stock, plus warrants to purchase a total of 871,840 additional shares of common stock, which resulted in dilution to our existing stockholders. Additionally, since April 2015, we have issued and sold 1,446,781 shares of our common stock in "at the market" offerings, which resulted in dilution to our existing stockholders.

Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our pledge of specified assets as collateral to secure our obligations under our existing loan and security agreement with Silicon Valley Bank may limit our ability to obtain additional debt financing.

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

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

We are an early-stage company. We were incorporated and commenced active operations in early 2008, and our operations to date have been limited to organizing and staffing our company, acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials. All of our product candidates which we are currently pursuing are still in preclinical development. We have not yet demonstrated our ability to successfully complete clinical development of any product candidate, obtain marketing approvals, manufacture at commercial scale, or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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

We expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We are considering alternatives to our current business strategy that could significantly impact our future operations and financial position.

We are in the process of reviewing a range of strategic alternatives that could result in potential changes to our current business strategy and future operations. As part of this process, we are reviewing alternatives with a goal of maximizing shareholder value. We have engaged an investment bank to advise us in this process. As a result of this process, we could determine to engage in one or more potential transactions, such as the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies, or to continue to operate our business in accordance with our existing business strategy. Pending any decision to change strategic direction, we are continuing our research and development activities in accordance with our existing business strategy while managing our cash position. We cannot provide any commitment regarding when or if this strategic review process will result in any type of transaction and no assurance can be given that we will determine to pursue a potential sale, strategic partnership or licensing arrangement. If we determine to pursue an alternative strategy or engage in a strategic transaction, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management. Because of the significant uncertainty regarding our future plans, we are not able to accurately predict the impact of a potential change in our existing business strategy.

Risks Related to the Discovery and Development of Our Product Candidates

We depend heavily on the success of EBI-031, our most advanced product candidate, which is still in preclinical development. If we are unable to successfully commence and complete our planned clinical program and obtain marketing approvals for EBI-031, or experience significant delays in doing so, or if after obtaining marketing approvals, we fail to commercialize EBI-031, our business will be materially harmed.

We are in the early stages of development of EBI-031. We plan to submit an IND for EBI-031 for the treatment of DME in the first half of 2016 to enable us to initiate clinical development of this product candidate.

The success of EBI-031 will depend on several factors, including the following:

- submitting an IND and commencing clinical development for EBI-031;
- completing clinical development of EBI-031 in patients with DME, uveitis or other indications;
- subject to obtaining favorable results from clinical trials, applying for and obtaining marketing approvals for EBI-031;
- establishing sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties, to effectively market and sell EBI-031;

- making arrangements with third-party manufacturers for commercial quantities of EBI-031 and receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities;
- acceptance of EBI-031, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies, including the existing standard of care;
- maintaining a continued acceptable safety profile of EBI-031 following approval;
- obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity; and
- protecting our rights in our intellectual property portfolio related to EBI-031.

Successful development of EBI-031 for use in broader patient populations and our ability, if it is approved, to broaden the label for EBI-031 will depend on similar factors. If we 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 successfully commercialize EBI-031, which would materially harm our business.

If clinical trials of EBI-031 or any other product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be delayed or unable to complete, the development and commercialization of EBI-031 or any other product candidate.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, including EBI-031, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans . Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome . A failure of one or more clinical trials can occur at any stage of testing . The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results . Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. For example, in May 2015, we announced top-line results from our Phase 3 clinical trial of our product candidate isunakinra in patients with moderate to severe dry eye disease. In this trial, there was no statistically significant difference between the isunakinra treated group and the vehicle control group on the co-primary endpoints. In addition, there were no statistically significant differences between the isunakinra treated group and the vehicle treated group on any secondary endpoints. Additionally, in January 2016, we announced top-line results from our Phase 3 clinical trial of isunakinra in patients with severe allergic conjunctivitis. In this trial, there was no statistically significant difference between the isunakinra treated group and the vehicle control group on the primary endpoint of ocular itching or on any secondary endpoints.

We may not conduct clinical trials of EBI-031 in the United States until we submit an IND to the FDA. We plan to submit an IND for EBI-031 for the treatment of DME in the first half of 2016.

Our prior clinical development efforts of isunakinra for the treatment of patients with dry eye disease and allergic conjunctivitis were not successful. We expended significant resources to pursue development of this product candidate and may in the future expend our limited resources to pursue development of a particular product candidate or indication and fail to capitalize on product candidates or indications that have a greater likelihood of clinical success or commercial potential.

We previously invested a significant portion of our efforts and financial resources in the development of isunakinra for the treatment of patients with dry eye disease and allergic conjunctivitis. Notwithstanding this significant investment, based on the results from our completed Phase 3 clinical trials in dry eye disease and allergic conjunctivitis, we do not plan to pursue further development of isunakinra.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater likelihood of clinical success or commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on research and development programs and product candidates for specific indications may not yield any commercially viable products. In addition, if we do not accurately evaluate the commercial potential or target market for a

particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize EBI-031 or any other product candidates that we may develop, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may decide, or regulators or institutional review boards may require us, to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not favorable or are only modestly favorable or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for EBI-031 or our other product candidates that we may develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In addition, some of our competitors have ongoing clinical trials for

product candidates that treat the same indications as EBI-031, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse or unacceptable side effects are identified during the development of EBI-031 or any other product candidates that we may develop, we may need to abandon or limit our development of EBI-031 or such other product candidates.

If EBI-031 or any of our other product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. We have no clinical safety data on human exposure to EBI-031. Many compounds that initially showed promise in clinical or early stage testing for treating ophthalmic disease have later been found to cause side effects that prevented further development of the compound.

We may not be successful in our efforts to use our AMP-Rx platform to build a pipeline of product candidates.

A key element of our strategy has been to use our proprietary AMP-Rx platform to rationally design, engineer and generate a pipeline of novel protein therapies and progress these therapies through clinical development for the treatment of a variety of ophthalmic diseases. Our research and development efforts to date have resulted in a pipeline of additional product candidates directed at the treatment of ophthalmic diseases. All of the product candidates which we are currently pursuing are in early preclinical research and have not been tested in humans. These and any other potential product candidates that we identify may not be suitable for continued preclinical or clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize our product candidates that we develop based upon our technological approach, we will not be able to obtain product revenues in future periods.

Risks Related to the Commercialization of Our Product Candidates

Even if EBI-031 or any other product candidate that we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for EBI-031 may be smaller than we estimate.

If EBI-031 or any other product candidate that we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Current treatments that are used for DME and uveitis include blockers of a protein called vascular endothelial growth factor, or VEGF, and low cost, off-label use of corticosteroids. These treatments are well established in the medical community, and doctors may continue to rely on these treatments rather than EBI-031, if and when it is approved for marketing by the FDA. As a result, healthcare professionals and third-party payors may choose to rely on such products rather than EBI-031. If EBI-031 does not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of EBI-031 or any other product candidate that we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments, including the existing standard of care;
- our ability to offer our products for sale at competitive prices, particularly in light of the lower cost of alternative treatments;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

Our assessment of the potential market opportunity for EBI-031 is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. If the actual market for EBI-031 is smaller than we expect, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to establish sales, marketing and distribution capabilities, we may not be successful in commercializing EBI-031 or any other product candidates that we may develop if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish sales, marketing and distribution capabilities, either ourselves or through collaborations or other arrangements with third parties.

In the future, we plan to build a focused sales and marketing infrastructure to market or co-promote EBI-031 and possibly other product candidates that we develop in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of EBI-031 or any other product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize EBI-031 or any other product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We expect to enter into arrangements with third parties to perform sales, marketing and distribution services in markets outside the United States. We may also enter into arrangements with third parties to perform these services in the United States if we do not establish our own sales, marketing and distribution capabilities in the United States or if we determine that such third-party arrangements are otherwise beneficial. Our product revenues and our profitability, if any, under any such third-party sales, marketing or distribution arrangements are likely to be lower than if we were to market, sell and distribute EBI-031 or any other product candidates that we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute EBI-031 or any other product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market EBI-031 or our other product candidates effectively. If we do not establish sales,

marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing EBI-031 or any other product candidates that we may develop.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to EBI-031 and our other current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

The current standard of care for DME includes anti-VEGF therapies and corticosteroids. Some patients with DME are effectively treated by the current standard of care therapies. Approved anti-VEGF therapies for treating DME include Lucentis (ranibizumab) and Eylea® (aflibercept). Off-label use of Avastin (bevacizumab) is also seen in DME. Approved corticosteroid therapies include Ozurdex (dexamethasone implant) and Iluvien (fluocinolone implant). Laser photocoagulation was historically the standard of care for treating DME, in particular for a subcategory of DME called clinically significant macular edema, and is still used to treat some DME patients. However, anti-VEGF therapy has been proven in clinical studies to have superior efficacy over laser photocoagulation.

New areas that are being investigated for pharmacologic treatment of DME include targets and pathways such as mammalian target of rapamycin, or mTOR, tie-2 activators, integrin antagonists, synthetic derivative of testosterone, intercellular adhesion molecule-1, or ICAM-1, matrix metalloproteinases, or MMPs, receptor for advance glycation products, or RAGE, renin-angiotensin system, bradykinin pathway inhibitors and others.

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 EBI-031 or other product candidates 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, our ability to compete may be affected in many cases by insurers or other third-party payors, particularly Medicare, seeking to encourage the use of generic products. Generic products are currently being used for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If EBI-031 or any other product candidate that we may develop achieves marketing approval, we expect that it will be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize EBI-031 or any other product candidate that we may develop, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

Our ability to commercialize EBI-031 or any other product candidates that we may develop successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers, managed care plans and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the

amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for EBI-031 or any other product that we commercialize and, even if they are available, the level of reimbursement may not be satisfactory.

Inadequate reimbursement may adversely affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize EBI-031 or any other product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop would compromise our ability to generate revenues and become profitable.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

There can be no assurance that our product candidates or any products that we may in-license, if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost-effective by third-party payors, that coverage and an adequate level of reimbursement will be available, or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

Our strategy of obtaining rights to product candidates and approved products for the treatment of a range of ophthalmic diseases through in-licenses and acquisitions may not be successful.

We may expand our product pipeline through opportunistically in-licensing or acquiring the rights to other products, product candidates or technologies for the treatment of ophthalmic diseases. The future growth of our business may depend in part on our ability to in-license or acquire the rights to approved products, additional product candidates or technologies. However, we may be unable to in-license or acquire the rights to any such products, product candidates or technologies from third parties. The in-licensing and acquisition of pharmaceutical products is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire products, product candidates or technologies 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 in-license or acquire the rights to the relevant product, product candidate or technology on terms that would allow us to make an appropriate return on our investment. Furthermore, we may be unable to identify suitable products, product

candidates or technologies within our area of focus. If we are unable to successfully obtain rights to suitable products, product candidates or technologies, our ability to pursue this element of our strategy could be impaired.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we develop.

We face an inherent risk of product liability exposure related to the use of EBI-031 and any other product candidates that we develop in human clinical trials and will face an even greater risk if we commercially sell any products that we develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

We currently hold $5.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $5.0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage as we expand our clinical trials. We will need to further increase our insurance coverage if we commence commercialization of EBI-031 or any other product candidate that receives marketing approval. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

We have entered into one collaboration and in the future may enter into collaborations with other third parties for the development or commercialization of our product candidates, including EBI-031. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

In May 2013, we entered into a collaboration and license agreement with ThromboGenics. Under the agreement, we and ThromboGenics are collaborating to identify protein or peptide therapeutics that directly modulate any of a specified set of targets in a novel pathway in retinal disease. This collaboration generally prohibits us, our affiliates and any entities which become affiliates of ours as a result of an acquisition of us by a third party, from researching, developing, manufacturing or commercializing any protein or peptide therapeutic that directly modulates one of the specified targets, except as otherwise provided in the agreement. This restriction may have the effect of preventing us from undertaking development and other efforts that may appear to be attractive to us.

We expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize EBI-031 in markets outside the United States. We also may enter into arrangements with third parties to perform these services in the United States if we do not establish our own sales, marketing and distribution capabilities in the United States or if we determine that such third-party arrangements are otherwise beneficial. We also may seek third-party collaborators for development and commercialization of other product candidates. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.
Our existing collaboration with ThromboGenics and any future collaborations that we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;

- collaborators may not pursue development and commercialization of our product candidates that receive marketing approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If our existing collaboration and license agreement with ThromboGenics, and any future collaborations that we enter into, do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. The initial research term concluded in November 2015. However the parties have agreed to continue the existing Collaboration and License Agreement to provide us the time required to complete additional research activities for no additional consideration. We expect the relevant data to become available in the second quarter of 2016. To date, no collaboration products have been identified. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours were to be involved in a business combination, it might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be harmed.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the

proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We have relied on third parties, such as CROs, to conduct our clinical trials of isunakinra and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of EBI-031 and our other product candidates. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would 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 responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We expect to contract with third parties for the manufacture of EBI-031 for clinical trials and expect to continue to do so in connection with the commercialization of EBI-031 and for clinical trials and commercialization of any other product candidates that we may develop. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of EBI-031 or any other of our product candidates. We rely, and expect to continue to rely, on third parties to manufacture clinical and commercial supplies of EBI-031, preclinical and clinical supplies of our other product candidates that we may develop and commercial supplies of products if and when any of our product candidates receives marketing approval. Our current and anticipated future dependence upon others for the manufacture of EBI-031 and any other product candidate or product that we develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. In addition, any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We currently rely exclusively on one third-party manufacturer to supply us with EBI-031 drug substance on a purchase order basis. We also rely on another third-party manufacturer to conduct fill-finish services on a purchase order basis. We do not currently have any contractual commitments for commercial supply of bulk drug substance for EBI-031 or for fill-finish services. We also do not currently have arrangements in place for redundant supply or a second source for bulk drug substance for EBI-031 or for fill-finish services. The prices at which we are able to obtain supplies of EBI-031 drug substance and fill-finish services may vary substantially over time and adversely affect our financial results.

If our third-party manufacturer for EBI-031 drug substance fails to fulfill our purchase orders or should become unavailable to us for any reason, we believe that there are a limited number of potential replacement manufacturers, and we likely would incur added costs and delays in identifying or qualifying such replacements. We could also incur additional costs and delays in identifying or qualifying a replacement manufacturer for fill-finish services if our existing third-party manufacturer should become unavailable for any reason. We may be unable to establish any agreements with such replacement manufacturers or to do so on acceptable terms. Even if we could transfer manufacturing to a different third party, the shift would likely be expensive and time consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need FDA approval before using or selling any products manufactured at that facility.

The FDA maintains strict requirements governing the manufacturing process for biologics. When a manufacturer seeks to modify or make even seemingly minor changes to that process, the FDA may require the applicant to conduct a comparability study that evaluates the potential differences in the product resulting from the change in the manufacturing process. The agency has issued several guidances on this point. In connection with our application for a license to market EBI-031 or other product candidates in the United States, we may be required to conduct a comparability study if the product we intend to market is supplied by a manufacturer different from the one who supplied the product evaluated in our clinical studies. Delays in designing and completing this study to the satisfaction of the FDA could delay or preclude our development and commercialization plans and thereby limit our revenues and growth.

Reliance on third-party manufacturers entails additional risks, including:

- EBI-031 and any other product candidates that we may develop may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under current good manufacturing practices, or cGMP, regulations;
- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Risks Related to Our Intellectual Property

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

Our success depends in large part on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We and our licensors have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not

be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned or licensed patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We may not be able to generate sufficient additional data on a timely basis, or at all. Moreover, changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

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

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

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

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

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the U.S. Patent and Trademark Office. The risks of being involved in such litigation and proceedings may increase as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. We may not be aware of all such intellectual property rights potentially relating to our product candidates and their uses. Thus, we do not know with certainty that EBI-031 or any other product candidate, or our commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are party to a number of license agreements and a collaboration agreement that impose, and, for a variety of purposes, we will likely enter into additional licensing and funding arrangements with third parties that may impose, diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. Under certain of our existing licensing agreements, we are obligated to pay royalties or make specified milestone payments on net product sales of product candidates or related technologies to the extent they are covered by the agreement. We also are obligated under certain of our existing license agreements to pay maintenance and other fees. We also have diligence and development obligations under certain of those agreements that we are required to satisfy. If we fail to comply with our obligations under current or future license and collaboration agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could diminish the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or

disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

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

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

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

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory and Marketing Approval of Our Product Candidates and Other Legal Compliance Matters

If we are not able to obtain required regulatory approvals, or there are delays in obtaining approvals, we will not be able to commercialize EBI-031 or any other product candidate that we may develop, and our ability to generate revenue will be materially impaired. The marketing approval process is expensive, time-consuming and uncertain. As a result, we cannot predict when or if we, or any collaborators we may have in the future, will obtain marketing approval to commercialize EBI-031 or any other product candidate.

To date, we have not obtained approval from the FDA or any foreign regulatory authority to market or sell any of our product candidates, including EBI-031. The failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. The activities associated with the development and commercialization of our product candidates, including EBI-031, including design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside the United States. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, especially if additional clinical trials are required, if approval is obtained at all. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety, purity and potency. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA, EMA or other regulatory authorities may determine that EBI-031 or any other product candidate that we may develop is not safe, effective or pure, is only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

The regulatory process can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Moreover, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate.

The different requirements of the EMA compared with the FDA may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post approval limitations or restrictions. If we experience delays in obtaining regulatory approvals, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

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

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

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

Our product candidates for which we intend to seek approval as biological products may face competition sooner than expected.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, abbreviated pathways for approval of biosimilar and interchangeable biological products were created. The BPCIA establishes legal authority for the FDA to review and approve biosimilars for marketing, as well as biosimilars that have been designated as "interchangeable" with a previously approved biologic, or reference product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a full BLA. This period of non-patent exclusivity runs concurrently with, but is independent of, periods of patent protection for the reference product.

We believe that any of our product candidates approved as a biological product under a full BLA should qualify for a 12-year period of exclusivity. However:

- the United States Congress could amend the BPCIA to significantly shorten this exclusivity period as has been previously proposed; and
- a potential competitor could seek and obtain approval of its own BLA during our exclusivity period instead of seeking approval of a biosimilar version.

The BPCIA is complex and is only beginning to be interpreted and implemented by the FDA. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes could compromise the future commercial prospects for our biological products. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear and will depend on a number of marketplace and regulatory factors that are still developing at both the federal and state levels of government.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad, and any approval we are granted for our product candidates in the United States would not assure approval of product candidates in foreign jurisdictions.

In order to market and sell EBI-031 and any other product candidate that we may develop in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Even if we, or any collaborators we may have in the future, obtain marketing approvals for EBI-031 or our other product candidates, the terms of those approvals, ongoing regulations and post-marketing restrictions may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators we may have in the future, must therefore comply with requirements concerning advertising and promotion for any of our products for which we or they
obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, if EBI-031 or any other product candidate that we may develop receives marketing approval, the accompanying label may limit the approved use of our product, which could limit sales of the product.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to physicians, recordkeeping, and potentially costly post-marketing studies or other clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval will be subject to a strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other federal and state regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. Violations of such requirements may lead to investigations alleging violations of the FDCA and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with customers and third-party payors may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates, including EBI-031, for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we

market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, which imposes obligations, including mandatory contractual terms, on covered healthcare providers, health plans and healthcare clearinghouses, as well as their business associates, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign 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; state and foreign 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 and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

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

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

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent product labeling and post-marketing testing and other requirements.

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

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

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

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we or our third-party manufacturers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur significant costs.

We and our third-party manufacturers are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the 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 employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards 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 and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical and business development expertise of Abbie Celniker, Ph.D., our President and Chief Executive Officer, Karen L. Tubridy, our Chief Development Officer, and Michael Goldstein, M.D., our Chief Medical Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. For example, in January 2016, Eric Furfine notified us of his resignation as our Chief Scientific Officer, and in June 2015, Gregory D. Perry notified us of his resignation as our Chief Financial and Business Officer. We do not maintain “key person” insurance for any of our executives or other employees.

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

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

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

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our

operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. 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 our product research, development and commercialization efforts could be delayed.

Risks Related to Our Common Stock

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

As of March 15, 2016 , our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock, in the aggregate, beneficially owned shares representing approximately 57.5% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of voting power may:

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

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

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

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

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

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

Our shares of common stock began trading on The NASDAQ Global Market on February 6, 2014. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares.

The price of our common stock has been volatile and may fluctuate in the future, which could result in substantial losses for our stockholders.

The trading price of our common stock has and may continue to fluctuate significantly. During the period from January 4, 2016 to March 15, 2016 , the closing sales price of our common stock ranged from a high of $3 per share to a low of $0.25 per share. Our stock price experienced significant volatility in May 2015 after we announced that we failed to meet either of the two co-primary endpoints in our Phase 3 clinical trial of isunakinra in patients with moderate to severe dry eye disease and in January 2016 after we announced that we failed to meet the primary endpoint in our Phase 3 clinical trial of isunakinra in patients with allergic conjunctivitis. Furthermore, the stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased their shares. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of EBI-031 or any other product candidate that we may develop;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key scientific or management personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional products, product candidates or technologies for the treatment of ophthalmic diseases, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class action litigation has often been instituted against that company. We also may face securities class action litigation if we cannot obtain regulatory approvals for or if we otherwise fail to commercialize EBI-031. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources.

If we fail to continue to meet all applicable continued listing requirements of The NASDAQ Global Market and NASDAQ determines to delist our common stock, the market liquidity and market price of our common stock could decline.

Our common stock is listed on The NASDAQ Global Market. In order to maintain that listing, we must satisfy minimum financial and other continued listing requirements. On March 3, 2016, we received the following notifications from the NASDAQ Listings Qualifications Department:

- For the prior 30 consecutive business days, the bid price of our common stock on The NASDAQ Global Market closed below the minimum $1.00 per share required for continued inclusion under NASDAQ Marketplace Rule 5810(c)(3)(A), or the Minimum Bid Price Rule.

- For the prior 30 consecutive business days, our stockholders' equity did not comply with the minimum stockholders' equity requirement of $5,000,000 for continued listing on The NASDAQ Global Market pursuant to NASDAQ Marketplace Rule 5810(c)(3)(D), or the Minimum Market Value Rule.

In accordance with NASDAQ Marketplace Rule 5810(c)(3)(A), we have 180 calendar days, or until August 30, 2016, to regain compliance with the Minimum Bid Price Rule. The NASDAQ Listings Qualifications Department informed us that if, at any time before August 30, 2016, the bid price of our common stock closes at $1.00 per share or more for a minimum of 10 consecutive business days, NASDAQ will provide written notification that we have achieved compliance with the Minimum Bid Price Rule, although NASDAQ may, in its discretion, require that an issuer maintain a bid price of at least $1.00 per share for a period in excess of 10 consecutive business days, but generally no more than 20 consecutive business days, before determining that the issuer has demonstrated an ability to maintain long-term compliance.

In the event we do not regain compliance with the Minimum Bid Price Rule by August 30, 2016, NASDAQ will provide written notification that our securities will be delisted from The NASDAQ Global Market. At that time, we may appeal NASDAQ's determination to delist our securities to a NASDAQ Listing Qualifications Panel. Alternatively, we could apply to transfer its listing to The NASDAQ Capital Market, provided that it meets all applicable requirements for initial listing on The NASDAQ Capital Market other than the Minimum Bid Price Rule. If such an application were approved and we otherwise maintain the listing requirements for The NASDAQ Capital Market, other than with respect to the Minimum Bid Price Rule, we would be afforded the remainder of an additional 180 calendar day grace period while listed on The NASDAQ Capital Market to regain compliance with the Minimum Bid Price Rule.

In accordance with NASDAQ Marketplace Rule 5810(c)(3)(D), we have 180 calendar days, or until August 30, 2016, to regain compliance with the Minimum Market Value Rule. The NASDAQ Listings Qualifications Department informed us that if, at any time before August 30, 2016, the market value of our publicly held shares closes at $5,000,000 or more for a minimum of 10 consecutive business days, NASDAQ will provide written notification that we have achieved compliance with the Minimum Market Value Rule, although NASDAQ may, in its discretion, require that we maintain a market value of our publicly held shares of at least $5,000,000 or more for a period in excess of 10 consecutive business days, but generally no more than 20 consecutive business days, before determining that we have demonstrated an ability to maintain long-term compliance.

In the event we do not regain compliance with the Minimum Market Value Rule by August 30, 2016, NASDAQ will provide written notification that our securities will be delisted from The NASDAQ Global Market. Alternatively, we could apply to transfer our listing to The NASDAQ Capital Market, provided that we meet all applicable requirements for initial listing on The NASDAQ Capital Market.

We have not yet determined what action, if any, we will take in response to these notices, although we intend to monitor the closing bid price of our common stock and the market value of our publicly held shares between now and August 30, 2016. We will consider available options if our common stock does not trade at a level likely to result in us regaining compliance with the Minimum Bid Price Rule and the Minimum Market Value Rule.

If we fail to continue to meet all applicable continued listing requirements of The NASDAQ Global Market in the future and NASDAQ determines to delist our common stock or transfer our listing from The NASDAQ Global Market to The NASDAQ Capital Market, an active trading market for our common stock may not be sustained and the market price of our common stock could decline. If an active trading market for our common stock is not sustained, it will be difficult for our stockholders to sell shares of our common stock without further depressing the market price of our common stock or at all. A delisting of our common stock also could make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2015 , we had federal net operating loss, or NOL, carryforwards of $120.0 million , state NOL carryforwards of $118.2 million and federal and state research and development tax credit carryforwards of $1.7 million and $1.2 million , respectively, available to reduce future taxable income. These federal and state NOL carryforwards and federal and state tax credit carryforwards expire at various dates beginning in 2029 through 2035, if not utilized. Utilization of these NOL and tax credit carryforwards may be subject to a substantial limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and comparable provisions of state, local and foreign tax laws due to changes in ownership of our company that have occurred previously or that could occur in the future. Under Section 382 of the Code and comparable provisions of state, local and foreign tax laws, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change by value in its equity ownership over a three year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes, such as research and development tax credits, to reduce

its post-change income may be limited. We have not completed a study to determine whether our IPO or "at the market" offering, our most recent private placements of our common stock and warrants to purchase shares of our common stock and other transactions that have occurred over the past three years may have triggered an ownership change limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we generate taxable income, our ability to use our pre-change NOL and tax credits carryforwards to reduce U.S. federal and state taxable income may be subject to limitations, which could result in increased future tax liability to us.

A significant portion of our total outstanding shares are eligible to be sold into the market, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of March 15, 2016 , we had outstanding 19,684,875 shares of common stock. Of these shares, 7,731,766 shares are restricted securities under Rule 144 under the Securities Act. Any of our remaining shares that are not restricted securities under Rule 144 under the Securities Act may be resold in the public market without restriction unless purchased by our affiliates.

Moreover, holders of an aggregate of 8,020,538 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. On April 9, 2014, we filed a registration statement registering all shares of common stock that we may issue under our equity compensation plans. As of March 15, 2016 , we had outstanding options to purchase an aggregate of approximately 2,538,914 shares of our common stock, of which options to purchase approximately 957,576 shares were vested. These shares can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an
emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K. In particular, in this Annual Report on Form 10-K, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We expect to continue, in our public reporting, to take advantage of some or all of the reporting exemptions available to emerging growth companies. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards . This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to delay such adoption of new or revised accounting standards, and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies.

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

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

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

For as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies as described in the preceding risk factor. We may remain an emerging growth company until the end of the 2019 fiscal year, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have annual gross revenues of $1 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an emerging growth company if we issue more than $1 billion of non-convertible debt over a three-year period.

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

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

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of our loan and security agreement with Silicon Valley Bank and any future debt agreements that we may enter into, may preclude us from paying dividends without the lenders' consent or at all. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our sole facility currently consists of approximately 11,022 square feet of office and laboratory space in Cambridge, Massachusetts that we occupy under a lease that expires on April 30, 2018.

Item 3. Legal Proceedings.

We are not currently subject 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 Issuer Purchases of Equity Securities.

Our common stock trades on the NASDAQ Global Market under the symbol "EBIO". Trading of our common stock commenced on February 6, 2014, following the completion of our initial public offering, or IPO. Prior to that time, there was no established public trading market for our common stock. The following table sets forth for the period indicated the high and low sale prices per share for our common stock as reported on the NASDAQ Global Market for the period indicated:

	Market Price	
	High	Low
First quarter 2014 (February 6, 2014 through March 31, 2014)	$ 19.33	$ 10.11
Second quarter 2014	$ 17.48	$ 10.01
Third quarter 2014	$ 14.07	$ 9.50
Fourth quarter 2014	$ 12.10	$ 10.00
First quarter 2015	$ 13.50	$ 8.92
Second quarter 2015	$ 13.78	$ 2.61
Third quarter 2015	$ 8.00	$ 2.25
Fourth quarter 2015	$ 3.30	$ 2.24

As of March 15, 2016 , we had approximately 32 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name.

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

Recent Sales of Unregistered Securities

We did not sell or issue any equity securities that were not registered under the Securities Act during the period covered by this Annual Report on Form 10-K.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Selected Financial Data.

You should read the following selected financial data together with our financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the statement of operations data for the years ended December 31, 2015 , 2014 and 2013 and the balance sheet data as of December 31, 2015 and 2014 from our audited financial statements included in this Annual Report on Form 10-K. We derived the statements of operations data for the years ended December 31, 2012 and 2011 and the balance sheet data as of December 31, 2013, 2012 and 2011 from our audited consolidated financial statements that are not included elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year Ended December 31,				
	2015	2014	2013	2012	2011
	(in thousands, except per share data)				
Statement of Operations Data:					
Collaboration revenue	$ 490	$ 2,243	$ 1,334	$ —	$ —
Other revenue	500	—	—	—	—
Total revenue	990	2,243	1,334	—	—
Operating expenses:					
Research and development	26,336	26,703	13,788	15,263	9,411
General and administrative	9,850	8,471	4,024	4,213	3,267
Total operating expenses	36,186	35,174	17,812	19,476	12,678
Loss from operations	(35,196)	(32,931)	(16,478)	(19,476)	(12,678)
Other expense:					
Other income (expense), net	3,139	(849)	(147)	(13)	3
Interest expense	(1,395)	(376)	(1,400)	(168)	(151)
Total other income (expense), net	1,744	(1,225)	(1,547)	(181)	(148)
Net loss and comprehensive loss	$ (33,452)	$ (34,156)	$ (18,025)	$ (19,657)	$ (12,826)
Cumulative preferred stock dividends and accretion of preferred stock discount	—	(519)	(3,857)	(3,111)	(1,452)
Net loss applicable to common stockholders	$ (33,452)	$ (34,675)	$ (21,882)	$ (22,768)	$ (14,278)
Net loss per share applicable to common stockholders —basic and diluted	$ (1.76)	$ (2.37)	$ (16.18)	$ (22.93)	$ (17.80)
Weighted-average number of common shares used in net loss per share applicable to common stockholders —basic and diluted	18,993	14,644	1,352	993	802

See Note 2 within the notes to our financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to calculate basic and diluted net loss per share applicable to common stockholders.

	As of December 31,				
	2015	2014	2013	2012	2011
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents	$ 36,079	$ 54,059	$ 7,942	$ 7,882	$ 700
Working capital	28,731	49,199	2,677	6,446	(1,229)
Total assets	36,825	55,000	11,237	9,503	2,665
Notes payable, net of current portion	9,763	9,749	2,876	1,769	325
Warrant liability	115	3,219	297	147	26
Convertible preferred stock	—	—	56,678	45,035	19,644
Accumulated deficit	(125,202)	(91,750)	(57,594)	(39,569)	(19,912)
Total stockholders' equity (deficit)	18,944	36,826	(54,332)	(39,296)	(19,791)

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and the notes to those financial statements appearing in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part I, Item IA, "Risk Factors" of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements.

Overview

We are a preclinical stage biopharmaceutical company with a proprietary protein engineering platform, called AMP-Rx, that we apply to the discovery and development of protein therapeutics to treat diseases of the eye. Our therapeutic approach is based on the role of cytokines in diseases of the eye, our understanding of the structural biology of cytokines and our ability to rationally design and engineer proteins to modulate the effects of cytokines. Cytokines are cell signaling molecules found in the body that can have important inflammatory effects. Our most advanced product candidate, which is still in preclinical development, is EBI-031, which we designed, engineered and generated using our AMP-Rx platform and are developing as an intravitreal injection for diabetic macular edema, or DME, and uveitis. In 2015, we initiated the necessary chemistry, manufacturing and control, or CMC, development work and nonclinical safety studies of EBI-031 to support the submission of an investigational new drug application, or IND, to the United States Food and Drug Administration, or FDA. If the results of these efforts and our additional preclinical studies of EBI-031 are favorable, we intend to submit an IND for EBI-031 for the treatment of DME to the FDA in the first half of 2016 for the purpose of conducting clinical trials. We hold worldwide commercialization rights to EBI-031.

We previously invested a significant portion of our efforts and financial resources in the development of our product candidate isunakinra (EBI-005) for the treatment of patients with dry eye disease and allergic conjunctivitis. Notwithstanding this significant investment, based on the negative results from our completed Phase 3 clinical trials in dry eye disease and allergic conjunctivitis, we do not plan to pursue further development of isunakinra.

We were incorporated and commenced active operations in early 2008, and our operations to date have been limited to organizing and staffing our company, acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials. To date, we have financed our operations primarily through private placements of our common stock and preferred stock and convertible bridge notes, venture debt borrowings and our initial public offering, or IPO, sales effected in an "at the market" offering through our agent, Cowen and Company, LLC, or Cowen, and, to a lesser extent, from a collaboration. Substantially all of our revenue to date has been collaboration revenue, which we first began to generate in 2013. We have devoted substantially all of our financial resources and efforts to research and development activities. We are still in the early stages of development of our product candidates, and we have not completed development of any drugs. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year.

Since inception, we have incurred significant operating losses. Our net loss was $33.5 million for the year ended December 31, 2015 , $34.2 million for the year ended December 31, 2014 and $18.0 million for the year ended December 31, 2013. As of December 31, 2015 , we had an accumulated deficit of $125.2 million .

We anticipate that we will continue to incur substantial expenses in connection with the advancement of our preclinical product candidate, EBI-031, including the expenses associated with our planned submission of an IND for EBI-031 for the treatment of DME in the first half of 2016 and our planned initiation of clinical trials of EBI-031 for the treatment of DME.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly initiating and completing clinical development of EBI-031 for the treatment of DME, uveitis or other indications and, if successful, seeking marketing approval for EBI-031. We also expect to devote additional financial resources to functions associated with operating as a public company. We also may devote additional financial resources to conducting research and development, if we determine to proceed into clinical development, initiating clinical trials of, and seeking regulatory approval for, our other product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we would need to devote substantial financial resources to commercialization efforts, including product manufacturing, marketing, sales and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital

when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Our future success is dependent on our ability to develop our product candidates and ultimately upon our ability to attain profitable operations. We are subject to a number of risks similar to other early-stage life science companies, including, but not limited to, successful discovery and development of our drug candidates, raising additional capital, development by our competitors of new technological innovations, protection of proprietary technology and market acceptance of our products. These factors raise substantial doubt about our ability to continue as a going concern. In order for us to continue operations beyond 2016 and be able to discharge our liabilities and commitments in the normal course of business, we have taken or will take the following steps, not all of which are entirely within our control:

- We engaged an investment bank to conduct a review of strategic alternatives with the goal of maximizing shareholder value. Potential strategic alternatives to be explored and evaluated during the review process may include the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies. We cannot provide any commitment regarding when or if this strategic review process will result in any type of transaction and no assurance can be given that we will determine to pursue a potential sale, strategic partnership or licensing arrangement.

- We do not see an immediate path forward for isunakinra and have implemented a plan to wind down the development activities associated with isunakinra.

- We have conducted a review of our operations and implemented a plan to reduce future operating expenses to align with current operating conditions.

- On March 1, 2016, we prepaid all outstanding amounts owed to Silicon Valley Bank, or SVB, under our Loan and Security Agreement with SVB. We continue to evaluate other financing alternatives to provide additional operating funds on terms that are consistent with our business plans.

We believe that our current cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2016. If we are unable to obtain adequate financing or engage in a strategic transaction on acceptable terms and when needed, we will be required to implement further cost reduction strategies. These factors, and the factors described above, continue to raise substantial doubt about our ability to continue as a going concern. In its report on our financial statements for the year ended December 31, 2015, our independent registered public accounting firm has included an explanatory paragraph about our ability to continue as a going concern.

On March 3, 2016, we received the following notifications from the NASDAQ Listings Qualifications Department:

- For the prior 30 consecutive business days, the bid price of our common stock on The NASDAQ Global Market closed below the minimum $1.00 per share required for continued inclusion under NASDAQ Marketplace Rule 5810(c)(3)(A) (the “Minimum Bid Price Rule”).

- For the prior 30 consecutive business days, our stockholders’ equity did not comply with the minimum stockholders’ equity requirement of $5,000,000 for continued listing on The NASDAQ Global Market pursuant to NASDAQ Marketplace Rule 5810(c)(3)(D) (the “Minimum Market Value Rule”).

In accordance with NASDAQ Marketplace Rule 5810(c)(3)(A), we have 180 calendar days, or until August 30, 2016, to regain compliance with the Minimum Bid Price Rule and the Minimum Market Value Rule.

Financial Operations Overview

Revenue

To date, we have not generated any revenues from the sale of products. Substantially all of our revenue to date has been derived from a collaboration and, to a lesser extent, from a license agreement. We do not expect to generate significant product revenue unless and until we obtain marketing approval for, and commercialize EBI-031.

We have generated collaboration revenue exclusively from our collaboration and license agreement with ThromboGenics N.V., or Thrombogenics, which we entered into in May 2013. Under the agreement, we and ThromboGenics are collaborating to identify protein or peptide therapeutics that directly modulate any of a specified set of targets in a novel pathway in retinal disease. We call the therapeutics that are identified, and whose modulation of one of the targets is confirmed, in the course of the research collaboration, collaboration products. The initial research term concluded in November 2015. However the parties

have agreed to continue the existing Collaboration and License Agreement to provide us the time required to complete additional research activities for no additional consideration. We expect the relevant data to become available in the second quarter of 2016. To date, no collaboration products have been identified. The agreement expires when all of ThromboGenics' payment obligations expire. We are responsible for specified non-clinical activities during the research term. ThromboGenics is responsible for all development, manufacturing and commercialization activities with respect to the collaboration products. We granted ThromboGenics an exclusive, sublicensable, worldwide royalty-bearing license under our rights in any intellectual property made in the course of this collaboration, as well as under any other intellectual property we control during the research term that is necessary for ThromboGenics to perform its obligations to research, develop, manufacture and commercialize collaboration products. During the term of the agreement, neither we nor ThromboGenics, nor our respective affiliates other than any entities which become affiliates as a result of an acquisition of us or ThromboGenics, are permitted to research, develop, manufacture or commercialize any protein or peptide therapeutic that directly modulates one of the specified targets, except as otherwise provided in the agreement.

In connection with the agreement, we received an upfront, non-refundable payment of $1.75 million, and are entitled to receive payment for our performance of activities under the agreement at a set rate per full time annual equivalent personnel for research services pursuant to the agreement. We identified three deliverables in the arrangement: the research license, the research services and our participation on the joint research committee, or JRC deliverable, and concluded that there are two units of accounting: a combined research license and research services deliverable and the JRC deliverable. The estimated selling price for the JRC deliverable was *de minimis* , and thus we allocated the fixed arrangement consideration to the combined unit of accounting. We are recognizing revenue using the proportional performance method by which the amounts are recognized in proportion to the costs incurred based on full time equivalent efforts. In addition, we are eligible to receive up to an aggregate of $10.0 million if ThromboGenics achieves specified preclinical and clinical development milestones and up to an aggregate of $15.0 million if ThromboGenics achieves specified regulatory milestones. There are no commercialization or sales based milestones under the agreement. ThromboGenics is obligated to pay us a low single digit royalty on the sale of collaboration products. We recognized collaboration revenue of $0.5 million in connection with this collaboration for the year ended December 31, 2015 and $2.2 million for the year ended December 31, 2014. To date, no collaboration products have been identified and therefore we do not expect that we will generate significant revenue from our collaboration with ThromboGenics in the future.

Research and Development Expenses

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

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- expenses incurred under agreements with clinical research organizations, or CROs, and investigative sites that conduct our clinical trials;
- expenses associated with developing manufacturing capabilities and manufacturing clinical study materials;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies; and
- expenses associated with preclinical and regulatory activities.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our clinical trials and other research and development activities;
- the efficacy and potential advantages of our product candidates compared to alternative treatments, including any standard of care;
- the market acceptance of our product candidates;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation; and
- the timing, receipt and terms of any marketing approvals.

A change in the outcome of any of these variables with respect to the development of EBI-031 or any other product candidate that we may develop could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials or other testing beyond those that we currently contemplate will be required for the completion of clinical development of EBI-031 or any other product candidate that we may develop, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

We allocate direct research and development expenses, consisting principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials, and costs related to manufacturing or purchasing clinical trial materials, to specific product programs. We do not allocate employee and contractor-related costs, costs associated with our platform and facility expenses, including depreciation or other indirect costs, to specific product programs because these costs are deployed across multiple product programs under research and development and, as such, are separately classified. The table below provides research and development expenses incurred for our isunakinra and EBI-031 product programs and other expenses by category. We did not allocate research and development expenses to any other specific product program during the periods presented:

	Year ended December 31,		
	2015	2014	2013
	(in thousands)		
Programs:			
Isunakinra (EBI-005)	$ 14,455	$ 19,820	$ 7,366
EBI-031	5,384	—	—
Total program expenses	19,839	$ 19,820	$ 7,366
Personnel and other expenses:			
Employee and contractor-related expenses	4,762	4,620	4,409
Platform-related lab expenses	620	855	997
Facility expenses	536	473	773
Other expenses	579	935	243
Total personnel and other expenses	6,497	6,883	6,422
Total research and development expenses	$ 26,336	$ 26,703	$ 13,788

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation, in executive, operational, finance, business development and human resource functions. Other general and administrative expenses include facility-related costs and professional fees for legal, patent, consulting and accounting services.

Other Income (Expense), Net

Other income and expense consists primarily of interest income earned on cash and cash equivalents, interest expense on outstanding debt, the gain or loss associated with the change in the fair value of our common and preferred stock warrant liability and the convertible notes that were carried at fair value, the loss on extinguishment of debt and the expense related to the issuance costs allocated to warrants measured at fair value.

Critical Accounting Policies and Significant Judgments and Estimates

This management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued research and development expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our audited financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We recognize revenue in accordance with Accounting Standards Codification, or ASC, 605, *Revenue Recognition* . Accordingly, we recognize revenue 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.

We record as deferred revenue any amounts received prior to satisfying the revenue recognition criteria. We classify as deferred revenue, current any amounts expected to be recognized as revenue within the 12 months following the balance sheet date. We classify as deferred revenue, net of current portion any amounts not expected to be recognized as revenue within the 12 months following the balance sheet date.

We evaluate multiple-element arrangements based on the guidance in ASC Topic 605-25, *Revenue Recognition-Multiple-Element Arrangements* , or ASC 605-25. Pursuant to the guidance in ASC 605-25, we evaluate multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that the delivered item has value to the customer on a standalone basis, and if the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in our control. In assessing whether an item has standalone value, we consider factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that can provide the undelivered items. The consideration received under the arrangement that is fixed or determinable is then allocated among the separate units of accounting using the relative selling price method. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE nor TPE is available.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, we recognize revenue from the combined unit of accounting over our contractual or estimated performance period for the undelivered items, which is typically the term of our research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement on a straight-line basis over the period we are expected to complete our performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (1) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item as a result of a specific outcome resulting from our performance to achieve the milestone; (2) the consideration relates solely to past performance; and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the

particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. We have concluded that certain of the preclinical and clinical development milestone payments pursuant to our collaboration and license arrangement with ThromboGenics are substantive. Accordingly, in accordance with ASC Topic 605-28, *Revenue Recognition-Milestone Method* , we will recognize revenue in its entirety upon successful accomplishment of these milestones, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, assuming all other revenue recognition criteria are met.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotes and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses are related to fees paid to CROs and other vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepayment expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in our reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

Stock-based Compensation

We account for all stock-based compensation payments to employees, directors and non-employees using an option pricing model for estimating fair value. Accordingly, stock-based compensation expense is measured based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We recognize compensation expense for the portion of the award that is ultimately expected to vest over the period during which the recipient renders the required services to us using the straight-line method. In accordance with authoritative guidance, we remeasure the fair value of non-employee stock-based awards as the awards vest, and recognize the resulting value, if any, as expense during the period the related services are rendered.

Significant Factors, Assumptions and Methodologies Used in Determining Fair Value

We apply the fair value recognition provisions of ASC Topic 718, *Compensation-Stock Compensation* , or ASC 718. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. We recognize stock-based compensation expense for service-based awards ratably over the requisite service period, which in most cases is the vesting period of the award. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the expected term of our stock options, the risk free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. As a new public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. We calculate expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants. During the periods we were a privately held company with a limited operating history, we utilized data from a representative group of public companies to estimate expected stock price volatility. We selected companies from the biopharmaceutical industry with similar characteristics to us, including those at a similar stage of development and with a similar therapeutic focus.

We use the "simplified method" to estimate the expected term of stock option grants to employees. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of our stock options, taking into consideration multiple vesting tranches. We utilize this method due to a lack of historical exercise data and the plain-vanilla nature of our share-based awards. We have never paid, and do not anticipate paying, any cash dividends in the foreseeable future, and therefore use an expected dividend yield of zero in the option-pricing model. The risk-free rate is based on the yield curve of U.S. Treasury securities with periods commensurate with the expected term of the options being valued. The fair value of each stock option granted to employees and directors is estimated on the date of grant using the Black-Scholes option-pricing model based on the assumptions noted in the following table:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.42-1.92%	1.67-2.02%	1.09-2.07%
Expected dividend yield	—%	—%	—%
Expected term (in years)	5.75-6	5.75-6	6
Expected volatility	69.06-74.11%	60.00-69.58%	72.13-77.80%

We are also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from our 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 that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates are revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest. Through December 31, 2015, actual forfeitures have not been material.

Emerging Growth Company Status

The Jumpstart our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards as required when they are adopted.

Results of Operations

Comparison of the Years Ended December 31, 2015 and 2014

	Year ended December 31,		
	2015	2014	Change
	(in thousands)		
Collaboration revenue	$ 490	$ 2,243	$ (1,753)
Other revenue	500	—	500
Total revenue	990	2,243	(1,253)
Operating expenses:			
Research and development	26,336	26,703	(367)
General and administrative	9,850	8,471	1,379
Total operating expenses	36,186	35,174	1,012
Loss from operations	(35,196)	(32,931)	(2,265)
Other expense, net	1,744	(1,225)	2,969
Net loss	$ (33,452)	$ (34,156)	$ 704

Revenue . Revenue was $1.0 million for the year ended December 31, 2015 compared to $2.2 million for the year ended December 31, 2014. The decrease of $1.3 million was largely due to less revenue recognized pursuant to the ThromboGenics collaboration and license agreement entered into in May 2013. The initial research term concluded in November 2015. However the parties have agreed to continue the existing Collaboration and License Agreement to provide us the time required to complete additional research activities for no additional consideration. The decrease was partially offset by $0.5 million of revenue recognized from a license agreement entered into in December 2015.

Research and development expenses . Research and development expenses were $26.3 million for the year ended December 31, 2015 compared to $26.7 million for the year ended December 31, 2014. The decrease of $0.4 million was primarily due to a one-time license fee paid in 2014. In addition, there was a decrease of $5.4 million of isunakinra-related development expenses. We initiated a pivotal Phase 3 clinical program evaluating isunakinra for the treatment of moderate to severe dry eye disease in early 2014 and completed this study in early 2015. Based on the results from this trial, we decided not to pursue further development of isunakinra in dry eye disease. We also initiated and completed a Phase 2 clinical trial to evaluate the use of isunakinra in patients with allergic conjunctivitis in 2014. Based on the results from this trial, we initiated a Phase 3 clinical program of isunakinra in patients with allergic conjunctivitis in the second half of 2015 and completed this trial in early 2016. Based on the trial results from both Phase 3 studies, we do not see an immediate path forward for isunakinra. This decrease in isunakinra-related development expenses was offset by increases in EBI-031 related development expenses of $5.4 million during the year ended December 31, 2015. In late 2014, we began undertaking the necessary CMC development work and nonclinical safety studies to support the submission of an IND to the FDA. We expect to submit an IND to the FDA in the first half of 2016.

General and administrative expenses . General and administrative expenses were $9.9 million for the year ended December 31, 2015 compared to $8.5 million for the year ended December 31, 2014. The increase of $1.4 million was primarily due to increased operating costs as a result of our transition from a private company to a public company, including legal, accounting, insurance and investor relations expenses. In addition, we incurred professional fees related to our pursuit of collaborative or other strategic opportunities during the year ended December 31, 2015.

Other income (expense), net . Other income (expense), net was $1.7 million for the year ended December 31 2015 compared to $(1.2) million for the year ended December 31, 2014. The change of $3.0 million was primarily due to the decrease in the fair value of our warrant liability partially offset by an increase in interest expense associated with the additional borrowings from SVB.

Comparison of the Years Ended December 31, 2014 and 2013

	Year ended December 31,		
	2014	2013	Change
		(in thousands)	
Collaboration revenue	$ 2,243	$ 1,334	$ 909
Operating expenses:			
Research and development	26,703	13,788	12,915
General and administrative	8,471	4,024	4,447
Total operating expenses	35,174	17,812	17,362
Loss from operations	(32,931)	(16,478)	(16,453)
Other expense, net	(1,225)	(1,547)	322
Net loss	$ (34,156)	$ (18,025)	$ (16,131)

Revenue . Revenue was $2.2 million for the year ended December 31, 2014 compared to $1.3 million for the year ended December 31, 2013. The increase of $0.9 million was due to revenue recognized pursuant to the ThromboGenics collaboration and license agreement entered into in May 2013.

Research and development expenses . Research and development expenses were $26.7 million for the year ended December 31, 2014 compared to $13.8 million for the year ended December 31, 2013. The increase of $12.9 million was primarily due to an increase of $12.5 million of isunakinra-related development expenses. In early 2014, we initiated a pivotal Phase 3 clinical program evaluating isunakinra for the treatment of moderate to severe dry eye disease. We also initiated and completed a Phase 2 clinical trial to evaluate the use of isunakinra in patients with allergic conjunctivitis in 2014. These increases in research and development expenses were partially offset by decreases in research and development expenses as a result of the completion of the Phase 1b/2a clinical trial of isunakinra in patients with moderate to severe dry eye disease in 2013.

General and administrative expenses . General and administrative expenses were $8.5 million for the year ended December 31, 2014 compared to $4.0 million for the year ended December 31, 2013. The increase of $4.4 million was primarily due to increased operating costs as a result of our transition from a private company to a public company, including legal, accounting,

insurance and investor relations expenses. In addition, stock-based compensation expense allocated to general and administrative expenses was $1.4 million for the year ended December 31, 2014 compared to $0.1 million for the year ended December 31, 2013.

Other expense, net . Other expense, net was $1.2 million for the year ended December 31, 2014 compared to $1.5 million for the year ended December 31, 2013. The decrease was primarily due to the change in the fair value of the convertible notes payable of $(1.0) million recorded in 2013 and none in 2014 partially offset by the loss on extinguishment of debt of $0.5 million and the expense related to the issuance costs allocated to warrants measured at fair value of $0.3 million, both recorded in 2014.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have incurred significant operating losses. Substantially all of our revenue to date has been collaboration revenue and, to a lesser extent, from a licensing agreement. To date, we have financed our operations primarily through private placements of our common stock, preferred stock and bridge notes convertible into our preferred stock, venture debt borrowings, our IPO, which we closed in February 2014, sales effected in an "at the market" offering through our agent, Cowen, and, to a lesser extent, from a collaboration.

In March 2015, we entered into a sales agreement, or the Sales Agreement, with Cowen, pursuant to which we may issue and sell shares of our common stock from time to time having an aggregate offering price of up to $40 million through Cowen, acting as our agent. Sales of our common stock through Cowen may be made by any method permitted that is deemed an “at the market offering” as defined in Rule 415 under the Securities Act of 1933, as amended, including sales made directly on or through the Nasdaq Global Market, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and/or any other method permitted by law. Cowen is not required to sell any specific amount, but acts as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices.

Shares sold pursuant to the Sales Agreement have been sold pursuant to a shelf registration statement, or the 2015 Shelf, which became effective on March 20, 2015 (File No 333-202676), as supplemented by a prospectus supplement dated March 11, 2015. Under the Sales Agreement, we pay Cowen a commission of up to 3% of the gross proceeds. As of December 31, 2015 , we had sold approximately 1,446,781 shares pursuant to the Sales Agreement, resulting in proceeds of approximately $12.7 million , net of commissions and issuance costs.

In November 2014, we amended our Loan and Security Agreement, or the Loan Agreement, with SVB to increase the amount we could borrow up to $15.0 million. We borrowed $10.0 million in 2014, and we borrowed the remaining $5.0 million in May 2015. In December 2015, we amended the Loan Agreement to change the repayment terms of the Loan Agreement under specified circumstances and to change the circumstances under which we were required to fund a cash collateral account with SVB in an amount equal to the outstanding amount under the Loan Agreement. As a result of the outcome of our Phase 3 clinical trial of isunakinra for the treatment of severe allergic conjunctivitis, we were required to fund a cash collateral account with SVB in an amount equal to approximately $15.1 million, representing the outstanding obligations under the Loan Agreement. On March 1, 2016, we prepaid all outstanding amounts owed to SVB, in an amount equal to approximately $14.9 million, and terminated the Loan Agreement.

Cash Flows

As of December 31, 2015, we had cash and cash equivalents of $36.1 million . Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

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

	Year ended December 31,		
	2015	2014	2013
	(in thousands)		
Net cash provided by (used in):			
Operating activities	$ (34,529)	$ (29,307)	$ (13,494)
Investing activities	(287)	(137)	—
Financing activities	16,836	75,561	13,554
Net increase in cash and cash equivalents	$ (17,980)	$ 46,117	$ 60

Operating activities. Net cash used in operating activities was $34.5 million for the year ended December 31, 2015 , and consisted primarily of a net loss of $33.5 million adjusted for non-cash items, including stock-based compensation expense of $2.5 million , depreciation expense of $0.4 million , a net change of $3.1 million in the fair value of the warrant liability and a net change in operating assets and liabilities of $(1.0) million .

Net cash used in operating activities was $29.3 million for the year ended December 31, 2014, and consisted primarily of a net loss of $34.2 million adjusted for non-cash items, including stock-based compensation expense of $2.4 million, loss on extinguishment of debt of $0.5 million, depreciation expense of $0.4 million, expense related to the issuance costs allocated to warrants measured at fair value of $0.3 million, change in fair value of warrant liability of $0.1 million and a net change in operating assets and liabilities of $1.1 million.

Net cash used in operating activities was $13.5 million for the year ended December 31, 2013, and consisted primarily of a net loss of $18.0 million adjusted for non-cash items, including stock-based compensation expense of $1.3 million, depreciation expense of $0.4 million, change in fair value of warrant liability of $0.2 million, change in fair value of convertible notes payable of $1.0 million and a net change in operating assets and liabilities of $1.6 million. The significant item in the net change in operating assets and liabilities include an increase in deferred revenue of $1.5 million due to the up-front payment related to the ThromboGenics collaboration.

Investing activities . Net cash used in investing activities consists of purchases of property and equipment. For the year ended December 31, 2015 , we purchased $0.3 million of property and equipment. For the year ended December 31, 2014, we purchased $0.1 million of property and equipment. We made no such purchases during the year ended December 31, 2013.

Financing activities . Net cash provided by financing activities for the year ended December 31, 2015 was $16.8 million and consisted primarily of net proceeds of $12.7 million from the issuance of common stock in connection with sales effected in an “at the market” offering through our agent, Cowen, and $5.0 million from additional borrowings under our loan with SVB. These amounts were partially offset by payments of notes payable of $0.9 million .

Net cash provided by financing activities for the year ended December 31, 2014 was $75.6 million and consisted primarily of net proceeds from the IPO and the net proceeds from the private placement of common stock completed in December 2014. We received aggregate net proceeds from the IPO of approximately $50.2 million, after deducting underwriting discounts and commissions and other offering expenses payable by us, of which $1.3 million were paid in 2013. We received aggregate net proceeds from the private placement of approximately $18.2 million, after deducting placement agent’s fees and other offering expenses payable by us, of which $1.3 million were paid in 2014.

Net cash provided by financing activities for the year ended December 31, 2013 was $13.6 million and consisted primarily of net proceeds from the issuance of series B preferred stock and convertible notes of $12.3 million to certain of our stockholders and additional borrowings under our debt facility of $3.0 million. These amounts were partially offset by deferred initial public offering costs of $1.3 million.

Funding Requirements

We anticipate that we will continue to incur substantial expenses in connection with the advancement of our preclinical product candidate, EBI-031, including the expenses associated with our planned submission of an IND for EBI-031 for the treatment of DME in the first half of 2016.

We will also incur substantial expenses if and as we:

- pursue the development of EBI-031 for additional indications, such as uveitis, or for use in other patient populations or, if it is approved, seek to broaden the label for EBI-031;
- continue the research and development of our other preclinical product candidates;
- seek to discover and develop additional product candidates;
- in-license or acquire the rights to other products, product candidates or technologies for the treatment of ophthalmic diseases;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish sales, marketing and distribution capabilities and scale up and validate external manufacturing capabilities to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific and management personnel;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and planned future commercialization efforts and our operations as a public company; and
- increase our insurance coverage as we commence clinical trials and potentially commercialize EBI-031.

As of December 31, 2015, we had cash and cash equivalents of $36.1 million . In March 2016, we prepaid all outstanding amounts and fees under the Loan Agreement with SVB, in an amount equal to approximately $14.9 million. We believe that our current cash and cash equivalents will be sufficient to fund our operating expenses into the fourth quarter of 2016. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

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

- the progress, costs and outcome of clinical development of EBI-031 for the treatment of DME and uveitis;
- the costs and timing of process development and manufacturing scale up and validation activities associated with EBI-031;
- the costs and timing of commercialization activities for EBI-031 if we receive, or expect to receive, marketing approval, including the costs and timing of establishing product sales, marketing, distribution and outsourced manufacturing capabilities;
- subject to receipt of marketing approval, the amount of revenue received from commercial sales of EBI-031;
- the progress, costs and outcome of developing EBI-031 for the treatment of additional indications or for use in other patient populations;
- our ability to establish collaborations on favorable terms, if at all, particularly manufacturing, marketing and distribution arrangements for our product candidates;
- the scope, progress, results and costs of preclinical development, laboratory testing and, if we determine to proceed into clinical development, clinical trials of our other product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we in-license or acquire rights to other products, product candidates or technologies for the treatment of ophthalmic diseases.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding, collaborations, strategic alliances, licensing arrangements and marketing and distribution arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as holders of our common stock. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, collaborations, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to

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

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2015:

	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
			(in thousands)		
Operating lease obligations(1)	$ 1,540	$ 642	$ 898	$ —	$ —
Debt obligations(2)	16,621	5,146	11,475	—	—
Total fixed contractual obligations	$ 18,161	$ 5,788	$ 12,373	$ —	$ —

(1) We lease office space at 215 First Street in Cambridge, Massachusetts under a non-cancelable operating lease that expires on April 30, 2018.
(2) Amounts include payments for interest on our debt obligations.

In May 2010, we entered into a $1.5 million secured debt facility with SVB. We borrowed an aggregate of $1.5 million under the debt facility in June and July 2010 and issued SVB promissory notes. In September 2012, we modified the terms of our secured debt facility with SVB to increase the amount we could borrow thereunder to $5.0 million. We borrowed $2.0 million under the debt facility in September 2012 and an additional $3.0 million under the debt facility in February 2013. In November 2014, we modified our secured debt facility with SVB to increase the amount we could borrow thereunder to $15.0 million. We borrowed an additional $10.0 million in November 2014, of which amount approximately $3.2 million was applied to the repayment of outstanding debt obligations to SVB under the debt facility, and we borrowed the remaining $5.0 million in May 2015. The debt facility carried a fixed interest rate of 3.75% above the prime lending rate. On March 1, 2016, we prepaid all outstanding amounts owed to SVB and terminated the Loan Agreement.

We also have obligations to pay royalties and to make future payments to third parties that become due and payable on the achievement of specified development, regulatory and commercial milestones. We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these contingent payments are not fixed and determinable. These commitments include potential milestone and royalty payments we may be required to make under our license agreement with The Schepens Eye Research Institute, Inc., or Schepens, under which we obtained an exclusive worldwide license under specified patents and technology owned or controlled by Schepens to research, develop, make, have made, use, sell, offer for sale and import products for the treatment of inflammation of the eye and adjoining tissues, or anti-IL-1 products, including isunakinra. See “Business—License and Collaboration Agreements” for additional information regarding our agreement with Schepens. In February 2016, we provided notice to Schepens of our termination of the License Agreement.

We enter into contracts in the normal course of business with CROs to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Net Operating Loss Carryforwards

As of December 31, 2015, we had $120.0 million of federal NOL carryforwards, state NOL carryforwards of $118.2 million and federal and state research and development tax credit carryforwards of $1.7 million and $1.2 million , respectively, available to reduce future taxable income. Due to our history of losses and lack of other positive evidence, we have determined that it is more likely than not that our deferred tax assets will not be realized, and therefore, the deferred tax assets were fully reduced by a valuation allowance. These federal and state NOL carryforwards and federal and state tax credit carryforwards expire at various dates beginning in 2029 through 2035, if not utilized. Utilization of the NOLs and general business tax credits carryforwards may be subject to a substantial limitation under Sections 382 and 383 of the Internal Revenue Code of 1986 as amended, which we refer to as the Code, due to changes in ownership of our company that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOLs and general business tax credits carryforwards that can be utilized annually to reduce future taxable income and tax, respectively. In general, an ownership

change, as defined by Section 382 of the Code, results from transactions increasing the ownership of "5-percent Shareholders" (as defined in the Code) in the stock of a corporation by more than 50 percentage points over a three-year period. We have not completed a study to determine the impact of this ownership change limitation on our NOL carryforwards under Section 382 of the Code. If we experienced a Section 382 ownership change in connection with our IPO or the private placement of our common stock in December 2014 or experience a Section 382 ownership charge as a result of future changes in our stock ownership, some of which changes are outside our control, the tax benefits related to the NOL carryforwards may be further limited or lost.

Off-balance Sheet Arrangements

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

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2015 , we had cash and cash equivalents of $36.1 million , primarily money market mutual funds consisting of U.S. government-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CROs and contract manufacturers globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the United States dollar are recorded based on exchange rates at the time such transactions arise. As of December 31, 2015 , substantially all of our total liabilities were denominated in the United States dollar.

Item 8. Financial Statements and Supplementary Data.

Our financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-27 of this Annual Report on Form 10-K.

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

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

The Company's management, with the participation of the Company's Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of the Company's disclosure controls and procedures as of December 31, 2015. 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 a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time period specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any 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. Based on the evaluation of the Company's disclosure controls and procedures as of December 31, 2015, the Company's Chief Executive Officer and Chief Financial Officer concluded that, as of such date, the Company's disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

The management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended. The Company's

internal control system was designed to provide reasonable assurance to the Company's management and board of directors regarding the preparation and fair presentation of published financial statements. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

The Company's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2015. In making this assessment, it used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in Internal Control—Integrated Framework (2013). Based on our assessment we believe that, as of December 31, 2015, the Company's internal control over financial reporting is effective based on those criteria.

This annual report does not include an attestation report of the company's registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by the company's registered public accounting firm pursuant to rules of the Securities and Exchange Commission that permit emerging growth companies, which we are, to provide only management's report in this annual report.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f)under the Exchange Act) that occurred during the three months ended December 31, 2015 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item is contained under the caption “Proposal 1- Election of Directors” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference.

Item 11. Executive Compensation.

Information required by this item is contained under the captions “Corporate Governance - Director Compensation” and “Information About Executive Compensation” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference.

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

Information required by this item relating to security ownership of certain beneficial owners and management is contained under the caption “Security Ownership of Certain Beneficial Owners and Management” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference. Information required by this item relating to securities authorized for issuance under equity compensation plans is contained under the caption “Information About Executive Compensation - Securities Authorized for Issuance Under Equity Compensation Plans” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference.

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

Information required by this item relating to transactions with related persons is contained under the caption “Corporate Governance - Certain Relationships and Related Transactions” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference. Information required by this item relating to director independence is contained under the caption “Corporate Governance - Determination of Independence” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

Information required by this item is contained under the caption “Corporate Governance - Independent Registered Public Accounting Firm Fees and Other Matters” in our 2016 proxy statement to be filed with the SEC within 120 days after December 31, 2015 and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) Financial Statements

The following financial statements and supplementary data are included in Item 8 of this Annual Report on Form 10-K.

(b) Exhibits

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding such exhibits, and are incorporated herein by reference.

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.

ELEVEN BIOTHERAPEUTICS, INC.

By: /s/ Abbie C. Celniker

Abbie C. Celniker, Ph.D.

President and Chief Executive Officer

March 24, 2016

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

/s/ Abbie C. Celniker **Abbie C. Celniker, Ph.D.**	Director, President and Chief Executive Officer (Principal Executive Officer)	March 24, 2016
/s/ John J. McCabe **John J. McCabe**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 24, 2016
/s/ Daniel S. Lynch **Daniel S. Lynch**	Chairman of the Board of Directors	March 24, 2016
/s/ David A. Berry **David A. Berry, M.D., Ph.D.**	Director	March 24, 2016
/s/ Paul G. Chaney **Paul G. Chaney**	Director	March 24, 2016
/s/ Jay S. Duker, M.D. **Jay S. Duker, M.D.**	Director	March 24, 2016
/s/ Wendy L. Dixon, Ph.D. **Wendy L. Dixon, Ph.D.**	Director	March 24, 2016
/s/ Barry J. Gertz, M.D., Ph.D. **Barry J. Gertz, M.D., Ph.D.**	Director	March 24, 2016
/s/ Jane V. Henderson **Jane V. Henderson**	Director	March 24, 2016
/s/ Cary G. Pfeffer **Cary G. Pfeffer, M.D.**	Director	March 24, 2016

EXHIBIT INDEX

Exhibit No.	Description
3.1	Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed with the SEC on February 18, 2014)
3.2	Amended and Restated By-laws of the Registrant (Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed with the SEC on April 16, 2015)
4.1	Specimen Stock Certificate evidencing the shares of common stock (Incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
4.2	Amended and Restated Investors' Rights Agreement of the Registrant (Incorporated by reference to Exhibit 4.2 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.1+	Amended and Restated 2009 Stock Incentive Plan (Incorporated by reference to Exhibit 10.1 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.2+	Form of Incentive Stock Option Agreement under the Amended and Restated 2009 Stock Incentive Plan (Incorporated by reference to Exhibit 10.2 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.3+	Form of Non-statutory Stock Option Agreement under the Amended and Restated 2009 Stock Incentive Plan (Incorporated by reference to Exhibit 10.3 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.4+	Form of Restricted Stock Agreement under the Amended and Restated 2009 Stock Incentive Plan (Incorporated by reference to Exhibit 10.4 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.5+	2014 Stock Incentive Plan (Incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.6+	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan (Incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.7+	Form of Non-statutory Stock Option Agreement under 2014 Stock Incentive Plan (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.8+	Form of Restricted Stock Unit Agreement under 2014 Stock Incentive Plan (Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the SEC on June 29, 2015)
10.9†	License Agreement dated July 13, 2010 by and between the Registrant and The Schepens Eye Research Institute, Inc. (Incorporated by reference to Exhibit 10.8 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.10†	Collaboration and License Agreement dated May 28, 2013 by and between the Registrant and ThromboGenics N.V. (Incorporated by reference to Exhibit 10.9 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.11	Loan and Security Agreement dated May 27, 2010 by and between the Registrant and Silicon Valley Bank, as modified (Incorporated by reference to Exhibit 10.10 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.12	Lease Agreement dated January 14, 2010 by and between the Registrant and ARE-MA Region No. 38, LLC, as amended (Incorporated by reference to Exhibit 10.11 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.13	Form of Indemnification Agreement by and between the Registrant and each of its directors and executive officers (Incorporated by reference to Exhibit 10.12 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.14+	2014 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.13 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.15+	Employment Agreement, dated December 23, 2013, by and between the Registrant and Abbie C. Celniker, Ph.D. (Incorporated by reference to Exhibit 10.14 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)

Exhibit No.	Description
10.16+	Employment Agreement, dated December 26, 2013, by and between the Registrant and Karen L. Tubridy, Pharm.D (Incorporated by reference to Exhibit 10.16 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)
10.17*+	Employment Agreement, dated August 28, 2015, by and between the Registrant and John J. McCabe
10.18+	Form of Director Restricted Stock Agreement under 2014 Stock Incentive Plan (Incorporated by reference to Exhibit 10.18 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)
10.19	Securities Purchase Agreement, dated November 24, 2014, by and among the Registrant and the persons party thereto (Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the SEC on December 1, 2014)
10.20	Form of Warrant to Purchase Common Stock, by and between the Registrant and the persons party thereto (Incorporated by reference to Exhibit 10.2 to our Current Report on Form 8-K filed with the SEC on December 1, 2014)
10.21	Registration Rights Agreement, dated November 24, 2014, by and among the Registrant and the persons party thereto (Incorporated by reference to Exhibit 10.3 to our Current Report on Form 8-K filed with the SEC on December 1, 2014)
10.22	Second Loan Modification, dated November 25, 2014, by and among the Registrant and Silicon Valley Bank (Incorporated by reference to Exhibit 10.22 to our Registration Statement on Form S-1 filed with the SEC on December 19, 2014)
10.23	Form of Warrant issued to Silicon Valley Bank and Life Science Loans, LLC dated November 25, 2014 (Incorporated by reference to Exhibit 10.23 to our Registration Statement on Form S-1 filed with the SEC on December 19, 2014)
10.24	Second Amendment to Lease, dated August 18, 2015, by and between the Registrant and ARE-MA Region No. 38, LLC (Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q/A filed with the SEC on November 14, 2015)
10.25*	Consent and Third Amendment to Loan and Security Agreement, dated November 25, 2014, by and among the Registrant and Silicon Valley Bank
10.26*†	Amendment #1 to License Agreement dated December 22, 2015 by and between the Registrant and The Schepens Eye Research Institute, Inc.
23.1*	Consent of Ernst & Young LLP
31.1*	Rule 13a-14(a) Certification of Principal Executive Officer
31.2*	Rule 13a-14(a) Certification of Principal Financial Officer
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. §1350
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

\+ This exhibit is a compensatory plan or arrangement in which executive officers or directors of the Company participate.

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Eleven Biotherapeutics, Inc.

We have audited the accompanying balance sheets of Eleven Biotherapeutics, Inc. (the "Company") as of December 31, 2015 and 2014, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2015. 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. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Eleven Biotherapeutics, Inc. at December 31, 2015 and 2014, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2015 in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has recurring losses from operations and has an accumulated deficit. In addition, subsequent to December 31, 2015, the Company was required to provide cash collateral in a separate bank account with the lender equal to the Company's then outstanding debt in accordance with its loan agreements with the lender. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 24, 2016

ELEVEN BIOTHERAPEUTICS, INC.
BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2015	2014
Assets		
Current assets:		
Cash and cash equivalents	$ 36,079	$ 54,059
Prepaid expenses and other current assets	232	342
Total current assets	36,311	54,401
Property and equipment, net	407	486
Restricted cash	94	94
Other assets	13	19
Total assets	$ 36,825	$ 55,000
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,246	$ 2,458
Accrued expenses	1,794	1,987
Notes payable, current portion (Note 14)	4,134	251
Deferred revenue, current portion	406	506
Total current liabilities	7,580	5,202
Other liabilities	423	4
Notes payable, net of current portion (Note 14)	9,763	9,749
Warrant liability	115	3,219
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share; 5,000,000 shares authorized at December 31, 2015 and 2014 and no shares issued and outstanding at December 31, 2015 and 2014	—	—
Common stock, $0.001 par value per share; 200,000,000 shares authorized at December 31, 2015 and 2014 and 19,619,124 and 17,933,260 shares issued and outstanding at December 31, 2015 and 2014, respectively	20	18
Additional paid-in capital	144,126	128,558
Accumulated deficit	(125,202)	(91,750)
Total stockholders' equity	18,944	36,826
Total liabilities and stockholders' equity	$ 36,825	$ 55,000

See accompanying notes.

ELEVEN BIOTHERAPEUTICS, INC.
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except per share data)

	Year Ended December 31,		
	2015	2014	2013
Revenue:			
Collaboration revenue	$ 490	$ 2,243	$ 1,334
Other revenue	500	—	—
Total revenue	990	2,243	1,334
Operating expenses:			
Research and development	26,336	26,703	13,788
General and administrative	9,850	8,471	4,024
Total operating expenses	36,186	35,174	17,812
Loss from operations	(35,196)	(32,931)	(16,478)
Other income (expense):			
Other income (expense), net	3,139	(849)	(147)
Interest expense	(1,395)	(376)	(1,400)
Total other income (expense), net	1,744	(1,225)	(1,547)
Net loss and comprehensive loss	$ (33,452)	$ (34,156)	$ (18,025)
Cumulative preferred stock dividends and accretion of preferred stock discount	—	(519)	(3,857)
Net loss applicable to common stockholders	$ (33,452)	$ (34,675)	$ (21,882)
Net loss per share applicable to common stockholders—basic and diluted	$ (1.76)	$ (2.37)	$ (16.18)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	18,993	14,644	1,352

See accompanying notes.

ELEVEN BIOTHERAPEUTICS, INC.
STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
	(in thousands, except share data)								
Balance at December 31, 2012	45,250,000	$45,035	—	$ —	1,205,038	$ 1	$ 272	$ (39,569)	$ (39,296)
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	286,837	1	34	—	35
Issuance of series B convertible preferred stock, net of issuance costs of $163,000	—	—	5,142,859	7,439	—	—	—	—	—
Issuance of series B convertible preferred stock upon the conversion of notes payable	—	—	2,060,986	4,204	—	—	—	—	—
Beneficial conversion feature of Series B preferred stock discount	—	—	—	(163)	—	—	163	—	163
Accretion of Series B preferred stock discount	—	—	—	163	—	—	(163)	—	(163)
Issuance of warrants for the purchase of common stock							1,685		1,685
Exercise of warrants	—	—	—	—	144,262	—	9	—	9
Stock-based compensation expense	—	—	—	—	—	—	1,260	—	1,260
Net loss	—	—	—	—	—	—	—	(18,025)	(18,025)
Balance at December 31, 2013	45,250,000	45,035	7,203,845	11,643	1,636,137	2	3,260	(57,594)	(54,332)
Initial public offering, net of issuance costs of $7.3 million	(45,250,000)	(45,035)	(7,203,845)	(11,643)	14,010,424	14	106,868	—	106,882
Issuance of common stock, net of issuance costs of $1.5 million	—	—	—	—	1,743,680	2	15,417	—	15,419
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	190,701	—	65	—	65
Exercise of warrants	—	—	—	—	352,318	—	15	—	15
Conversion of preferred stock warrant to common stock warrant	—	—	—	—	—	—	247	—	247
Issuance of common stock warrants in connection with notes payable	—	—	—	—	—	—	254	—	254
Stock-based compensation expense	—	—	—	—	—	—	2,432	—	2,432
Net loss	—	—	—	—	—	—	—	(34,156)	(34,156)
Balance at December 31, 2014	—	—	—	—	17,933,260	18	128,558	(91,750)	36,826
Issuance of common stock, net of issuance costs of $819,000	—	—	—	—	1,446,781	2	12,648	—	12,650
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	239,083	—	63	—	63
Issuance of common stock warrants in connection with notes payable	—	—	—	—	—	—	328	—	328
Stock-based compensation expense	—	—	—	—	—	—	2,529	—	2,529
Net loss	—	—	—	—	—	—	—	(33,452)	(33,452)
Balance at December 31, 2015	—	$ —	—	$ —	19,619,124	$ 20	$ 144,126	$ (125,202)	$ 18,944

See accompanying notes.

ELEVEN BIOTHERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2015	**2014**	**2013**
Operating activities			
Net loss	$ (33,452)	$ (34,156)	$ (18,025)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	366	410	438
Non-cash interest expense	108	36	36
Stock-based compensation expense	2,529	2,432	1,260
Change in fair value of warrant liability	(3,104)	123	150
Change in fair value of convertible notes payable, included in interest expense	—	—	991
Loss on extinguishment of debt	—	459	—
Expense related to issuance costs allocated to warrants measured at fair value	—	276	—
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	110	(259)	167
Restricted cash	—	—	40
Accounts payable	(1,212)	1,021	(211)
Accrued expenses	226	1,315	190
Deferred revenue	(100)	(964)	1,470
Net cash used in operating activities	(34,529)	(29,307)	(13,494)
Investing activities			
Purchases of property and equipment	(287)	(137)	—
Net cash used in investing activities	(287)	(137)	—
Financing activities			
Proceeds from issuance of convertible notes payable	—	—	3,500
Proceeds from issuance of notes payable, net of debt issuance costs	5,000	9,883	3,000
Payments on equipment financing and notes payable	(877)	(4,633)	(511)
Proceeds from issuance of series B convertible preferred stock, net of issuance costs	—	—	8,837
Proceeds from issuance of common stock and common stock warrants, net of issuance costs	12,650	70,237	—
Proceeds from exercise of common stock options and common stock warrants	63	74	31
Deferred initial public offering costs	—	—	(1,303)
Net cash provided by financing activities	16,836	75,561	13,554
Net (decrease) increase in cash and cash equivalents	(17,980)	46,117	60
Cash and cash equivalents at beginning of period	54,059	7,942	7,882
Cash and cash equivalents at end of period	$ 36,079	$ 54,059	$ 7,942
Supplemental non-cash financing activities			
Conversion of Series A and Series B preferred stock into 8,260,444 shares of common stock	$ —	$ 56,678	$ —
Conversion of preferred stock warrants into common stock warrants	$ —	$ 247	$ —
Conversion of notes payable and accrued interest thereon into Series B convertible preferred stock	$ —	$ —	$ 4,204
Issuance of warrants to purchase common stock	$ 328	$ 3,300	$ 1,685
Supplemental cash flow information			
Cash paid for interest	$ 930	$ 335	$ 264

See accompanying notes.

ELEVEN BIOTHERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

Eleven Biotherapeutics, Inc. (the “Company”), formerly known as Denovo Therapeutics, Inc. and Newco LS14, Inc., a Delaware corporation formed on February 25, 2008, is a biopharmaceutical company with a proprietary protein engineering platform, called AMP-Rx, that it applies to the discovery and development of protein therapeutics to treat diseases of the eye. The Company's most advanced product candidate, which is still in preclinical development, is EBI-031, which the Company designed, engineered and generated using its AMP-Rx platform and is developing as an intravitreal injection for diabetic macular edema, or DME, and uveitis. In 2015, the Company initiated the necessary chemistry, manufacturing and control, or CMC, development work and nonclinical safety studies of EBI-031 to support the submission of an investigational new drug application ("IND") to the United States Food and Drug Administration ("FDA").

On May 28, 2013 , the Company entered into a collaboration and license agreement with ThromboGenics N.V (“ThromboGenics”). Under the agreement, the Company and ThromboGenics are collaborating to identify protein or peptide therapeutics that directly modulate any of a specified set of targets in a novel pathway in retinal disease (See Note 3).

These financial statements have been prepared in accordance with U.S. generally accepted accounting principles (“GAAP”).

Liquidity

The Company has financed its operations to date primarily through private placements of its common stock and preferred stock and convertible bridge notes, venture debt borrowings and its initial public offering ("IPO") and as of December 31, 2015, the Company had cash and cash equivalents totaling approximately $36.1 million , net working capital of $28.7 million and an accumulated deficit of $125.2 million . Additionally, as described in Note 14, in January 2016, as a result of the outcome of the Company’s Phase 3 clinical trial of its lead product candidate, isunakinra (EBI-005), for the treatment of severe allergic conjunctivitis, the Company was required to fund a cash collateral account with Silicon Valley Bank ("SVB") in an amount equal to approximately $15.1 million , representing the outstanding obligations under the Loan and Security Agreement with SVB dated May 27, 2010, as amended on September 4, 2012, November 25, 2014 and December 4, 2015 (the “Loan Agreement”). In March 2016, the Company prepaid all outstanding amounts owed to SVB and terminated the Loan Agreement with existing cash on hand.

The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. The Company is subject to a number of risks similar to other early-stage life science companies, including, but not limited to, successful discovery and development of its product candidates, raising additional capital with favorable terms, development by its competitors of new technological innovations, protection of proprietary technology and market acceptance of the Company’s products. The successful discovery and development of product candidates requires substantial working capital which may not be available to the Company on favorable terms. These factors raise substantial doubt about the Company’s ability to continue as a going concern. In order for the Company to continue operations beyond 2016 and be able to discharge its liabilities and commitments in the normal course of business, the Company has taken or will take the following steps, not all of which are entirely within the Company’s control:

- The Company engaged an investment bank to conduct a review of strategic alternatives to maximize shareholder value. Potential strategic alternatives to be explored and evaluated during the review process may include the sale of the Company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of the Company’s proprietary technologies. The Company cannot provide any commitment regarding when or if this strategic review process will result in any type of transaction and no assurance can be given that the Company will determine to pursue a potential sale, strategic partnership or licensing arrangement.

- The Company does not see an immediate path forward for isunakinra (EBI-005) and has implemented a plan to wind down the development activities associated with isunakinra.

- The Company has conducted a review of its operations and implemented a plan to reduce operating expenses to align with current operating conditions.

- As described in Note 14, on March 1, 2016, the Company prepaid all outstanding amounts owed to SVB under the Loan Agreement. The Company continues to evaluate other financing alternatives to provide additional working capital on terms that are consistent with the Company's business plans.

The Company believes that its cash and cash equivalents at December 31, 2015 of $36.1 million will be sufficient to fund the Company's current operating plan into the fourth quarter of 2016. If the Company is unable to obtain adequate financing or engage in a strategic transaction on acceptable terms and when needed, it will be required to implement further cost reduction strategies. These factors, and the factors described above, continue to raise substantial doubt about the Company's ability to continue as a going concern. The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

2. Significant Accounting Policies

Use of Estimates

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

Revenue Recognition

To date, the Company's revenue has been primarily from the collaboration and license agreement with ThromboGenics (See Note 3) and, to a lesser extent, from a license agreement.

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") 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. Amounts expected to be recognized as revenue within the twelve months following the balance sheet date are classified in current liabilities. Amounts not expected to be recognized as revenue within the twelve months following the balance sheet date are classified as deferred revenue, net of current portion.

The Company evaluates multiple-element arrangements based on the guidance in ASC Topic 605-25, *Revenue Recognition-Multiple-Element Arrangements* ("ASC 605-25"). Pursuant to the guidance in ASC 605-25, the Company evaluates multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires the Company to make judgments about the individual deliverables and whether

such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use a deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that can provide the undelivered items. The consideration received under the arrangement that is fixed or determinable is then allocated among the separate units of accounting using the relative selling price method. The Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price ("BESP") if neither VSOE nor TPE is available. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, the Company recognizes revenue from the combined unit of accounting over the Company's contractual or estimated performance period for the undelivered elements, which is typically the term of the Company's research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (1) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from its performance to achieve the milestone, (2) the consideration relates solely to past performance and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, assuming all other revenue recognition criteria are met.

Research and Development Costs

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company's proprietary protein engineering platform called AMP-Rx and its protein-based therapeutics, including isunakinra and EBI-031. The research and development costs include personnel-related costs, stock-based compensation, facilities, research-related overhead, clinical trial costs, manufacturing costs and other contracted services, license fees, and other external costs.

In certain circumstances, the Company is required to make advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the advance payments are deferred and are expensed when the activity has been performed or when the goods have been received.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees and directors, including grants of employee stock options, to be recognized as expense in the statements of operations based on their grant date fair values. For stock options granted to employees and to members of the Board of Directors for their services on the Board of Directors, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense, net of estimated forfeitures, equal to the grant date fair value of stock options on a straight-line basis over the requisite service period . For awards subject to both performance and service-based vesting conditions, the Company recognizes stock-based compensation expense using an accelerated recognition method.

The Company expenses restricted stock awards and restricted stock units to employees and directors based on the fair value of the award on a straight-line basis over the associated service period of the award. Awards of restricted stock to non-employees are adjusted through stock-based compensation expense at each reporting period end to reflect the current fair value of such awards and expensed on a straight-line basis.

The Company records the expense for stock option grants subject to performance-based milestone vesting using the accelerated attribution method over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

Share-based payments issued to non-employees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC 718 and ASC Topic 505, *Equity* . For equity instruments granted to non-employees, the Company recognizes stock-based compensation expense on a straight-line basis.

During the years ended December 31, 2015 , 2014 and 2013 , the Company recorded stock-based compensation expense, which was allocated as follows in the statements of operations (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Research and development expense	$ 1,032	$ 1,069	$ 1,150
General and administrative expense	1,497	1,363	110
	$ 2,529	$ 2,432	$ 1,260

No related tax benefits were recognized for the years ended December 31, 2015 , 2014 and 2013 .

Income Taxes

The Company provides for income taxes using the liability method. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2015 and 2014 , the Company did not have any significant uncertain tax positions.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the years ended December 31, 2015 , 2014 and 2013 , comprehensive loss was equal to net loss.

Cash and Cash Equivalents

The Company considers highly liquid investments with a maturity of 3 months or less when purchased to be cash equivalents.

Concentrations of Credit Risk and Off-Balance-Sheet Risk

The Company has no significant off-balance-sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash and cash equivalents. The Company places its cash and cash equivalents in a custodian account in accredited financial institutions.

Fair Value of Financial Instruments

The fair value hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three broad levels as follows: Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities; Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The following table presents information about the Company's financial assets and liabilities that have been measured at fair value, and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value. The Company determines the fair value of the common stock warrants (See Note 9) using Level 3 inputs.

The following table summarizes the assets and liabilities measured at fair value on a recurring basis at December 31, 2015 (in thousands):

Description	December 31, 2015	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash and cash equivalents	$ 36,079	$ 36,079		
Restricted cash	94	94		
Total assets	$ 36,173	$ 36,173	$ —	$ —
Liabilities:				
Warrant liability	$ 115	$ —	$ —	$ 115
Total liabilities	$ 115	$ —	$ —	$ 115

The following table summarizes the assets and liabilities measured at fair value on a recurring basis at December 31, 2014 (in thousands):

Description	December 31, 2014	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash and cash equivalents	$ 54,059	$ 54,059	$ —	$ —
Restricted cash	94	94	—	—
Total assets	$ 54,153	$ 54,153	$ —	$ —
Liabilities:				
Warrant liability	$ 3,219	$ —	$ —	$ 3,219
Total liabilities	$ 3,219	$ —	$ —	$ 3,219

The carrying amounts reflected in the balance sheets for prepaid expenses and other current assets, other assets, accounts payable and accrued expenses approximate their fair values at December 31, 2015 and 2014 , due to their short-term nature. At December 31, 2015 , the carrying value of the notes payable approximates fair value.

There have been no changes to the valuation methods during the years ended December 31, 2015 and 2014 . The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between levels during the years ended December 31, 2015 and 2014 .

Property and Equipment

Property and equipment consists of lab equipment, furniture and fixtures, computer equipment, software, and leasehold improvements. Expenditures for maintenance and repairs are recorded to expense as incurred. Major betterments are capitalized as additions to property and equipment. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-Lived Assets

The Company periodically evaluates its long-lived assets for potential impairment in accordance with ASC Topic 360, *Property, Plant and Equipment* . Potential impairment is assessed when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the assets, considering a number of factors, including past operating results, budgets and economic projections, market trends and product development cycles. If impairments are identified, assets are written down to their estimated fair value. The Company has not recognized any impairment charges through December 31, 2015 .

Warrant Liability

The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. These warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a component of other expense, until the earlier of their exercise or expiration or upon the completion of a liquidation event. The following table sets forth a summary of changes in the fair value of the Company's common stock warrant liability, which represented a recurring measurement classified within Level 3 of the fair value hierarchy, wherein fair value was estimated using significant unobservable inputs (in thousands):

Beginning balance, January 1, 2015	$ 3,219
Change in fair value of common stock warrants	(3,104)
Ending balance, December 31, 2015	$ 115

Segment Information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate

resources and assess performance. The Company views its operations and manages its business in one operating segment. The Company operates in one geographic segment.

Subsequent Events (See Note 14)

The Company considers events or transactions that occur after the balance sheet date, but prior to the issuance of the financial statements, to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated through the date these financial statements were issued.

Net Loss Per Share

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

The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect or the exercise prices were greater than the average market price of the common shares.

	As of December 31,		
	2015	**2014**	**2013**
Convertible preferred stock	—	—	8,260,444
Stock options	1,803,574	1,438,528	1,346,238
Unvested restricted stock	41,657	125,027	163,353
Restricted stock units	150,932	—	—
Common stock warrants	926,840	899,340	333,799
Preferred stock warrants	—	—	30,708
	2,923,003	2,462,895	10,134,542

Recent Accounting Pronouncements

In the second quarter of 2014, the Financial Accounting Standards Board (FASB) issued guidance applicable to revenue recognition that will be effective for the Company for the year ending December 31, 2018. The new guidance must be adopted using either a full retrospective approach for all periods presented or a modified retrospective approach. Earlier application is permitted only as of annual reporting periods beginning after December 15, 2016, including interim reporting periods within that reporting period. The new guidance applies a more principles-based approach to recognizing revenue. The Company is evaluating the new guidance and the expected effect on the Company's financial statements.

In August 2014, the FASB issued Accounting Standards Update No. 2014-15, *Going Concern (Subtopic 205-40)* ("ASU 2014-15"). ASU 2014-15 requires management of all entities to evaluate whether there are conditions and events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the financial statements are issued (or available to be issued when applicable). The guidance is effective for fiscal years beginning after December 15, 2016 and for interim periods within that fiscal year. The Company does not expect the adoption of this guidance to have a material effect on the Company's financial statements, but may require further disclosure in its financial statements once adopted.

In April 2015, the FASB issued Accounting Standard Update No. 2015-3, " *Interest – Imputation of Interest (Subtopic 835-30)* ("ASU 2015-3")." ASU 2015-3 requires debt issuance costs related to a recognized debt liability to be presented in the balance sheet as a direct deduction from the carrying amount of the debt liability, consistent with debt discounts. The recognition and measurement guidance for debt issuance costs are not affected by the new amendment. The new guidance will be applied on a retrospective basis to each prior reporting period presented. Upon transition, the Company is required to comply with

applicable disclosures for a change in accounting principle. The amendment is effective for financial statements issued for fiscal years beginning after December 15, 2015, and interim periods within those fiscal years. Early adoption is permitted. The Company does not expect the adoption of this guidance to have a material effect on the Company's financial statements.

In November 2015, the FASB issued Accounting Standard Update No. 2015-17, *Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). ASU 2015-17 requires companies to classify all deferred tax assets and liabilities as noncurrent on the balance sheet instead of separating deferred taxes into current and noncurrent amounts. The guidance is effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted. The guidance may be adopted on either a prospective or retrospective basis. The Company does not expect the adoption of this guidance to have a material effect on the Company's financial statements.

In January 2016, the FASB issued Accounting Standard Update No. 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities* ("ASU 2016-01"). ASU 2016-01 requires entities to measure equity investments that do not result in consolidation and are not accounted for under the equity method at fair value, and recognize any changes in fair value in net income unless the investments qualify for the new measurement alternative. For financial liabilities measured using the fair value option in Accounting Standards Codification 825, *Financial Instruments* , entities will need to present any change in fair value caused by a change in instrument-specific credit risk (own credit risk) separately in other comprehensive income. ASU 2016-01 also changes certain disclosure requirements and other aspects of current GAAP. It does not change the guidance for classifying and measuring investments in debt securities and loans. The guidance is effective for annual periods, beginning after December 15, 2017, including interim periods within those annual periods. Early adoption is not permitted. The Company does not expect the adoption of this guidance to have a material effect on the Company's financial statements.

In February 2016, the FASB issued Accounting Standard Update No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"). ASU 2016-02 addresses the financial reporting of leasing transactions. Under current guidance for lessees, leases are only included on the balance sheet if certain criteria, classifying the agreement as a capital lease, are met. This update will require the recognition of a right-of-use asset and a corresponding lease liability, discounted to the present value, for all leases that extend beyond 12 months. For operating leases, the asset and liability will be expensed over the lease term on a straight-line basis, with all cash flows included in the operating section of the statement of cash flows. For finance leases, interest on the lease liability will be recognized separately from the amortization of the right-of-use asset in the statement of operations and the repayment of the principal portion of the lease liability will be classified as a financing activity while the interest component will be included in the operating section of the statement of cash flows. This guidance is effective for annual and interim reporting periods beginning after December 15, 2018. Early adoption is permitted. The Company has not yet completed the analysis of how adopting this guidance will affect our financial statements.

3. Collaboration Agreement

On May 28, 2013 , the Company entered into the collaboration and license agreement with ThromboGenics. Under this agreement, the Company and ThromboGenics are collaborating to identify protein or peptide therapeutics that directly modulate any of a specified set of targets in a novel pathway in retinal disease. The Company and ThromboGenics jointly own any know-how made by or on behalf of either party in the course of the research and any patent rights claiming such know-how. The Company has granted ThromboGenics an exclusive, sublicenseable, royalty-bearing license under the Company's rights in these patent rights and know-how, as well as under any other patent rights and know-how that the Company controls during the research term that are necessary for ThromboGenics to perform its obligations to research, develop, manufacture and commercialize collaboration products.

ThromboGenics has funded certain research and development services performed by the Company during the research term, which is initially thirty (30) months and automatically extends to the extent that the parties mutually agree in writing. The activities under the agreement are governed by a Joint Research Committee ("JRC"). The JRC is responsible for overseeing the research activities under the agreement. The JRC will disband at the end of the research term. The initial research term concluded in November 2015. However the parties have agreed to continue the existing Collaboration and License Agreement to provide the Company the time required to complete additional research activities for no additional consideration. The Company expects the relevant data to become available in the second quarter of 2016. To date, no collaboration products have been identified.

The Company received a $1.75 million upfront payment and will receive a set rate per annual full time equivalent personnel working on the collaboration, which will be paid quarterly in advance. The Company is also eligible to receive up to an

aggregate of $25.0 million in milestone payments and may also receive low single-digit royalties on sales of any commercialized products resulting from the collaboration. There are no commercialization or sales-based milestones under the agreement.

The agreement expires when all of ThromboGenics' payment obligations expire. The agreement provides that either party may terminate the agreement in the event of the other party's insolvency, bankruptcy or comparable proceedings, or if the other party materially breaches the agreement and does not cure such breach during a specified cure period. The Company may terminate the agreement if ThromboGenics or any of its affiliates or licensees challenges the patent rights licensed to ThromboGenics. ThromboGenics may terminate the agreement for convenience by providing the Company with notice following the end of the research term. There are no refund provisions in this agreement.

The Company accounts for this agreement pursuant to ASC 605-25. The Company identified the following deliverables in this agreement:

- an exclusive license to the Company's intellectual property that is necessary for ThromboGenics to perform its obligations during the research term. ("Research License Deliverable");
- the Company's obligation to provide research services ("Research Services Deliverable"); and
- the Company's participation on the JRC ("JRC Deliverable").

The Company determined that the licenses to future collaboration product candidates are contingent upon the identification of future product candidates as a result of the Research Services, and as such, have not been identified as a separate deliverable at the inception of the arrangement.

The Company determined that the Research License Deliverable did not have standalone value from the Research Services Deliverable because the License is not sold separately and could not be resold on a standalone basis. While the intellectual property rights granted to ThromboGenics under this agreement are sublicensable, the Company determined that the Research License Deliverable does not have value without the Research Services Deliverable as the Company's intellectual property could not be sold separately or utilized to develop product candidates without the expertise of the Company that is provided through the Research Services Deliverable. The Company concluded that ThromboGenics does not have the expertise to perform the specialized research activities and such expertise is not readily available in the marketplace. As such, the Company has accounted for the Research License Deliverable and the Research Services Deliverable as a combined unit of accounting. The Company determined that the JRC Deliverable has standalone value from the Research License Deliverable and the Research Services Deliverable (the combined unit of account). The Company has determined that the best estimate of selling price of the JRC Deliverable is de minimis, and thus the non-contingent arrangement consideration has been allocated to the combined unit of accounting.

The Company is recognizing the arrangement consideration using the proportional performance method, by which the amounts are recognized in proportion to the costs incurred based on full time equivalent personnel efforts. The Company recorded revenue of $0.5 million , $2.2 million and $1.3 million for the year ended December 31, 2015 , 2014 and 2013 , respectively. The costs incurred by the Company related to the research activities are recorded as research and development expense in the statement of operations and comprehensive loss.

The potential milestone payments under this agreement are comprised of (i) up to an aggregate of $10.0 million of milestone payments due upon the achievement of specified preclinical and clinical development milestone events, and (ii) up to an aggregate of $15.0 million in milestone payments due upon the achievement of specified regulatory milestone events. The Company believes that certain of the preclinical and clinical development milestone payments are consistent with the definition of substantive milestones, and, accordingly, the Company will recognize these payments upon the achievement of such milestones, if any, in the period that such milestone is achieved. The remaining clinical development and regulatory milestone payments were not considered substantive and will be recognized upon achievement of the revenue recognition criteria of ASC 605. Factors considered in the evaluation of whether the milestones are substantive included the degree of risk associated with performance of the milestone, the level of effort and investment required, whether the milestone consideration was reasonable relative to the deliverables and whether the milestone was earned at least in part based on the Company's performance.

As of December 31, 2015 , the Company had not received any milestone or royalty payments.

4. Property and Equipment

Property and equipment and related accumulated depreciation are as follows ($ in thousands):

	Estimated Useful Life (Years)	December 31, 2015	December 31, 2014
Lab equipment	5	$ 1,961	$ 1,795
Furniture and fixtures	4	107	107
Computer equipment	3	171	206
Software	3	25	25
Leasehold improvements	Lesser of useful life or remaining lease term	100	100
		2,364	2,233
Less accumulated depreciation and amortization		(1,957)	(1,747)
Total property and equipment, net		$ 407	$ 486

Depreciation expense amounted to $366,000 , $410,000 and $438,000 for the years ended December 31, 2015 , 2014 and 2013 , respectively.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2015	December 31, 2014
Development costs	$ 931	$ 834
Employee compensation	573	874
Professional fees	194	195
Interest	88	84
Other	8	—
	$ 1,794	$ 1,987

6. Indebtedness

Term Loan

In May 2010, the Company entered into the Loan Agreement with SVB, pursuant to which the Company could borrow up to $1.5 million . The Loan Agreement was secured by substantially all of the Company's assets, excluding its intellectual property. Outstanding borrowings bore interest at a fixed per annum rate equal to 8.25% . The Company borrowed the entire $1.5 million in two equal advances in June 2010 and July 2010, and principal and interest payments were due through September 2013.

In September 2012, the Company modified the Loan Agreement with SVB such that the Company was able to borrow up to $5.0 million (the "First Loan Modification Agreement"). On September 4, 2012, the Company borrowed $2.0 million under the First Loan Modification Agreement, of which $0.5 million of the proceeds was used to repay the outstanding balance of the original Loan and Security Agreement. The interest rate on the amount borrowed in 2012 was fixed at 5.75% per annum. On February 1, 2013, the Company borrowed the remaining loan amount of $3.0 million under the First Loan Modification Agreement. The interest rate on the amount borrowed in 2013 was fixed at 5.75% per annum. The Company made interest-only payments until October 1, 2013, and was required to make consecutive equal monthly payments of principal, plus accrued interest, over the remaining term. The Company accounted for the amendment as a modification, as the terms of the amendment were not substantially different from the original terms of the Loan Agreement.

In November 2014, the Company modified the Loan Agreement with SVB such that the Company was able to increase the amount it may borrow under this venture debt facility to $15.0 million (the "Second Loan Modification Agreement"). On November 25, 2014, the Company borrowed a first tranche of $10.0 million , of which amount approximately $3.2 million was

applied to the repayment of outstanding debt obligations to SVB under the First Loan Modification Agreement, including accrued interest. The Company borrowed the remaining $5.0 million on May 11, 2015. The interest rate for each tranche was set at the funding date for such tranche at 3.75% above the prime lending rate published in the Wall Street Journal. The interest rate on the amount borrowed in 2014 was fixed at 7.00% per annum.

The Company accounted for the Second Loan Modification Agreement as an extinguishment as the terms of the Second Loan Modification Agreement were substantially different from the original terms of the Loan Agreement, and recorded a loss on extinguishment of $0.5 million , which was recorded in other expenses on the Statement of Operations and Comprehensive Loss. The warrants issued in connection with the debt (see Note 9) were treated as part of the extinguishment loss.

In connection with the Second Loan Modification Agreement, the Company issued to SVB and Life Science Loans, LLC warrants to purchase a total of 27,500 shares of the Company's common stock at a per share exercise price of $11.04 (the "Warrants"). In connection with the Company's draw-down of $5.0 million in May 2015 the Warrants automatically became exercisable for the purchase of an additional 27,500 shares of common stock at a per share exercise price of $11.83 . The exercise price and the number of shares are subject to adjustment upon a merger event, reclassification of the shares of common stock, subdivision or combination of the shares of common stock or certain dividend payments. The Warrants may be exercised on a cashless basis at any time. The Warrants are exercisable until November 24, 2024 and will be exercised automatically on a net issuance basis if not exercised prior to the expiration date and if the then-current fair market value of one share of common stock is greater than the exercise price then in effect.

On December 4, 2015, the Company entered into a Consent and Third Amendment to Loan and Security Agreement (the "Third Loan Amendment") with SVB in connection with the assignment of the Company's proprietary Supermin ™ albumin variant assets to a third party pursuant to a Patent Assignment and License Agreement dated as of December 4, 2015.

The Third Loan Amendment modified the repayment terms of the Loan Agreement under specified circumstances and the circumstances under which the Company was required to fund a cash collateral account with SVB in an amount equal to the outstanding amount under the Loan Agreement. As a result of the Company's Phase 3 clinical trial of isunakinra for the treatment of severe allergic conjunctivitis, which constituted a "Study Discontinuation Event" pursuant to the terms of the Loan Agreement, the Company was required to fund a cash collateral account with SVB in an amount equal to approximately $15.1 million , representing the outstanding obligations under the Loan Agreement.

The Company accounted for the Third Loan Amendment as a modification as the terms of the Third Loan Amendment were not substantially different from the terms of the Second Loan Amendment. The Company recorded a debt discount of $328,000 , which is being accreted as interest expense over the remaining term of the loan. The Company recorded interest expense of $102,000 for the year ended December 31, 2015. The offsetting credit to the debt discount was recorded as additional paid-in-capital.

The Company also accreted the final payment over the term of the debt using the effective interest method. As of December 31, 2015 , the Company had accreted $354,000 of the final payment. The Company also evaluated the debt for embedded features that need to be bifurcated, noting that the contingent interest feature and events of default were required to be bifurcated, but were concluded to be de minimis in value at inception and at December 31, 2015 . At December 31, 2015 and 2014 , $14.1 million and $10.0 million were outstanding on the term loan under the Loan Agreement, respectively. On March 1, 2016, the Company prepaid all outstanding amounts owed to SVB and terminated the Loan Agreement (See Note 14).

Scheduled principal payments on outstanding debt, as of December 31, 2015 , are as follows (in thousands):

2016	$	4,263
2017		4,978
2018		4,883
	$	14,124

7. Commitments and Contingencies

Operating Lease

The Company leases its corporate headquarters under an operating lease that is scheduled to expire on April 30, 2018. The Company recorded $494,000 , $416,000 and $725,000 in rent expense for the years ended December 31, 2015 , 2014 and 2013 , respectively. The operating lease requires the Company to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed below.

The minimum aggregate future lease commitment at December 31, 2015 is as follows (in thousands):

2016	$	642
2017		671
2018		227
	$	1,540

The Schepens Eye Research Institute, Inc. / The Massachusetts Eye and Ear Infirmary

In July 2010, the Company entered into a license agreement with The Schepens Eye Research Institute, Inc. (“Schepens”), pursuant to which Schepens granted the Company an exclusive royalty-bearing license, with the right to grant sublicenses, to certain intellectual property rights for the development of IL-1blocker for ophthalmic indications. The Company is obligated to pay Schepens up to $4.7 million and issue up to 105,000 shares of its common stock in milestone payments, contingent upon the issuance of certain patents. In addition, the Company is obligated to pay Schepens a tiered single-digit royalty based on net sales of the licensed product. During the year ended December 31, 2014, the Company paid Schepens and expensed $350,000 upon the achievement of a clinical milestone. The Company terminated the agreement with Schepens subsequent to December 31, 2015 (See Note 14).

Legal Contingencies

The Company does not currently have any contingencies related to ongoing legal matters.

8. Common Stock

The voting dividend and liquidation rights of holders of shares of common stock are subject to and qualified by the rights, powers and preferences of the holders of the shares of preferred stock. The Company’s common stock has the following characteristics:

Voting

The holders of common stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of common stock shall not be entitled to vote on any amendment to the Company’s certificate of incorporation that relates solely to the terms of one or more outstanding series of preferred stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more such series, to vote thereon. There shall be no cumulative voting.

Dividends

Dividends may be declared and paid on the common stock from funds lawfully available thereof as and when determined by the Board of Directors of the Company and subject to any preferential dividend or other rights of any then outstanding preferred stock.

Liquidation

Upon the dissolution or liquidation of the Company, whether voluntary or involuntary, holders of common stock will be entitled to receive all assets of the Company available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding preferred stock.

Reserved for Future Issuance

The Company has reserved the following shares of stock:

	As of December 31,	
	2015	2014
Unvested restricted stock	41,657	125,027
Restricted stock units	150,932	—
Options to purchase common stock	2,319,772	1,904,107
Warrants to purchase common stock	926,840	899,340
Employee stock purchase plan	157,480	—
	3,596,681	2,928,474

Reverse Stock Split

On January 21, 2014, the board of directors and the stockholders of the Company approved a one-for-6.35 reverse stock split of the Company's issued and outstanding common stock, which was effected on January 21, 2014. Stockholders entitled to fractional shares as a result of the reverse stock split received a cash payment in lieu of receiving fractional shares. The Company's historical share and per share information related to issued and outstanding common stock and outstanding options and warrants exercisable for common stock have been retroactively adjusted to give effect to this reverse stock split. Shares of common stock underlying outstanding stock options and other equity instruments convertible into common stock were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the agreements governing such securities.

Initial Public Offering

On February 11, 2014, the Company completed its IPO, whereby the Company sold 5,750,000 shares of its common stock (inclusive of 750,000 shares of common stock sold by the Company pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering) at a price of $10.00 per share. The shares began trading on the Nasdaq Global Market on February 6, 2014. The aggregate net proceeds received by the Company from the offering were approximately $50.2 million , after deducting underwriting discounts and commissions and other offering expenses payable by the Company. Upon the closing of the IPO, all outstanding shares of convertible preferred stock converted into 8,260,444 shares of common stock; and warrants exercisable for convertible preferred stock were automatically converted into warrants exercisable for 30,708 shares of common stock, resulting in the reclassification of the related convertible preferred stock warrant liability to additional paid-in capital. Additionally, the Company is now authorized to issue 200,000,000 shares of common stock and 5,000,000 shares of preferred stock.

Securities Purchase Agreement

On December 2, 2014, the Company issued and sold 1,743,680 shares of its common stock, par value $0.001 per share (the "Shares") and warrants to purchase 871,840 shares of common stock (the "Common Warrants") in a private placement. Investors paid $11.47 per Share and also received a Common Warrant to purchase one half of one share of common stock for every one Share purchased. The Common Warrants are exercisable at an exercise price of $15.00 per share and expire three years from the date of issuance. The Company received net proceeds from the offering of approximately $18.2 million after deducting placement agent's fees and other offering expenses payable by the Company.

At-the-Market Facility

In March 2015, the Company entered into a sales agreement (the "Sales Agreement") with Cowen & Company, LLC ("Cowen"), pursuant to which the Company may issue and sell shares of its common stock from time to time having an aggregate offering price of up to $40 million through Cowen, acting as its agent. Sales of the Company's common stock through Cowen may be made by any method permitted that is deemed an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended, including sales made directly on or through the Nasdaq Global Market, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and/or any other method permitted by law. Cowen is not required to sell any specific amount, but acts as the Company's sales agent using commercially reasonable efforts consistent with its normal trading and sales practices.

Shares sold pursuant to the Sales Agreement have been sold pursuant to a shelf registration statement, or the 2015 Shelf, which became effective on March 20, 2015 (File No 333-202676), as supplemented by a prospectus supplement dated March 11, 2015. Under the Sales Agreement, the Company pays Cowen a commission of up to 3% of the gross proceeds. As of December 31, 2015 , the Company had sold approximately 1,446,781 shares pursuant to the Sales Agreement, resulting in proceeds of approximately $12.7 million , net of commissions and issuance costs.

9. Common Stock Warrants

On November 25, 2014, the Company issued Warrants to purchase a total of 27,500 shares of common stock to SVB and Life Science Loans, LLC at an exercise price of $11.04 per share in connection with the Second Loan Modification Agreement (See Note 6). In connection with the Company's drawdown of an additional $5.0 million pursuant to the Loan Agreement in May 2015, the Warrants automatically became exercisable for the purchase of an additional 27,500 shares of common stock at a per share exercise price of $11.83 . The Warrants are exercisable immediately and have a ten -year life. The Warrants were initially valued at $0.3 million each using the Black-Scholes option-pricing model. The following assumptions were used in valuing the Warrants:

	May 11, 2015	November 25, 2014
Risk-free interest rate	2.28%	2.27%
Expected dividend yield	—%	—%
Expected term (in years)	10	10
Expected volatility	94.60%	79.28%

On December 2, 2014, the Company issued 871,840 warrants to purchase shares of common stock at an exercise price of $15.00 per share (the “PIPE Warrants”) in connection with a private placement of common stock (See Note 8). The PIPE Warrants are exercisable immediately and have a three -year life. Upon certain events, the Company is required to settle the PIPE Warrants for cash. As a result, the Company has classified the PIPE Warrants as a liability.

The Company allocated $3.0 million to the PIPE Warrants with the residual proceeds allocated to the common stock. The fair value of the PIPE Warrants was determined using the Black-Scholes option pricing model. The fair value of the PIPE Warrants is re-measured at each reporting date using then-current assumptions With changes in fair value charged to other income (expense) on the statement of operations and comprehensive loss. As of December 31, 2015 and 2014, the PIPE Warrants were valued using the Black-Scholes option-pricing model at $0.1 million and $3.2 million , respectively. The following assumptions were used in valuing the PIPE Warrants:

	December 31, 2015	December 31, 2014	December 2, 2014
Risk-free interest rate	1.06%	1.10%	0.96%
Expected dividend yield	—%	—%	—%
Expected term (in years)	1.92	2.92	3
Expected volatility	70.67%	56.79%	57.28%

The change in fair value of $ (3.1) million and $0.2 million was recorded as other (income) expense in the accompanying statement of operations for the year ended December 31, 2015 and 2014 , respectively. As of December 31, 2015 , none of the PIPE Warrants had been exercised.

10. Share-Based Payments

2009 Stock Incentive Plan

The Company maintains the Eleven Biotherapeutics, Inc. 2009 Stock Incentive Plan (the “2009 Plan”), as amended and restated, for employees, directors, consultants, and advisors to the Company. Upon the closing of the Company’s IPO in February 2014, the Company ceased granting stock incentive awards under the 2009 Plan. The 2009 Plan provided for the grant of incentive and non-qualified stock options and restricted stock grants as determined by the Board of Directors. Under the 2009 Plan, stock options could not be granted at less than fair value on the date of the grant. Furthermore, the exercise price of

ISOs granted to an employee, who, at the time of grant, is a 10% shareholder, could not be less than 110% of the fair value on the date of grant.

Terms of stock option agreements, including vesting requirements, are determined by the Board of Directors, subject to the provisions of the 2009 Plan. Options and restricted stock awards granted by the Company generally vest ratably over four years , with a one -year cliff for new employee awards, and are exercisable from the date of grant for a period of ten years . Restricted stock issuances and early exercises of stock options are subject to the Company's right of repurchase at the original issuance price, which right lapses over the vesting period of the stock. For options and restricted stock awards granted to date, the exercise price equaled the estimated fair value of the common stock as determined by the Board of Directors on the date of grant.

2014 Stock Incentive Plan

In December 2013, the Company's 2014 Stock Incentive Plan (the "2014 Plan") was adopted by the Board of Directors and was approved by the Company's stockholders in January 2014. The 2014 Plan became effective immediately prior to the closing of the Company's IPO in February 2014. The 2014 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The number of shares of the Company's common stock reserved for issuance under the 2014 Plan is the sum of (1) 708,661 shares, plus (2) the number of shares (up to 1,347,821 shares) equal to (a) 1,586 shares (representing the number of shares reserved for issuance under the 2009 Plan that remained available for future issuance as of the effectiveness of the 2014 Plan) and (b) the number of shares of the Company's common stock subject to outstanding awards under the Company's 2009 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased without having been fully exercised or resulting in any common stock being issued, plus (3) an annual increase, to be added on the first day of each fiscal year, equal to the lowest of 1,102,362 shares of the Company's common stock, 4% of the number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year and an amount determined by the Company's board of directors. On January 1, 2015, the
Company increased the number of shares reserved for issuance under the 2014 Plan by 722,331 shares.

The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2014 Plan.
However, incentive stock options may only be granted to the Company's employees.

A summary of the Company's stock option activity and related information follows:

	Shares	Weighted-Average Exercise Price	Remaining Contractual Life (in years)
Outstanding at December 31, 2014	1,438,528	$ 4.93	7.86
Granted	802,828	8.66	
Exercised	(78,585)	0.74	
Cancelled or forfeited	(359,197)	7.40	
Outstanding at December 31, 2015	1,803,574	$ 6.28	7.78
Exercisable at December 31, 2015	855,711	$ 4.80	7.11
Vested and expected to vest at December 31, 2015 (1)	1,589,145	$ 6.58	7.88

(1) Represents the number of vested options, plus the number of unvested options expected to vest.

The total intrinsic value of options vested and expected to vest as of December 31, 2015 was $1.2 million . The total intrinsic value of options exercised for the years ended December 31, 2015 , 2014 and 2013 was $768,000 , $921,000 and $170,000 , respectively. The total fair value of employee options vested for the years ended December 31, 2015 , 2014 and 2013 was $1.8 million , $1.3 million and $40,000 , respectively.

Restricted Stock

From time to time, upon approval by the Board of Directors, certain employees and advisors have been granted restricted shares of common stock. These shares of restricted stock are subject to repurchase rights. Accordingly, the Company has recorded the proceeds from the issuance of restricted stock as a liability in the balance sheets. The restricted stock liability is reclassified into

stockholders' equity as the restricted stock vests. A summary of the status of unvested restricted stock as of December 31, 2015 and 2014 , and changes during the year ended December 31, 2015 are presented below:

	Restricted Stock	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2014	125,027	$ 5.39
Granted	6,660	4.03
Vested	(90,030)	2.67
Unvested at December 31, 2015	41,657	$ 11.05

The Company issued 6,660 and 3,000 shares of restricted stock to non-employees during the years ended December 31, 2015 and 2014 , respectively. No restricted stock was granted to non-employees during the year ended December 31, 2013. The non-employee restricted stock is revalued as it vests. There were 1,787 shares of non-employee unvested restricted stock outstanding at December 31, 2015 . The expense related to the restricted stock granted to non-employees for the years ended December 31, 2015 , 2014 and 2013 was $45,000 , $58,000 and $481,000 , respectively.

Restricted Stock Units

From time to time, upon approval by the Board of Directors, certain employees have been granted restricted stock units. A summary of the status of restricted stock units is presented below:

	Restricted Stock Units	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2014	—	$ —
Granted	221,400	2.82
Vested	(70,468)	2.76
Unvested at December 31, 2015	150,932	$ 2.85

The Company did not issue any restricted stock units to non-employees during the years ended December 31, 2015 , 2014 and 2013 .

Performance-Based Stock Options

The Company has granted stock options to the founders of the Company, which contain both performance-based and service-based vesting criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain preclinical and clinical development milestones related to the Company's product candidates. Stock-based compensation expense associated with these performance-based stock options is recognized if the performance condition is considered probable of achievement using management's best estimates. There was no expense recorded for milestone based vesting awards during the year ended December 31, 2015 . During the years ended December 31, 2014 and 2013 , management determined that a performance-based milestone was achieved and recorded stock-based compensation expense of $293,000 and $106,000 , respectively. The remaining milestones were not deemed to be probable of achievement as of December 31, 2015. As of December 31, 2015 , unrecognized compensation expense related to performance based awards was $352,000 .

Stock-Based Compensation Expense

The fair value of each stock option granted to employees and directors was estimated on the date of grant using the Black-Scholes option-pricing model based on the assumptions noted in the following table:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.42-1.92%	1.67-2.02%	1.09-2.07%
Expected dividend yield	—%	—%	—%
Expected term (in years)	5.75-6	5.75-6	6
Expected volatility	69.06-74.11%	60.00-69.58%	72.13-77.80%

Volatility

Since the Company has only been publicly traded since February 6, 2014 , it does not have relevant historical data to support its expected volatility. As such, the Company has used a weighted-average of expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies. For purposes of identifying representative companies, the Company considered characteristics such as stage of development and area of therapeutic focus. The expected volatility has been determined using a weighted-average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to continue to consistently apply this process using the same similar entities until a sufficient amount of historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

Risk-Free Rate

The risk-free rate is based on the yield curve of U.S. Treasury securities with periods commensurate with the expected term of the options being valued.

Expected Term

The Company uses the "simplified method" to estimate the expected term of stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of the Company's stock options, taking into consideration multiple vesting tranches. The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's share-based awards.

Dividends

The Company has never paid, and does not anticipate paying, any cash dividends in the foreseeable future, and therefore uses an expected dividend yield of zero in the option-pricing model.

Forfeitures

The Company is also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from its estimates. The Company uses 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 that actual forfeitures differ from the Company's estimates, the difference is recorded as a cumulative adjustment in the period the estimates are revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Using the Black-Scholes option-pricing model, the weighted-average per share grant date fair values of options granted to employees in 2015 , 2014 and 2013 were $5.60 , $8.68 and $4.07 , respectively. The expense related to the options granted to employees for the years ended December 31, 2015 , 2014 and 2013 were $2.0 million , $1.6 million and $0.2 million , respectively.

The Company did not grant stock options to non-employees during the years ended December 31, 2015 and 2014. The Company granted 231,968 stock options to non-employees during the year ended December 31, 2013 with weighted-average exercise prices of $1.77 per share.

The fair value of each non-employee stock option granted is estimated using the Black-Scholes option-pricing model based on assumptions noted in the following table:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.19-2.26%	1.67-2.04%	1.82-2.99%
Expected dividend yield	0.00%	0.00%	0.00%
Expected option life (years)	10	10	10
Expected stock price volatility	67.24-92.40%	57.65-80.98%	76.28-78.14%

The total number of non-employee stock options outstanding at December 31, 2015 was 332,041 . The non-employee stock options are revalued as they vest. The Company calculated the value of the stock options using the Black-Scholes option-pricing model. The expense related to the options granted to non-employees for the years ended December 31, 2015 , 2014 and 2013 were $168,000 , $504,000 and $486,000 , respectively.

Employee Stock Purchase Plan

On January 21, 2014, the Company's Board of Directors adopted its 2014 Employee Stock Purchase Plan ("2014 ESPP"), which was subsequently approved by the Company's stockholders and became effective upon the closing of the Company's IPO on February 6, 2014. The 2014 ESPP authorizes the initial issuance of up to a total of 157,480 shares of the Company's common stock to participating employees. The first offering period under the 2014 ESPP opened on September 15, 2015. As of December 31, 2015, no shares have been issued pursuant to the 2014 ESPP.

11. Income Taxes

A reconciliation of the expected income tax benefit (expense) computed using the federal statutory income tax rate to the Company's effective income tax rate was as follows:

	Year Ended December 31,		
	2015	2014	2013
Income tax benefit computed at federal statutory tax rate	34.00%	34.00%	34.00%
State taxes, net of federal benefit	5.59	5.05	4.67
General business credits and other credits	1.77	1.33	4.28
Permanent differences	2.38	(1.29)	(3.52)
Change in valuation allowance	(43.74)	(39.09)	(39.43)
Total	— %	— %	— %

The Company has incurred net operating losses, or NOLs, from inception. At December 31, 2015 , the Company has federal and state NOL carryforwards of $120.0 million and $118.2 million , respectively, available to reduce future taxable income, that expire beginning in 2029 through 2035 . The Company also had federal and state research and development tax credit carryforwards of $1.7 million and $1.2 million, respectively, available to reduce future tax liabilities that expire beginning in 2025 through 2035. Included in the federal and state net operating losses are deductions attributable to excess tax benefits from the exercise of stock options of $0.7 million . The tax benefits attributable to these deductions are credited directly to additional paid-in capital when realized.

Under the provisions of the Internal Revenue Code, certain substantial changes in the Company's ownership may result in a limitation on the amount of NOL carryforwards and research and development credit carryforwards that may be utilized annually to reduce future taxable income and taxes payable. The Company has not determined if a limitation has occurred.

The Company's deferred tax assets consist of the following (in thousands):

	December 31,	
	2015	2014
Deferred tax assets:		
Net operating loss carryforwards	$ 46,749	$ 33,267
Research and development credit carryforwards	2,462	1,979
Accruals and other	1,385	948
Capitalized license and organization costs	66	73
Capitalized start-up costs	278	309
Depreciation	21	—
Total gross deferred tax asset	50,961	36,576
Deferred tax liability	—	(18)
Valuation allowance	(50,961)	(36,558)
Net deferred tax asset	$ —	$ —

As required by ASC 740, *Income Taxes* ("ASC 740"), management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are composed principally of NOL carryforwards and research and development credit carryforwards. Management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and, as a result, a valuation allowance of $51.0 million and $36.6 million has been established at December 31, 2015 and 2014 , respectively. The change in the valuation allowance was $14.4 million for the year ended December 31, 2015 . At December 31, 2015 and for prior periods, the Company had no unrecognized tax benefits. The Company has not, as yet, conducted a study of its research and development credit carryforwards. Such a study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amount is being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits, and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations and comprehensive loss if an adjustment were required.

The Company applies the accounting guidance in ASC 740 related to accounting for uncertainty in income taxes. The Company's reserves related to taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. As of December 31, 2015 and 2014 , the Company had no unrecognized tax benefits. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

The Company files income tax returns in the U.S. federal tax jurisdiction and the Massachusetts state jurisdiction. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available. The Company does not have any international operations as of December 31, 2015 . There are currently no federal or state audits in process.

12. Related-Party Transaction

The landlord from which the Company leases its corporate headquarters under an operating lease purchased 250,000 shares of series A preferred stock at $1.00 per share, the price paid by the other investors, after execution of the lease (See Note 7).

13. Defined Contribution Benefit Plan

The Company sponsors a 401(k) retirement plan, in which substantially all of its full-time employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company made matching contributions of $62,000 to this plan during the year ended December 31, 2015 . The Company did not provide any contributions to this plan during the years ended December 31, 2014 and 2013.

14. Subsequent Events

On January 15, 2016, the Company announced top-line results from the Company's Phase 3 clinical trial of isunakinra for the treatment of severe allergic conjunctivitis. As a result of the outcome of this trial, which constituted a "Study Discontinuation

Event" pursuant to the terms of the Loan Agreement, the Company was required to fund a cash collateral account with SVB in an amount equal to approximately $15.1 million , representing the outstanding obligations under the Loan Agreement.

On February 10, 2016, the Company provided notice to The Schepens Eye Research Institute, Inc. ("Schepens") of the Company's termination of the License Agreement dated July 13, 2010, as amended, between the Company and Schepens (the "License Agreement"), to be effective 60 days following receipt of such notice by Schepens.

On March 1, 2016, the Company prepaid all outstanding amounts owed to SVB under the Loan Agreement. The outstanding principal amount under the Loan Agreement was $13.7 million . In addition, the Company paid $0.1 million in accrued interest and $1.1 million in prepayment and other fees.

15. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for 2015 and 2014 . The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	2015				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
	(in thousands, except per share data)				
Total revenue	$ 244	$ 114	$ 67	$ 565	$ 990
Total operating expenses	7,841	8,516	9,426	10,403	36,186
Loss from operations	(7,597)	(8,402)	(9,359)	(9,838)	(35,196)
Net loss	(6,524)	(6,906)	(9,693)	(10,329)	(33,452)
Net loss applicable to common stockholders	(6,524)	(6,906)	(9,693)	(10,329)	(33,452)
Net loss per share applicable to common stockholders—basic and diluted	$ (0.36)	$ (0.36)	$ (0.50)	$ (0.53)	$ (1.76)

	2014				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
	(in thousands, except per share data)				
Total revenue	$ 568	$ 761	$ 539	$ 375	$ 2,243
Total operating expenses	7,757	8,806	11,141	7,470	35,174
Loss from operations	(7,189)	(8,045)	(10,602)	(7,095)	(32,931)
Net loss	(7,222)	(8,121)	(10,674)	(8,139)	(34,156)
Net loss applicable to common stockholders	(7,741)	(8,121)	(10,674)	(8,139)	(34,675)
Net loss per share applicable to common stockholders—basic and diluted	$ (0.80)	$ (0.51)	$ (0.66)	$ (0.49)	$ (2.37)

August 28,, 2015

Personal & Confidential
Mr. John McCabe
17 Brookside Farm Lane
Sudbury, MA 01776

Dear John:

It is my pleasure to confirm that, as of August 12, 2015, you have been promoted to the position of Senior Vice President, Finance for Eleven Biotherapeutics, Inc. ("the Company" or "Eleven Bio") initially reporting to Abbie Celniker, PhD, Chief Executive Officer ("CEO"). This letter summarizes important details about your employment and constitutes an amendment and restatement of the letter agreement between you and the Company dated April 26, 2012. This letter agreement shall be effective as of August 28, 2015 (the "Effective Date").

1. **Full-Time and Best Efforts** : As Eleven Bio's Senior Vice President, Finance, which is a full-time position, we expect that you will devote substantially all of your working time to the performance of your Company duties in a satisfactory manner and to the best of your abilities at all times. You shall not engage in any other business or occupation during your employment here, including, without limitation, any activity that conflicts with the interests of the Company, interferes with the proper and efficient performance of your duties for the Company, or interferes with your exercise of judgment in the Company's best interests. Notwithstanding the foregoing, nothing herein shall preclude you from serving, with the prior written consent of the CEO and/or Board of Directors (the "Board"), as a member of the boards of directors or advisory boards of non-competing businesses and charitable organizations; *provided, however* , that such activities shall be limited by you so as not to interfere, individually or in the aggregate, with your performing your job

2. **Compensation** : You currently receive a bi-weekly salary of $10,192.31 (equivalent to $265,000 when annualized) effective as of August 1, 2015, which will be subject to all applicable tax reporting and withholding. You will be considered for a merit review in conjunction with your performance review (which generally are conducted annually) and consistent with the Company's compensation practices, as determined by the Board.

3. **Annual Bonus** : For the 2015 fiscal year, you will be eligible for an annual target bonus of up to 20% of your base salary (after giving effect to payment of the one-time retention bonus previously approved by the Compensation Committee of the Board) contingent upon your individual and our Company performance. For the 2016 fiscal year and subsequent fiscal years,

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you will be eligible for an annual target bonus of up to 25% of your base salary contingent upon your individual and our Company performance. The determination of whether a bonus will be granted, and the amount of any such bonus, will be determined by the Company in its reasonable good faith discretion. All annual bonuses, if any, will be payable no later than March 15 of the year following the year in which they were earned. Please note that you must be employed on the date bonuses, if any, are paid, in order to be eligible for such a payment.

4. **Restricted Stock; Options** : The Board will review annually the allocation of stock among employees and you will be eligible to be considered for additional annual grants of restricted stock or stock options.

5. **Employee Benefits; Expenses** : The Company offers a comprehensive benefit package that includes group health, dental and vision plans as well as life and disability and time-off benefits. Your eligibility to participate in these plans and receive benefits thereunder is subject to the plan documents governing such benefits. Notwithstanding the foregoing, you understand and agree that nothing contained herein will require the Company to establish or maintain any fringe benefits and any such benefits may be modified, amended, terminated or cancelled at any time by the Company in its sole and absolute discretion.

During your employment, the Company shall pay (or promptly reimburse you) for documented, out-of-pocket expenses reasonably incurred by you in performing your job, which are consistent with the Company's policies in effect from time to time with respect to business expenses, subject to the Company's requirements with respect to reporting of such expenses.

Please also note that all in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by you during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

6. **Vacation Time** : As a full time employee of the Company, you are eligible for up to fifteen (15) paid vacation days that are accrued on a monthly basis at a rate of 1.25 days (10 hours) per month of full time employment. The use of vacation is governed by the Company's vacation pay policy.

7. **Term of Employment** : It is important for you to understand that you are an employee "at will". This means that you have the right to terminate your employment relationship with Eleven Bio at any time for any or no reason. Similarly, the Company has the right to terminate its

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employment relationship with you at any time for any or no reason. Your employment and this letter will be governed by the laws of Massachusetts.

8. **Severance Benefits** : Notwithstanding the foregoing, in the event that Eleven Bio terminates your employment without Cause or you resign with Good Reason (in either case a "Qualifying Termination"), you will be eligible for the benefits outlined in sub-paragraphs A or B (the "Severance Benefits"), subject to the terms set forth in this letter:

A. If a Qualifying Termination occurs: (i) Eleven Bio will pay you severance in the form of continuation of your base salary for a total of twelve (12) months, such amount to be paid in accordance with the Company's then current payroll practices, except as otherwise specified in this letter, beginning on the Company's first regular payroll date that occurs after the Payment Date (as defined below); and (ii) subject to the terms and conditions provided for in COBRA, and subject to your timely election of COBRA and copayment of premium amounts at the active employee's rate, the Company shall pay its then current share of premium payments for group health and dental program after the termination date through (1) your severance period as outlined above, or (2) the date you become employed with benefits substantially comparable to the benefits provided under the corresponding Company plan, or (3) the date you become ineligible for COBRA benefits; *provided, however* , that such Company-paid premiums may be recorded as additional income pursuant to Section 6041 of the Internal Revenue Code of 1986, as amended (the "Code") and not entitled to any tax qualified treatment to the extent necessary to comply with or avoid the discriminatory treatment prohibited by the Patient Protection and Affordable Care Act of 2010 and the Health Care and Education Reconciliation Act of 2010 or Section 105(h) of the Code. You shall be responsible for the entire COBRA premium should you elect to maintain this coverage after the earlier of the dates specified in sections 8.A.(ii) (1)-(3) above.

B. If a Qualifying Termination occurs within twelve (12) months after a Change in Control Transaction (as defined below), then: (i) you will be eligible for the same severance payments and COBRA premium assistance as set forth in sections 8.A.(i)-A.(ii) above, subject to the same terms, conditions, and limitations as described therein; and (ii) the vesting of 100% of your then outstanding unvested equity grants shall be accelerated, such that all unvested equity grants vest and become fully exercisable or non-forfeitable as of the termination date.

For the sake of clarity, it shall not be a "Qualifying Termination" if your employment terminates because of your death or due to your suffering a Disability (as defined below).

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C. The Severance Benefits will be subject to the following terms:

i. Solely for purposes of Section 409A of the Code, each salary continuation payment is considered a separate payment.

ii. Any severance or other benefits under this offer letter will begin only upon the date of your "separation from service" (as defined under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h)) which occurs on or after the date of termination of the employment. To the extent that the termination of your employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) (as the result of further services that are reasonably anticipated to be provided by you to the Company, or any of its parents, subsidiaries or affiliates, at the time your employment terminates), any severance benefits payable that constitute deferred compensation under Section 409A of the Code shall be delayed until after the date of a subsequent event constituting a separation from service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h). For purposes of clarification, this section shall not cause any forfeiture of benefits on your part, but shall only act as a delay until such time as a "separation from service" occurs.

Further, if you are a "specified employee" (as that term is used in Section 409A of the Code and regulations and other guidance issued thereunder) on the date your separation from service becomes effective, any severance benefits payable hereunder that constitute non-qualified deferred compensation under Section 409A of the Code shall be delayed until the earlier of (i) the business day following the six-month anniversary of the date your separation from service becomes effective, and (ii) the date of your death, but only to the extent necessary to avoid such penalties under Section 409A of the Code. On the earlier of (A) the business day following the six-month anniversary of the date your separation from service becomes effective, and (B) your death, the Company shall pay you in a lump sum the aggregate value of the non-qualified deferred compensation that the Company otherwise would have paid you prior to that date as described above. Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A of the Code. The Company makes no representation or warranty and shall have no liability to you or any other person if any provision of this Agreement is determined to constitute deferred compensation subject to Section 409A of the Code, but do not satisfy an exemption from, or the conditions of, Section 409A of the Code.

iii. Eleven Bio's obligations to make the above payments and provide the above benefits will be contingent upon your execution of and compliance with a comprehensive severance agreement and release of claims (the "Release"), which Release must be signed and any applicable revocation period with respect thereto must have expired by the thirtieth (30 th) day following your termination of employment (such 30 th day, the

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"Payment Date"). In addition, you must comply with all post-employment obligations, including those in the Employee Non-Competition, Non- Solicitation, Confidentiality and Assignment Agreement that you signed as a condition of employment.

iv. You agree to give prompt written notice of any reemployment during the Severance Period which results in eligibility for comparable medical and dental benefits. If the Company makes any overpayment of COBRA Benefits, you agree to promptly return any such overpayment to the Company. The foregoing shall not create any obligation on your part to seek reemployment after the date of termination of your employment.

9. Definitions : For purposes of this letter agreement, "for Cause" shall mean the Company has complied with the "Cause Process", as defined below, following your committing one or more of the following (each a "Cause Condition"): (i) an act of material dishonesty involving the Company, embezzlement, or misappropriation of assets or property of the Company; (ii) gross negligence or willful misconduct in connection with the performance of your duties, theft, fraud or breach of fiduciary duty to the Company; (iii) your willful, sustained, or repeated failure to substantially perform the duties or obligations of your position (other than due to illness or injury); (iv) a violation of federal or state securities law; (v) the conviction of a felony or any crime involving moral turpitude, including a plea of nolo contendre; (vi) a material breach of any of the Company's written policies related to conduct or ethics; or (vii) a material breach of the Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement (copy attached) executed in accordance with your initial letter agreement.

"Cause Process" shall mean that (i) the Company reasonably determines, in good faith, that one of the Cause Conditions has occurred; (ii) the Company notifies you in writing of the first occurrence of the Cause Condition within thirty (30) days of becoming aware of such condition; (iii) the Company cooperates in good faith with your efforts, for a period not less than thirty (30) days following such notice (the "Cause Cure Period"), to remedy the Cause Condition; (iv) notwithstanding such efforts, the Cause Condition continues to exist; and (v) the Company terminates your employment within thirty (30) days after the end of the Cause Cure Period, provided that the Company will not be required to provide a Cause Cure Period in the event that a Cause Condition (x) is of the type described in clauses (i), (ii), (iv), (v) or (vii) of the first sentence of this paragraph; (y) is incapable of being cured; or (z) is required to be publicly disclosed under applicable securities law.

If you cure to the Company's satisfaction any Cause Condition during the applicable Cause Cure Period, Cause shall be deemed not to have occurred. If the Company is not required to provide a Cause Cure Period, the Cause Process will be satisfied if the Company notifies you in writing of the first occurrence of the Cause Condition within thirty (30) days of the CEO becoming aware of such condition and terminates your employment within thirty (30) days of such notice. You are eligible for no more than two "cure" opportunities during your employment.

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"Change in Control Transaction" shall mean (i) a merger or consolidation of the Company with or into another corporation under circumstances where the stockholders of the Company immediately prior to such merger or consolidation do not own after such merger or consolidation shares representing at least fifty percent (50%) of the voting power of the Company or the surviving, resulting or parent corporation, as the case may be, (ii) a transfer of shares representing fifty percent (50%) or more of the voting power of the Company to any person who was not, on the Effective Date, a holder of stock of any class or preference or any stock option of the Company, (iii) a liquidation of the Company, or (iv) a sale or other disposition of all or substantially all of the Company's assets.

"Good Reason" shall mean you have complied with the "Good Reason Process" as defined below, following the occurrence of one or more of the following events: (i) any material adverse change in your compensation, title, or material responsibilities, (ii) the relocation of your primary place of work more than thirty (30) miles from your residence on the Effective Date of this Agreement, or (iii) the material breach by the Company of any provision of this letter agreement or any other employment-related agreement between the Company and you (as defined below).

"Good Reason Process" shall mean that (i) you reasonably determine in good faith that one of the foregoing "Good Reason" conditions has occurred; (ii) you notify the Company in writing of the first occurrence of the Good Reason condition within thirty (30) days of the first occurrence of such condition; (iii) you cooperate in good faith with the Company's efforts, for a period not less than thirty (30) days following such notice (the "Cure Period") to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) you terminate your employment within thirty (30) days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred. Notwithstanding the foregoing, should you be suspended pending any investigation, such suspension shall not be grounds for "Good Reason."

"Disability" shall mean your inability (as determined by the Company in good faith) to perform the essential functions of your position due to physical or mental disability (after taking into account the Company's obligation to provide reasonable accommodations in accordance with the Americans with Disabilities Act of 1990 or analogous state law), which continues for a period of 90 days (whether or not consecutive) during any 12-month period. In connection with any determination regarding your possible Disability, you shall have the right to provide to the Company, and the Company shall consider in good faith, any physical or mental evaluation performed by a competent physician of your selection.

10. **Modified Section 280G Cutback** : Notwithstanding any other provision of this Agreement, except as set forth in Section 10.B, in the event that the Company undergoes a "Change in Ownership or Control" (as defined below), the following provisions shall apply:

A. The Company shall not be obligated to provide to you any portion of any "Contingent Compensation Payments" (as defined below) that you would otherwise be entitled to receive to the extent necessary to eliminate any "excess

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parachute payments" (as defined in Section 280G(b)(1) of the Code) for you. For purposes of this Section 10, the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Payments" and the aggregate amount (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-30 or any successor provision) of the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Amount."

B. Notwithstanding the provisions of Section 10.A, no such reduction in Contingent Compensation Payments shall be made if (1) the Eliminated Amount (computed without regard to this sentence) exceeds (2) 100% of the aggregate present value (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-31 and Q/A-32 or any successor provisions) of the amount of any additional taxes that would be incurred by you if the Eliminated Payments (determined without regard to this sentence) were paid to you (including state and federal income taxes on the Eliminated Payments, the excise tax imposed by Section 4999 of the Code payable with respect to all of the Contingent Compensation Payments in excess of your "base amount" (as defined in Section 280G(b)(3) of the Code), and any withholding taxes). The override of such reduction in Contingent Compensation Payments pursuant to this Section 10.B shall be referred to as a "Section 10.B Override." For purpose of this paragraph, if any federal or state income taxes would be attributable to the receipt of any Eliminated Payment, the amount of such taxes shall be computed by multiplying the amount of the Eliminated Payment by the maximum combined federal and state income tax rate provided by law.

C. For purposes of this Section 10 the following terms shall have the following respective meanings:

i. "Change in Ownership or Control" shall mean a change in the ownership or effective control of the Company or in the ownership of a substantial portion of the assets of the Company determined in accordance with Section 280G(b)(2) of the Code.

ii. "Contingent Compensation Payment" shall mean any payment (or benefit) in the nature of compensation that is made or made available (under this Agreement or otherwise) to a "disqualified individual" (as defined in Section 280G(c) of the Code) and that is contingent (within the meaning of Section 280G(b)(2)(A)(i) of the Code) on a Change in Ownership or Control of the Company.

D. Any payments or other benefits otherwise due to you following a Change in Ownership or Control that could reasonably be characterized (as determined by

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the Company) as Contingent Compensation Payments (the "Potential Payments") shall not be made until the dates provided for in this Section 10.D. Within 30 days after each date on which you first become entitled to receive (whether or not then due) a Contingent Compensation Payment relating to such Change in Ownership or Control, the Company shall determine and notify you (with reasonable detail regarding the basis for its determinations) (1) which Potential Payments constitute Contingent Compensation Payments, (2) the Eliminated Amount and (3) whether the Section 10.B Override is applicable. Within 30 days after delivery of such notice to you, you shall deliver a response to the Company (the "Executive Response") stating either (A) that you agree with the Company's determination pursuant to the preceding sentence or (B) that you disagrees with such determination, in which case you shall set forth (x) which Potential Payments should be characterized as Contingent Compensation Payments, (y) the Eliminated Amount, and (z) whether the Section 10.B Override is applicable. In the event that you fail to deliver an Executive Response on or before the required date, the Company's initial determination shall be final. If you state in the Executive Response that you agree with the Company's determination, the Company shall make the Potential Payments to you within three (3) business days following delivery to the Company of the Executive Response (except for any Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). If you state in the Executive Response that you disagree with the Company's determination, then, for a period of sixty (60) days following delivery of the Executive Response, you and the Company shall use good faith efforts to resolve such dispute. If such dispute is not resolved within such 60-day period, such dispute shall be settled exclusively by arbitration in Cambridge, Massachusetts, in accordance with the rules of the American Arbitration Association then in effect. Judgment may be entered on the arbitrator's award in any court having jurisdiction. The Company shall, within three (3) business days following delivery to the Company of the Executive Response, make to you those Potential Payments as to which there is no dispute between the Company and you regarding whether they should be made (except for any such Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). The balance of the Potential Payments shall be made within three (3) business days following the resolution of such dispute.

E. The Contingent Compensation Payments to be treated as Eliminated Payments shall be determined by the Company by determining the "Contingent

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Compensation Payment Ratio" (as defined below) for each Contingent Compensation Payment and then reducing the Contingent Compensation Payments in order beginning with the Contingent Compensation Payment with the highest Contingent Compensation Payment Ratio. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio, such Contingent Compensation Payment shall be reduced based on the time of payment of such Contingent Compensation Payments with amounts having later payment dates being reduced first. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio and the same time of payment, such Contingent Compensation Payments shall be reduced on a pro rata basis (but not below zero) prior to reducing Contingent Compensation Payment with a lower Contingent Compensation Payment Ratio. The term "Contingent Compensation Payment Ratio" shall mean a fraction the numerator of which is the value of the applicable Contingent Compensation Payment that must be taken into account by you for purposes of Section 4999(a) of the Code, and the denominator of which is the actual amount to be received by you in respect of the applicable Contingent Compensation Payment. For example, in the case of an equity grant that is treated as contingent on the Change in Ownership or Control because the time at which the payment is made or the payment vests is accelerated, the denominator shall be determined by reference to the fair market value of the equity at the acceleration date, and not in accordance with the methodology for determining the value of accelerated payments set forth in Treasury Regulation Section 1.280G-1Q/A-24(b) or (c)).

F. The provisions of this Section 10 are intended to apply to any and all payments or benefits available to you under this Agreement or any other agreement or plan of the Company under which you receive Contingent Compensation Payments.

11. General: By signing below, you represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing or limiting you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter. You also agree that you will not disclose to anyone at the Company, bring onto Company premises, or use in the course of your employment at the Company, any confidential information or trade secrets belonging to any former employer or to any other entity.

After the Effective Date, this letter (and the plans, documents, and policies referenced herein) shall constitute our entire agreement regarding the terms and conditions of your employment with the Company and shall supersede any prior agreements or other promises or statements (whether oral or written) regarding the terms of employment. Notwithstanding the foregoing, the

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Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement dated April 23, 2012 and your obligations thereunder remain in full force and effect.

The terms described herein cannot be modified except in writing by you and the Company.

We are thrilled you are continuing as part of the leadership team at Eleven. Please contact me or Barbara if you have any questions or need more information.

Sincerely,

/s/Abbie Celniker

Abbie Celniker, PhD
President and CEO

I accept the above terms of employment as stated:

/s/ John J. McCabe August 31, 2015
John McCabe Date

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CONSENT AND THIRD AMENDMENT
TO
LOAN AND SECURITY AGREEMENT

This **CONSENT AND THIRD AMENDMENT TO LOAN AND SECURITY AGREEMENT** (this "Amendment" or the "Third Amendment") is entered into this 4 th day of December, 2015, by and between **SILICON VALLEY BANK** ("Bank") and **ELEVEN BIOTHERAPEUTICS, INC.** , a Delaware corporation ("Borrower").

RECITALS

A. Bank and Borrower have entered into that certain Loan and Security Agreement dated as of May 27, 2010, as amended by that certain First Loan Modification Agreement by and between Bank and Borrower dated as of September 4, 2012, and as further amended by that certain Second Loan Modification Agreement by and between Bank and Borrower dated as of November 25, 2014 (as the same may from time to time be further amended, modified, supplemented or restated, the "Loan Agreement"). Bank has extended credit to Borrower for the purposes permitted in the Loan Agreement.

B. Bank has extended credit to Borrower for the purposes permitted in the Loan Agreement.

C. Borrower has notified Bank that it intends to assign all of its right, title and interest in the Eleven Patents, the Eleven Improvements, the inventory of Eleven Albumin, the Eleven Agreement and other Eleven Technology (each as defined in the Assignment Agreement (defined below)) to Novozymes Biopharma DK A/S, a Danish corporation ("Novozymes") (the "Assignment") pursuant to the terms and conditions of that certain Patent Assignment and License Agreement to be entered into by and between Borrower and Novozymes, a final form of which has been provided to Bank (the "Assignment Agreement").

D. Borrower has requested that Bank (i) consent to the Assignment and the other specific items set forth in Section 2 of this Amendment and (ii) amend the Loan Agreement to make certain revisions thereto as more fully set forth herein.

E. Bank has agreed to (i) consent to the Assignment and the other specific items set forth in Section 2 of this Amendment and (ii) amend certain provisions of the Loan Agreement, but only to the extent, in accordance with the terms, subject to the conditions and in reliance upon the representations and warranties set forth below.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2. Consent. Subject to the terms of Section 3 below, Bank hereby consents to the Borrower (a) entering into and performing the Assignment, (b) receiving inbound licenses of Intellectual Property in connection with the Assignment under the Assignment Agreement and (c) making royalty payments in connection with the Assignment under the Assignment Agreement, and hereby agrees that the transactions described in clauses (a) through and including (c) above shall not, in and of themselves, constitute an "Event of Default" under: (i) Section 5.2 of the Loan Agreement (relative to Borrower being the sole owner of its Intellectual Property), (ii) Section 6.7(b) of the Loan Agreement (relative to Borrower providing written notice to Bank of entering or becoming bound by any Restricted License, and Borrower taking steps to obtain the consent of, or waiver by, the licensors thereunder as provided in such Section 6.7(b)), (iii) Section 7.1 of the Loan Agreement (relative to dispositions), (iv) Section 7.2(a) of the Loan Agreement (relative to Borrower engaging in a new line of business), (v) Section 7.4 of the Loan Agreement (relative to Borrower making royalty payments to the extent such payments constitute Indebtedness), or (vi) Section 7.5 of the Loan Agreement (relative to assignments of Intellectual Property and Collateral pursuant to the Assignment). Contemporaneously with the consummation of the Assignment, Bank releases its security interest in the Eleven Patents, the Eleven Improvements, the inventory of Eleven Albumin, the Eleven Agreement and other Eleven Technology (each as defined in the Assignment Agreement).

3. Effectiveness; Application of Proceeds . This Amendment shall be deemed effective upon and subject to the due execution and delivery to Bank of this Amendment by each party hereto. The provisions of Section 2 of this Amendment (but not any other provision of this Amendment) shall be void and of no effect if the Assignment Agreement is not fully executed on or before December 4, 2015. Within two (2) Business Days of receipt by Borrower, Borrower shall apply the net cash proceeds actually received by Borrower as an up-front cash payment pursuant to Section 3.1 of the Assignment Agreement (the "Proceeds") on account of the Obligations of Borrower to Bank. Borrower and Bank acknowledge and agree that the Proceeds applied on account of the Obligations of Borrower to Bank shall be applied to (in whole or in part, as the case may be) the next to occur of any regularly scheduled payment or payments of outstanding principal (in chronological order of maturity) or accrued interest to Bank pursuant to the Loan Agreement. Bank (a) waives any prepayment premium payable with respect to any such application of Proceeds, and (b) acknowledges that the Proceeds may be subject to withholding taxes and bank fees which could reduce the cash payment actually received by Borrower to be less than the amount of Five Hundred Thousand Dollars ($500,000.00) set forth in Section 3.1 of the Assignment Agreement. Borrower agrees to pay Bank's reasonable and documented legal fees and expenses in connection with this Amendment.

4. Amendments to Loan Agreement.

4.1 Section 2.1.3(c) (Repayment). Section 2.1.3(c) is deleted in its entirety and replaced with the following:

" (c) Repayment . Commencing on December 1, 2015 and continuing on each Payment Date thereafter, Borrower shall repay each 2014 Growth Capital Advance in thirty-six (36) consecutive equal monthly installments of principal and interest, as calculated by Bank, based upon: (i) the amount of such 2014 Growth Capital Advance, (ii) the interest rate set forth in Section 2.2(a)(iii), and (iii) an amortization

schedule equal to thirty-six (36) consecutive months; provided, however , that if the Deferral Event occurs on or before May 31, 2016, then, at Borrower's election (the "IO Election") (A) beginning with the first Payment Date to occur on or after the Deferral Event and continuing on the five (5) immediately succeeding consecutive Payment Dates thereafter, Borrower shall make monthly installments of accrued interest instead of monthly installments of principal and interest (for the sake of clarity, beginning with the seventh Payment Date to occur after the Deferral Event and continuing on each Payment Date thereafter, Borrower shall resume making monthly installments of principal and interest), and (B) the amortization schedule set forth in clause (iii) above shall be recalculated as (1) thirty (30) consecutive months minus (2) the number of Payment Dates on and after December 1, 2015 but prior to the Deferral Event. All outstanding and accrued and unpaid interest under each 2014 Growth Capital Advance and all other outstanding Obligations with respect to the 2014 Growth Capital Advances are due and payable in full on the 2014 Growth Capital Maturity Date."

4.2 Section 13.1 (Definitions). The following new definition is added to appear alphabetically in Section 13.1:

" **Deferral Event** " means the determination by Bank in Bank's sole but reasonable discretion that, on or before May 31, 2016, Borrower has satisfied Borrower's primary efficacy endpoint, and has achieved statistical significance for a named secondary endpoint, in each case described in the clinical trial protocol and statistical analysis plan with respect to Borrower's phase 3 clinical trial of EBI-005 for the treatment of allergic conjunctivitis that is ongoing as of December 4, 2015.

4.3 Section 13.1 (Definitions). The definition of "Final Payment Percentage" appearing in Section 13.1 is deleted in its entirety and replaced with the following:

" **Final Payment Percentage** " is, for each 2014 Growth Capital Advance, six percent (6.0%), provided, however, that upon the occurrence of the IO Election, the Final Payment Percentage for each 2014 Growth Capital Advance shall be six and one-quarter of one percent (6.25%).

4.4 Section 13.1 (Definitions). The definition of "Study Discontinuation Event" appearing in Section 13.1 is deleted in its entirety and replaced with the following:

"Study Discontinuation Event " means the determination by Bank in Bank's sole but reasonable discretion that any one (1) of the following has occurred: (a) Borrower's phase 3 clinical trial of EBI-005 for the treatment of allergic conjunctivitis, that is ongoing as of December 4, 2015, is terminated as a result of any safety issue, (b) Borrower fails to satisfy the primary efficacy endpoint described in the clinical trial protocol and statistical analysis plan with respect to Borrower's phase 3 clinical trial of EBI-005 for the treatment of allergic conjunctivitis that is ongoing as of December 4, 2015, or (c) a clinical hold is imposed, and is not released within a reasonable time period under the circumstances determined by

Bank in its sole but reasonable discretion, by the United States Food and Drug Administration preventing the further advancement of the Borrower's clinical development of EBI-005 for the treatment of allergic conjunctivitis.

5. Limitation of Amendments.

5.1 This Amendment is effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right or remedy which Bank may now have or may have in the future under or in connection with any Loan Document.

5.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, except as herein amended, are hereby ratified and confirmed and shall remain in full force and effect. The Existing Loan Documents are hereby amended wherever necessary to reflect the consent and changes specifically set forth above.

6. Representations and Warranties. To induce Bank to enter into this Amendment, Borrower hereby represents and warrants to Bank as follows:

6.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties expressly refer to a specific date, in which case they are true and correct as of such date), and (b) no Event of Default has occurred and is continuing;

6.2 Borrower has the power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

6.3 The organizational documents of Borrower delivered to Bank on or before the date of this Amendment remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

6.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized by Borrower;

6.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not contravene (a) any material Requirement of Law binding on or affecting Borrower, (b) any order, judgment or decree of any Governmental Authority binding on Borrower, or (c) the organizational documents of Borrower;

6.6 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, (a) do not require any order, consent, approval, license, authorization

or validation of, or filing, recording or registration with, or exemption by any Governmental Authority binding on Borrower, except as already has been obtained or made and except for the disclosure and filing of this Amendment with the SEC and (b) do not constitute an event of default under any material agreement by which Borrower is bound; and

6.7 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

7. Ratification of Perfection Certificate . Borrower hereby ratifies, confirms and reaffirms, all and singular, the terms and disclosures contained in a certain Perfection Certificate dated as of December 4, 2015 between Borrower and Bank, and acknowledges, confirms and agrees the disclosures and information Borrower provided to Bank in said Perfection Certificate have not changed, as of the date hereof. Borrower and Bank hereby acknowledge and agree that all references in the Loan Agreement to "Perfection Certificate" shall mean and include the Perfection Certificate as described herein.

8. Integration . This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements. All prior agreements, understandings, representations, warranties, and negotiations between the parties about the subject matter of this Amendment and the Loan Documents merge into this Amendment and the Loan Documents.

9. Prior Agreement . The Loan Documents are hereby ratified and reaffirmed and shall remain in full force and effect. This Amendment is not a novation and the terms and conditions of this Amendment shall be in addition to and supplemental to all terms and conditions set forth in the Loan Documents. In the event of any conflict or inconsistency between this Amendment and the terms of such documents, the terms of this Amendment shall be controlling, but such document shall not otherwise be affected or the rights therein impaired.

10. Counterparts. This Amendment may be executed in any number of counterparts and all of such counterparts taken together shall be deemed to constitute one and the same instrument.

11. Governing Law. This Amendment and the rights and obligations of the parties hereto shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts.

[Signature page follows.]

IN WITNESS WHEREOF, the parties hereto have caused this Amendment to be duly executed and delivered as a sealed instrument under the laws of the Commonwealth of Massachusetts as of the date first written above.

BANK	**BORROWER**
SILICON VALLEY BANK	ELEVEN BIOTHERAPEUTICS, INC.
By: /s/ Ryan Roller Name: Ryan Roller Title: Vice President	By: /s/ Abbie Celniker Name: Abbie Celniker Title: CEO and President

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Double asterisks denote omissions.

Exhibit 10.26

AMENDMENT # 1 TO LICENSE AGREEMENT

This Amendment # 1 to License Agreement (the " First Amendment ") is effective as of December 22, 2015 (the " First Amendment Effective Date ") and amends the License Agreement made effective as of July 13, 2010 (" Agreement ") by and between Eleven Biotherapeutics, Inc. (" LICENSEE ") and The Schepens Eye Research Institute, Inc. (" LICENSOR ").

1. **Terms.** Capitalized terms used in this First Amendment and not defined below shall have the respective meanings given to such terms in the Agreement. References to sections are references to sections of the Agreement and not of this First Amendment.

2. **Effects of First Amendment** . This First Amendment amends the Agreement solely to the extent expressly provided below as of the First Amendment Effective Date. In all other respects, the Agreement continues in full force and effect and is ratified in all respects. Any references in the Agreement to the "Agreement" will be deemed to mean the Agreement as amended by this First Amendment. The provisions of the Agreement apply to this First Amendment except to the extent this First Amendment amends any such provisions. If there is a conflict between the provisions of this First Amendment and the Agreement, the provisions of this First Amendment control.

3. **Amendments** .

3.1 **Amendment to Section 1.47** . Section 1.47 is hereby amended by deleting it in its entirety and replacing it with the following:

"Valid Claim" means (a) an unexpired claim of an issued patent within the Licensed Patents which has not been found to be unpatentable, invalid or unenforceable by an unreversed and unappealable decision of a court or other authority in the subject country or (b) a claim of an application within the Licensed Patents that has been pending for less than [**] years from the date of the first substantive office action (for claims filed in the United States) or the date of the first regional or national phase Examiner's report (for claims filed outside of the United States) (the **"Application Pending Period"**); provided, that, in no event shall the Application Pending Period exceed [**] years from the Effective Date.

3.2 **Amendment to Section 3.1** . Section 3.1 is hereby amended by deleting it in its entirety and replacing it with the following:

LICENSEE shall pay to LICENSOR a non-creditable, non-refundable, one-time, upfront license fee of [**] U.S. Dollars ($[**]).

LICENSOR acknowledges that LICENSEE has made such payment.

3.3 **Amendment to Exhibit A** . Exhibit A is amended by deleting it in its entirety and replacing it with Exhibit A hereto.

4. *[Signature page follows]*

IN WITNESS WHEREOF, the duly authorized representatives of the Parties have executed this Amendment # 1 to License Agreement effective as of the First Amendment Effective Date.

ELEVEN BIOTHERAPEUTICS, INC.

By: /s/ Abbie C. Celniker
Name: Abbie C. Celniker, Ph.D.
Title: President & Chief Executive Officer

Date: January 27, 2016

THE SCHEPENS EYE RESEARCH INSTITUTE, INC.

By: /s/ Ojas P. Mehta
Name: Ojas P. Mehta, JD
Title: Director, Intellectual Property & Commercial Ventures

Date: Dec. 22, 2015

[Signature page to Amendment # 1 to License Agreement]

Exhibit A

Licensed Patents

[**]

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-202676) of Eleven Biotherapeutics, Inc.,

(2) Registration Statement (Form S-8 No. 333-202677) pertaining to the Eleven Biotherapeutics, Inc. 2014 Stock Incentive Plan, and

(3) Registration Statement (Form S-8 No. 333-195170) pertaining to the Eleven Biotherapeutics, Inc. Amended and Restated 2009 Stock Incentive Plan;

of our report dated March 24, 2016, with respect to the financial statements of Eleven Biotherapeutics, Inc. included in this Annual Report (Form 10-K) of Eleven Biotherapeutics, Inc. for the year ended December 31, 2015.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 24, 2016

Exhibit 31.1

Rule 13a-14(a) CERTIFICATION

I, Abbie C. Celniker, certify that:

1. I have reviewed this Annual Report on Form 10-K of Eleven Biotherapeutics, 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 in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ Abbie C. Celniker

Abbie C. Celniker
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 24, 2016

Exhibit 31.2

Rule 13a-14(a) CERTIFICATION

I, John J. McCabe, certify that:

1. I have reviewed this Annual Report on Form 10-K of Eleven Biotherapeutics, 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 in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ John J. McCabe

John J. McCabe
Chief Financial Officer
(Principal Financial Officer)

Dated: March 24, 2016

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. §1350

In connection with the Annual Report on Form 10-K of Eleven Biotherapeutics, Inc. (the "Company") for the fiscal year ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. Section 1350, that, to the best of their knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Abbie C. Celniker

Abbie C. Celniker
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 24, 2016

/s/ John J. McCabe

John J. McCabe
Chief Financial Officer
(Principal Financial Officer)

Dated: March 24, 2016