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 whether 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 28, 2013, the last day of the registrant’s most recently completed second fiscal quarter, the registrant’s common stock was not publicly traded. The registrant’s common stock began trading on the NASDAQ Global Market on February 6, 2014. As of March 21, 2014, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $76.6 million, based on the closing price of the registrant’s common stock on March 21, 2014.

Number of outstanding shares of Common Stock as of March 21, 2014: 16,240,985
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### ELEVEN BIOTHERAPEUTICS, INC.

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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-005 for the treatment of dry eye disease and allergic conjunctivitis, 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;
- our ability to successfully develop our product candidates and complete our planned clinical programs;
- interim results from a clinical trial and whether they will be predictive of the final results of the trial or results of early clinical studies and whether they will be indicative of the results of future studies;
- expectations regarding regulatory approvals, including the requirements for marketing approval of EBI-005, 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-005 and our other product candidates, and the ability of EBI-005 and our other product candidates to meet existing or future regulatory standards;
- the potential advantages of EBI-005;
- our estimates regarding the potential market opportunity for EBI-005 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-005 and our other product candidates;
- our ability to maintain our collaboration with ThromboGenics N.V., enter into and successfully complete other collaborations or in-license or acquire rights to other products, product candidates or technologies for the treatment of eye diseases;
- 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 clinical-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 is EBI-005, which we designed, engineered and generated using our AMP-Rx platform and are developing as a topical treatment for dry eye disease and allergic conjunctivitis. In 2013, we completed a Phase 1b/2a clinical trial of EBI-005 in patients with moderate to severe dry eye disease. In early 2014, we initiated a pivotal Phase 3 clinical program evaluating EBI-005 for the treatment of moderate to severe dry eye disease. We also initiated a Phase 2 clinical trial to evaluate the use of EBI-005 in patients with allergic conjunctivitis in early 2014. We hold worldwide commercialization rights to EBI-005.

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 therapeutics candidates that target cytokines we believe are central to diseases of the eye. We are conducting research and development programs directed at both diseases of the front of the eye, such as dry eye disease and allergic conjunctivitis, and diseases of the back of the eye, such as diabetic macular edema, or DME, and uveitis. Our EBI-005 program is based on the role that elevated levels of the inflammatory cytokine interleukin-1, or IL-1, play in the initiation and maintenance of the inflammation and pain associated with dry eye disease and the redness and itching associated with allergic conjunctivitis. We also are conducting additional discovery efforts for the treatment of diseases of the back of the eye based on the role that other cytokines play in these diseases.

Dry eye disease affects the ocular surface and is characterized by symptoms of dryness, pain, discomfort and irritation. If dry eye disease is left untreated or becomes severe, patients may suffer chronic ocular pain and distortion of vision that can significantly reduce their quality of life. Dry eye disease is one of the leading causes of patient visits to eye care professionals in the United States. According to Market Scope, LLC, or Market Scope, a publisher of research and analysis on the ophthalmic market, approximately 68 million people in the United States, European Union, Japan and other developed markets have dry eye disease, including approximately 26 million people who suffer from the moderate to severe form of dry eye disease. According to Market Scope, approximately 19 million people in the United States have dry eye disease, including approximately seven million people who suffer from the moderate to severe form of dry eye disease.

The current standard of care for moderate to severe dry eye disease includes artificial tears and topical anti-inflammatory and immune-modulating drugs. The anti-inflammatory and immune-modulating drug market for the treatment of moderate to severe dry eye disease consists primarily of Restasis, which is approved for use in the United States, and off-label use of corticosteroids. Restasis is a topically applied, ophthalmic formulation of the immune-modulating drug cyclosporine. Restasis is not approved for the treatment of the symptoms of dry eye disease, but only for increasing tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with dry eye disease. In clinical trials, approximately 17% of patients reported ocular burning following the use of Restasis. We believe that there remains a significant unmet medical need for new treatments for patients suffering from moderate to severe dry eye disease.

We designed our Phase 1b/2a clinical trial of EBI-005 principally to assess safety in dry eye disease patients and secondarily, to measure efficacy in order to inform the design of our Phase 3 clinical trials. In our Phase 1b/2a trial, EBI-005 was generally well tolerated. While we did not power our Phase 1b/2a trial to measure efficacy with statistical significance, and the differences from baseline that we observed in the EBI-005 treatment groups were not statistically significant when compared to differences from baseline in patients who received vehicle control, we observed the following in this trial:

- on the primary efficacy endpoint of change in patient symptoms as assessed by a patient questionnaire called the ocular surface disease index, or OSDI, an improvement in patients treated with EBI-005 from baseline at six weeks;
- on the secondary efficacy endpoint of change in total corneal fluorescein staining, or CFS, a measure of ocular surface injury, an improvement in patients treated with EBI-005 from baseline at six weeks;
- on the painful or sore eyes question of the OSDI, a greater improvement from baseline at six weeks in patients treated with EBI-005 compared to improvement from baseline at six weeks in patients in the vehicle control group; and
- fewer artificial tears used by patients treated with EBI-005 compared with patients in the vehicle control group, and this difference was statistically significant.
Our pivotal Phase 3 clinical program will consist of two Phase 3 clinical trials evaluating the safety and efficacy of EBI-005 for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year. We began randomizing and treating patients in our first Phase 3 trial in January 2014. Based on our estimates regarding patient enrollment, we expect to have top-line data from our first Phase 3 trial available in early 2015. We also expect to initiate our separate safety trial in 2014. We currently intend to initiate our second Phase 3 trial after reviewing top-line data from our first Phase 3 trial. If the results of both of our Phase 3 trials and our separate safety trial are favorable, we plan to submit a Biologics License Application, or BLA, to the U.S. Food and Drug Administration, or FDA, seeking approval of EBI-005 for the treatment of dry eye disease in the United States in the second half of 2016.

In addition to our clinical development of EBI-005 in dry eye disease, in March 2014, we began randomizing and treating subjects in our Phase 2 clinical trial of EBI-005 in patients with allergic conjunctivitis who have not responded adequately to antihistamines and mast cell stabilizers, drugs that inhibit the release of histamine by cells of the immune system. Allergic conjunctivitis is an inflammatory disease of the conjunctiva, the membrane covering the inside of the eyelids and white part of the eye, primarily from a reaction to allergy-causing substances such as pollen or pet dander. Our preclinical product candidates include EBI-029 for the treatment of DME, a serious disease of the central portion of the retina known as the macula, and EBI-028 for the treatment of uveitis, which is an inflammatory disease of the middle layer of the eye known as the uvea.

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 a protein called vascular endothelial growth factor, or 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:

• **Complete clinical development of and seek marketing approval for EBI-005 for the treatment of dry eye disease.** Currently, we are devoting most of our efforts to completing the clinical development of EBI-005. We have initiated a pivotal Phase 3 clinical program consisting of two Phase 3 clinical trials evaluating the safety and efficacy of EBI-005 for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year. We began randomizing and treating patients for our first Phase 3 trial in January 2014. Based on our estimates regarding patient enrollment, we expect to have top-line data from our first Phase 3 trial available in early 2015. We also expect to initiate our separate safety trial in 2014. We currently intend to initiate our second Phase 3 trial after reviewing top-line data from our first Phase 3 trial. If the results of both of our Phase 3 trials and our separate safety trial are favorable, we plan to submit a BLA to the FDA, seeking approval of EBI-005 for the treatment of dry eye disease in the United States in the second half of 2016.

• **Expand use of EBI-005 for additional ocular indications.** We are evaluating other ocular surface diseases in which we believe elevated levels of IL-1 signaling play a role in the underlying biology of the disease and for which we believe EBI-005 treatment may be beneficial. We have initiated a Phase 2 clinical trial to assess the potential therapeutic benefit of EBI-005 for the treatment of allergic conjunctivitis in patients who have not responded adequately to antihistamines and mast cell stabilizers. In March 2014, we began randomizing and treating patients in this Phase 2 trial. We expect that top-line data from this Phase 2 trial could be available before the end of 2014.

• **Maximize commercial potential of EBI-005.** We hold worldwide commercialization rights to EBI-005. We believe that the specialists in the United States who treat most of the moderate to severe dry eye disease patients are sufficiently concentrated that if EBI-005 receives marketing approval in the United States, we could effectively promote EBI-005 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-005 in the United States. We intend to enter into strategic collaborations for the development and commercialization of EBI-005 outside of the United States.

• **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-005 and our other product candidates using our AMP-Rx platform. Our two most advanced preclinical product candidates are EBI-029 for the treatment of DME and EBI-028 for the treatment of uveitis. Both of these product candidates are in early preclinical research and may require further optimization. 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 apply our proprietary AMP-Rx platform to design, engineer and generate protein therapeutics that can modulate a specific novel pathway in retinal disease and that have key pharmaceutical attributes. This collaboration provides us with funding for the specific program that is the subject of the collaboration and allows 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.

### 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.
Ocular Surface Diseases

Ocular surface diseases are disorders of the surface of the cornea, the transparent layer that forms the front of the eye, and the conjunctiva, the membrane covering the inside of the eyelids and white part of the eye. These diseases include dry eye disease and allergic conjunctivitis. Patients with ocular surface diseases may suffer from difficulty with routine visual activities, loss of vision, discomfort, infections, erosion of the cornea, ulcerations and scarring of the cornea. We believe that the optimal approach to treatment of diseases of the ocular surface is a potent active ingredient formulated with a comfortable solution, or vehicle, for topical delivery.

Dry Eye Disease

Dry eye disease is a potentially debilitating disease of the eye that may, in its most severe forms, have sight-threatening corneal complications. Dry eye disease often is classified as mild, moderate or severe based on clinical symptom severity. Dry eye disease is one of the leading causes of patient visits to eye care professionals in the United States. According to Market Scope, approximately 68 million people in the United States, European Union, Japan and other developed markets have dry eye disease, including approximately 26 million people who suffer from the moderate to severe form of dry eye disease. According to Market Scope, approximately 19 million people in the United States have dry eye disease, including approximately seven million people who suffer from the moderate to severe form of dry eye disease.

Current Treatments. The current standard of care for moderate to severe dry eye disease includes artificial tears and topical anti-inflammatory and immune-modulating drugs. Artificial tears act as a wetting agent. They are available as over-the-counter treatments and are usually considered the first line of therapy for patients with mild disease. Artificial tears are effective supplements to other therapies in the treatment of moderate to severe dry eye disease, but they generally are not sufficient as a monotherapy. The anti-inflammatory and immune-modulating drug market for the treatment of moderate to severe dry eye disease consists primarily of Restasis, which is approved for use in the United States, and off-label use of corticosteroids. There are no drugs approved in the European Union for the treatment of dry eye disease.

Corticosteroids applied topically, or directly to the surface of the eye, have been shown to be effective in the treatment of moderate to severe dry eye disease. However, topically applied corticosteroids have been associated with a higher risk of developing glaucoma and cataracts and an increased risk of ocular infection. These are serious side effects that significantly limit the use of corticosteroids.

Restasis is a topically applied, ophthalmic formulation of the immune-modulating drug cyclosporine. Restasis is not approved for the treatment of the symptoms of dry eye disease, but only for increasing tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with dry eye disease. Annual worldwide sales of Restasis have increased from approximately $444 million in
2008 to approximately $940 million in 2013. In clinical trials, Restasis increased tear production, a sign of dry eye disease, after six months of treatment in approximately 15% of treated patients as compared to approximately 5% of patients in the control groups. These increases in tear production generally were observed between three and six months after initiation of treatment. In these same clinical trials, approximately 17% of patients reported ocular burning following the use of Restasis. We believe that there remains a significant unmet medical need for new treatments for patients suffering from moderate to severe dry eye disease.

**Biology.** At the onset of dry eye disease, the tear film that is necessary for maintaining the health of the surface of the eye and for providing clear vision breaks down. The precise causes of the breakdown are not well understood but may include hormonal changes, infection or inflammation of the eye, the use of drugs with drying effects such as anti-depressants, contact lens use, smoke and very dry air. Without adequate wetting, the surface of the eye becomes stressed. The symptoms of dry eye disease include discomfort, pain, burning, itching and visual disturbance.

We believe that stress on the ocular surface as a result of the loss of an adequate tear film leads to the signs and symptoms of dry eye disease. As a result of this stress on the ocular surface, various cells and tissues of the eye produce inflammatory mediators, such as the cytokines interleukin-1alpha, or IL-1α, and interleukin-1beta, or IL-1β. These cytokines, which we refer to together as IL-1, bind to the IL-1 receptor found on many different cell types in the cornea and conjunctiva. This binding and the resulting receptor signaling initiate and maintain an inflammatory response in the tissues of the eye. The resulting inflammation then leads to the further local production of inflammatory cytokines. This cascade of inflammation results in a state of chronic inflammation and ocular surface damage. This damage is indicative of dry eye disease and can be measured by the staining of the ocular surface with the dye fluorescein, a measure known as CFS.

IL-1α and IL-1β also can bind to the IL-1 receptor on nerve cells. This binding and the resulting receptor signaling stimulates nerve cells, triggers nociception, or feelings of pain, and can result over time in chronic hyperalgesia, or increased sensitivity to pain. Nociception and hyperalgesia lead to patient reported symptoms of discomfort, ocular pain, which patients may report as soreness, stinging or burning, and difficulty with routine visual activities, such as using a computer, driving a car or watching television. These subjective symptoms of dry eye disease can be evaluated through a variety of patient-reported and physician-reported assessments. These usually take the form of questionnaires which provide data that can be scored to provide a quantitative measure of symptom severity.

As depicted in the graphic below, stress on the ocular surface leads to the excess production of IL-1. IL-1 initiates and maintains both inflammatory and neural responses in the tissues of the eye. The inflammatory response results in ocular surface damage, a sign of dry eye disease. The inflammatory response also results in continued production of IL-1 and chronic inflammation, which manifests as various symptoms of dry eye disease. The neural response results in feelings of and hypersensitivity to pain, which are persistent symptoms of dry eye disease.

The biological activities of IL-1 suggest that blocking IL-1 receptor signaling should have a dual function and reduce both a sign of dry eye disease, specifically ocular surface inflammation and injury, and a symptom of dry eye disease, specifically ocular pain and discomfort. In the case of dry eye disease, IL-1α and IL-1β, acting independently or in concert, both drive IL-1 receptor signaling. As a result, a therapy that blocks only IL-1α or IL-1β may not have the desired effect of completely blocking IL-1 receptor signaling and alleviating the signs and symptoms of dry eye disease. We believe that a better approach is to block the IL-1 receptor itself so neither IL-1α nor IL-1β can bind to the receptor and trigger receptor signaling.
Our most advanced product candidate is EBI-005, a recombinant protein which binds with the IL-1 receptor and blocks, or antagonizes, IL-1 receptor signaling. We have designed, engineered and generated EBI-005 using our AMP-Rx platform and are developing EBI-005 as a topical, eye-drop treatment for dry eye disease and allergic conjunctivitis. EBI-005 prevents the binding of both IL-1α and IL-1β to the IL-1 receptor. When the IL-1 receptor is blocked by EBI-005, the IL-1 receptor is unable to transmit the biological signals that we believe are responsible for pain, discomfort, itching and inflammation in ocular surface diseases.

**Design and Attributes of EBI-005**

We designed EBI-005 based on our understanding of the molecular structure of the IL-1 receptor and two of the molecules, or ligands, that are known to bind effectively to this receptor, IL-1β and IL-1 receptor antagonist, or IL-1Ra. We engineered EBI-005 to combine the portions of IL-1β and IL-1Ra having desirable biophysical properties and IL-1 receptor binding characteristics. We engineered EBI-005 as a pure antagonist to the IL-1 receptor, which means that EBI-005 binds to the IL-1 receptor without triggering receptor signaling. We also designed EBI-005 to have the following product attributes that we believe improve its potential utility as a topical therapeutic:

- **Rapid onset of action.** We have designed EBI-005 to be a potent blocker of IL-1. In a biochemical study of receptor binding, EBI-005 bound more rapidly and up to 500 times more strongly to the IL-1 receptor than the natural ligands IL-1β and IL-1Ra. In a mouse model of dry eye disease, treatment with EBI-005 resulted in a greater reduction in CFS from baseline at seven days and at 11 days when compared to the reduction in CFS from baseline with IL-1Ra treatment. We believe the potency of EBI-005 may result in a rapid onset of symptomatic relief.

- **Comfortable for patients.** We have optimized EBI-005 for topical, ophthalmic delivery and have formulated it with a preservative-free comfortable solution, or vehicle, for delivery as an eye drop. We believe patient comfort is an important factor in patient compliance and physician recommendation of a topical drug for diseases of the ocular surface.

- **Convenient dosing.** We have designed EBI-005 to bind tightly to the IL-1 receptor and block it for an extended period of time. We have measured the duration of this receptor binding in biochemical tests outside the body, or *in vitro*. Based on these tests and our understanding of the natural cycling of the IL-1 receptor from the cell surface to the cell interior, we believe EBI-005 remains bound to an IL-1 receptor during the entire period the receptor is present on the surface of a cell. We believe a long duration of receptor binding may allow for a convenient dosing schedule.

- **Stable dosage form.** We designed EBI-005 to be a thermally stable protein product. In analytical tests, EBI-005 was stable for at least five months at room temperature. We believe room temperature stability without the need for refrigeration is an important convenience for patients.
EBI-005 Binds Tightly to and Blocks the IL-1 Receptor

We believe IL-1 plays a central role in dry eye disease and that EBI-005 has the potential to treat both the signs and symptoms of dry eye disease by binding tightly to and blocking the transmission of biological signals by the IL-1 receptor. EBI-005 blocks the inflammatory and neuropathic activities of IL-1 by binding to the IL-1 receptor during both the initiation and maintenance of the cycle of pain and inflammation in dry eye disease.

Proof of Concept Clinical Trial with Anakinra, an IL-1 Blocker

In 2013, the peer-reviewed journal *JAMA Ophthalmology* published the results of an exploratory Phase 1/2 clinical trial in 75 patients conducted by one of our scientific co-founders, Dr. Reza Dana, at the Massachusetts Eye and Ear Infirmary using another IL-1 blocker, anakinra, to treat moderate to severe dry eye disease. Anakinra is approved for subcutaneous administration for the treatment of rheumatoid arthritis and is marketed under the brand name Kineret. For this proof-of-concept study, the investigators compounded, or reformulated, anakinra in eye drops at two different concentrations for topical administration. In this double masked, placebo controlled study, patients with dry eye disease received either anakinra or a placebo control consisting of the vehicle, which was a commercially available eye drop the investigators used to formulate anakinra for topical, ophthalmic application. The investigators in this trial required patients who were using anti-inflammatory therapies, including Restasis, to discontinue their use for 30 days prior to enrollment and throughout this trial. Patients were allowed to continue their use of artificial tears and therapies other than anti-inflammatory therapies. Thirty patients received anakinra at the lower dose of 25 mg/ml and 15 patients received anakinra at the higher dose of 50 mg/ml. Thirty patients received vehicle control. Patients were treated for 12 weeks with a follow up at 16 weeks.

In this trial, there was an improvement in CFS, a sign of dry eye disease, in patients treated with anakinra from baseline at six weeks and at 12 weeks. We believe that the magnitude of the CFS response was clinically relevant for the lower dose anakinra treatment group at six weeks and at 12 weeks. We believe that the magnitude of the CFS response was clinically relevant for the higher dose anakinra treatment group only at six weeks. However, none of these differences was statistically significant when compared to the difference from baseline observed in patients who received vehicle control. We determine statistical significance based on a widely used, conventional statistical
method that establishes the p-value of clinical results. Typically, a p-value of 0.05 or less represents statistical significance. There also was an improvement in patient symptoms as measured by the OSDI score in patients treated with anakinra from baseline at six weeks and at 12 weeks. We believe that the magnitude of improvement in patient symptoms as measured by the OSDI score was clinically relevant for both the lower dose and higher dose anakinra treatment groups at six weeks and at 12 weeks, and the differences from baseline at six weeks and at 12 weeks were statistically significant for both the lower dose and higher dose anakinra treatment groups when compared to the differences from baseline observed in patients who received vehicle control.

We subsequently conducted an additional, retrospective analysis of the results of this trial. In this analysis, we observed in patients treated with anakinra that the improvement from baseline at six weeks and at 12 weeks in pain and discomfort, as measured by the painful or sore eyes question on the OSDI, was the largest contributor to the improvement in patient symptoms as measured by the OSDI score. We then analyzed the data on pain and discomfort and observed a statistically significant improvement from baseline in pain and discomfort, as measured by the painful or sore eyes question on the OSDI, in the lower dose anakinra treatment group at six weeks (p=0.01) and at 12 weeks (p=0.04) and higher dose anakinra treatment group at six weeks (p=0.01) and at 12 weeks (p=0.04) compared to the improvement from baseline in the vehicle control group. We believe that the clinical experiences with anakinra are relevant to our development of EBI-005 because the therapeutic targets and mechanisms of action of anakinra and EBI-005 are similar. However, based on our studies of the biophysical characteristics of anakinra, we do not believe that it can be formulated for topical ophthalmic delivery in a convenient format on a commercial basis because at the concentration shown to be effective in the anakinra trial, anakinra is not stable under the conditions encountered during vialing in a standard blow-fill-seal vial configuration. We believe that the blow-fill-seal vial configuration is the most cost-effective process for delivering a preservative-free eye drop. We believe that a drug for dry eye disease should be preservative-free because chronic exposure to preservatives may irritate the ocular surface. In addition, based on our own biochemical studies, we do not believe that the particular formulation of anakinra used in the anakinra trial can be used for topical ophthalmic delivery in a convenient format on a commercial basis because at the concentration shown to be effective in the anakinra trial:

- anakinra is not stable in solution when agitated, which means that routine handling of a topical, ophthalmic formulation of anakinra by a patient could result in a change in the concentration of anakinra received by the patient upon dosing; and
- anakinra is not stable at room temperature. We believe room temperature stability without the need for refrigeration is an important convenience for patients.

Clinical Development of EBI-005

We have completed two clinical trials with EBI-005. In 2012, after submitting an investigational new drug application, or IND, to the FDA for the purpose of conducting clinical trials for the treatment of dry eye disease, we completed a Phase 1 clinical trial evaluating the safety and tolerability of EBI-005 in healthy volunteers. In 2013, we completed a Phase 1b/2a clinical trial evaluating the safety, tolerability and biological activity of EBI-005 in patients with moderate to severe dry eye disease. We have initiated a pivotal Phase 3 clinical program consisting of two Phase 3 clinical trials evaluating the safety and efficacy of EBI-005 for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year. We began randomizing and treating patients in our first Phase 3 trial in January 2014. Based on our estimates regarding patient enrollment, we expect to have top-line data from our first Phase 3 trial available in early 2015. We expect to initiate our separate safety trial in 2014.

In November 2013, we submitted to the FDA the protocol for our first pivotal Phase 3 clinical trial of EBI-005 and data supporting our change to a larger-scale manufacturing process for the production of EBI-005 to be used in this Phase 3 clinical trial. The FDA is not obligated to comment on our submissions within any specified time period or at all or to affirmatively clear or approve any clinical trial, and we are not obligated to wait for clearance or approval of the FDA to commence any clinical trial. On March 24, 2014, we received a letter from the FDA requesting additional information regarding the characterization of EBI-005 produced using our larger-scale manufacturing process based on the FDA’s product quality review of our November 2013 submission. We have responded to the FDA with the information the FDA requested.

We currently intend to initiate our second Phase 3 trial after reviewing top-line data from our first Phase 3 trial. If the results of both of our Phase 3 trials and our separate safety trial are favorable, we plan to submit a BLA with the FDA seeking approval of EBI-005 for the treatment of dry eye disease in the United States in the second half of 2016.

We designed our Phase 1b/2a trial to evaluate the safety and tolerability of EBI-005 and to provide us with insights regarding dose, patient selection and efficacy endpoints for the design of our Phase 3 trials. When we evaluated the results of the anakinra trial, we concluded that we would need to conduct a clinical trial in approximately 650 patients in order to determine with statistical significance a difference in improvements in one sign and one symptom of dry eye disease between patients treated with EBI-005 at concentrations of 5 mg/ml and 20 mg/ml and a vehicle control.

We believed that a trial with approximately 650 patients as our first clinical trial of EBI-005 in patients with dry eye disease was impractical. Accordingly, we designed our Phase 1b/2a trial as a smaller trial to determine if treatment with EBI-005 would result in the magnitude of change from baseline on CFS scores, OSDI scores and OSDI scores specifically on the painful or sore eyes question that had been observed by Dr. Dana with anakinra treatment. CFS is a quantitative measure of the severity of dry eye disease and
is a widely used and validated sign of dry eye disease. CFS is measured on a scale from zero, which means no staining and no sign of damage, to a maximum of between three and 15, depending on the particular scale used, which means extensive staining and damage. The OSDI is a commonly used 12-item questionnaire that is designed to determine how a patient experiences the feeling of dry eye disease, the impact that dry eye disease has on routine visual function and what environmental triggers exacerbate symptoms. The OSDI score is a composite of the scores on the individual questions and ranges from zero, which means the patient is experiencing no symptoms, to 100, which means the patient is experiencing severe symptoms. Individual questions in the OSDI, which have scores that range from zero to four, also can be evaluated as measures of specific symptoms.

We formulate the active pharmaceutical ingredient of EBI-005 with a preservative-free solution, or vehicle, for topical, ophthalmic delivery as an eye drop. In descriptions of our clinical trials in this Annual Report on Form 10-K, we refer to this formulation also as EBI-005. The vehicle is a proprietary mixture of excipients that are commonly used in eye drops. In each of our clinical trials the placebo control group receives vehicle, which is the same as the EBI-005 formulation used in the trial except that it contains none of the EBI-005 active pharmaceutical ingredient.

We tested EBI-005 at concentrations of 5 mg/ml and 20 mg/ml in our Phase 1b/2a trial. We analyzed efficacy data by first combining both EBI-005 dose groups, as specified in the statistical analysis plan, into a single combined EBI-005 treatment group and then by individual EBI-005 dose groups. We designed our Phase 1b/2a trial to evaluate differences in patient responses to EBI-005 on multiple efficacy endpoints without an expectation of achieving statistical significance compared to vehicle control. We believed that the results of our Phase 1b/2a trial would provide a foundation for making informed choices regarding dose of EBI-005, patient eligibility criteria and measures of clinical efficacy for our Phase 3 trials. As described below, we have incorporated our evaluations of the results of our Phase 1b/2a trial into the design of our pivotal Phase 3 clinical program. The pivotal Phase 3 clinical program described in this Annual Report on Form 10-K is based on our current protocols and is subject to change with respect to the planned second Phase 3 clinical trial and the separate clinical trial evaluating the safety of treatment with EBI-005 for one year.

**Pivotal Phase 3 Clinical Program of EBI-005 for the Treatment of Dry Eye Disease**

Our pivotal Phase 3 clinical program will consist of two Phase 3 clinical trials to evaluate the safety and efficacy of EBI-005 from baseline at 12 weeks at a concentration of 5 mg/ml for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 at the same concentration for one year. We plan to conduct each of our Phase 3 trials in approximately 650 patients. We began randomizing and treating patients in our first Phase 3 trial in January 2014. We plan to conduct our first Phase 3 trial at up to 40 centers in the United States. If the results of our first Phase 3 trial are favorable, we currently intend to initiate our second Phase 3 trial after reviewing top-line data from our first Phase 3 trial. We will conduct each of our Phase 3 trials in an outpatient setting in a natural environment. We will not use a controlled adverse environment chamber.

We have designed our pivotal Phase 3 clinical program based on the results we observed in our Phase 1b/2a clinical trial of EBI-005 for the treatment of dry eye disease. We met with the FDA’s Division of Transplant and Ophthalmology Products in July 2013 to discuss our planned pivotal Phase 3 clinical program. Based in part on the discussions at that meeting, we believe that if the results of both of our Phase 3 trials are favorable, they will be sufficient, together with our separate safety trial, to support a BLA submission to the FDA seeking approval of EBI-005 for the treatment of dry eye disease in the United States.

We are evaluating the development of EBI-005 in Europe in addition to the United States and have sought and received scientific advice from the European Medicine Agency’s, or EMA, Committee for Medicinal Products for Human Use, or CHMP, regarding European registration requirements for EBI-005 for the treatment of dry eye disease. The scientific advice received indicates that the requirements for European registration in dry eye disease will differ from the requirements for registration in the United States and our pivotal Phase 3 clinical program is not consistent with the advice of the CHMP. We will continue to evaluate the scientific advice received from the EMA and plan to further discuss with the EMA a registration plan for EBI-005 in moderate to severe dry eye disease for the European Union.

**Phase 3 Clinical Trial Endpoints**

Based on our communications with the FDA, we believe that in order to support a BLA submission to the FDA seeking approval of EBI-005 in the United States, we must demonstrate in two Phase 3 clinical trials a statistically significant improvement in at least one sign and one symptom of dry eye disease in patients treated with EBI-005 compared to improvement on the same sign and symptom in patients receiving vehicle. We will specify a sign and a symptom as co-primary endpoints in our Phase 3 trials. In the first Phase 3 trial we have defined one co-primary endpoint as a change in CFS score, a sign of dry eye disease, from baseline at week
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12 with EBI-005 treatment compared to change from baseline at week 12 with vehicle control. We have defined the other co-primary endpoint as improvement in pain and discomfort as measured by the painful or sore eyes question on the OSDI, a symptom of dry eye disease, from baseline at week 12 with EBI-005 treatment compared to change from baseline at week 12 with vehicle control.

We have included the change in the OSDI score from baseline at week 12 with EBI-005 treatment compared to change from baseline at week 12 with vehicle control as another measure of change in symptoms and as a secondary endpoint in our first Phase 3 trial. We also included as secondary endpoints in our first Phase 3 trial changes in CFS in specified regions of the cornea from baseline at week 12 with EBI-005 treatment compared to changes from baseline at week 12 with vehicle control. Other secondary endpoints in our first Phase 3 trial include the evaluation of the change in all primary and secondary endpoints from baseline at week nine. In addition to efficacy endpoints, other secondary endpoints in this Phase 3 trial include the evaluation of the safety, tolerability and immunogenicity, or the tendency to elicit an antibody response, of EBI-005 after 12 weeks of dosing.

If we demonstrate a statistically significant improvement from baseline in the EBI-005 treatment group relative to the improvement from baseline in the vehicle control group on a pre-specified secondary endpoint in the first of our Phase 3 trials, we may decide to substitute that secondary endpoint as a co-primary endpoint in our second Phase 3 trial prior to initiation of this second Phase 3 trial. If we demonstrate a statistically significant improvement from baseline in the EBI-005 treatment group relative to the improvement from baseline in the vehicle control group on the substituted co-primary endpoint in the second Phase 3 trial, we may combine the results of the evaluation of the pre-specified secondary endpoint in the first Phase 3 trial with the results of the substituted pre-specified co-primary endpoint in the second Phase 3 trial, in support of our application for marketing approval of EBI-005. Based on our meeting with the FDA in July 2013, we believe that, although it would be a review issue at the time of our application for marketing approval, the FDA may consider this an acceptable means of meeting the requirement that we duplicate in two Phase 3 trials a statistically significant improvement on a clinically relevant sign or symptom.

Phase 3 Clinical Trial Design

Each of our Phase 3 trials will be a double masked, randomized, placebo controlled study. Patients will be screened on the basis of eligibility criteria at a first visit. We expect that patients who qualify for enrollment will receive topical administration in each eye three times per day for one week of vehicle. At the conclusion of this one-week run-in period, we will reassess patients against additional eligibility criteria. Those patients who qualify under these additional criteria will be randomly assigned, or randomized, to either an EBI-005 treatment group or a vehicle control group. We refer to the time at which we randomize a patient as baseline.

Eligible patients will be at least 18 years of age, with moderate to severe dry eye disease. Eligibility criteria also will include the following:

- OSDI score greater than or equal to 23 and less than or equal to 75 at screening. A score greater than or equal to 23 and less than or equal to 32 is considered moderate dry eye disease. A score greater than or equal to 33 is considered severe dry eye disease.
- OSDI score greater than or equal to 19 and less than 50 at randomization.
- CFS score of greater than or equal to six and less than 15 on the National Eye Institute, or NEI, scale at screening. A score greater than or equal to six and less than 15 is consistent with moderate to severe dry eye disease.
- CFS score of greater than or equal to five and less than 15 on the NEI scale at randomization.

During our Phase 1b/2a trial of EBI-005, we observed greater variability in clinical response in patients who had an OSDI score greater than or equal to 50 at randomization. We believe this increased variability in clinical response made it more difficult to detect differences between the combined EBI-005 treatment groups and the vehicle control group on the primary and secondary efficacy endpoints. In our Phase 3 trials, we will exclude patients with an OSDI score greater than or equal to 50 at randomization because we believe this criteria will reduce variability in clinical response and improve our ability to detect differences between the EBI-005 treatment group and the vehicle control group on the co-primary and secondary efficacy endpoints.

Patients who are randomized will receive topical administration in each eye three times per day for 12 weeks of EBI-005 at 5 mg/ml or vehicle control beginning at randomization. The patients will undergo study evaluations at weeks one, three, six, nine and 12 following randomization. The last dose of EBI-005 will be completed 12 weeks after randomization. We will require patients to attend a final visit three weeks after their week 12 visit.
The timeline for our first Phase 3 trial of EBI-005 and number of patients, or subjects, to be randomized into the EBI-005 treatment and vehicle control groups are depicted in the graphic below.

The following aspects of the design of our Phase 3 trials are based on the results we observed in our Phase 1b/2a trial of EBI-005 for the treatment of dry eye disease:

**Eligibility Criteria—OSDI Score.** Our Phase 3 trials of EBI-005 will include patients with OSDI scores at screening greater than or equal to 23 and less than or equal to 75 and with OSDI scores at randomization greater than or equal to 19 and less than 50. In a retrospective analysis of the results of our Phase 1b/2a trial, in which we included patients with OSDI scores at screening greater than or equal to 23 and less than 90 and with OSDI scores at randomization greater than or equal to 19, we observed in patients with OSDI scores less than 50 at randomization less variability in clinical response than we observed in patients with OSDI scores greater than or equal to 50 at randomization. Therefore, we have designed our Phase 3 trials to exclude at randomization patients with an OSDI score greater than or equal to 50. We believe this will make it more likely that our Phase 3 trials will confirm the trend of greater improvement in clinical response from baseline in the combined EBI-005 treatment groups relative to the improvement from baseline in vehicle control group that we observed in our Phase 1b/2a trial. We also have designed our Phase 3 trials to exclude at screening patients with an OSDI score greater than 75, as compared to greater than or equal to 90 in our Phase 1b/2a trial. We believe we can increase the likelihood of recruiting patients who will have an OSDI score less than 50 at randomization by excluding patients with OSDI scores greater than 75 at screening.

**Eligibility Criteria—CFS Score.** We will include patients with CFS scores greater than or equal to six and less than 15 on the NEI scale at screening or greater than or equal to five and less than 15 on the NEI scale at randomization. These are the same criteria we used in our Phase 1b/2a trial, except that we did not exclude patients with a CFS score of 15 at randomization in our Phase 1b/2a trial. The determination of CFS score is made by microscopic examination of the cornea by the physician who has to assess the extent of staining in each of five regions of the ocular surface. We have developed an eye-piece for the microscope that projects a grid pattern onto the cornea that divides it into the five regions to be assessed. We believe this helps the physician and reduces some of the subjectivity inherent in the assessment. By reducing the subjectivity, we believe we generate a more reliable data set for statistical analysis.

**Use of Rescue Artificial Tears.** We will restrict the use of rescue artificial tears by patients in our Phase 3 trials. In our Phase 1b/2a trial, we measured artificial tear usage by patients as a pre-specified exploratory endpoint. Mean and median artificial tear usage were significantly higher in patients in the vehicle control group than those in the EBI-005 treatment groups. We believe that the use of artificial tears by patients in the vehicle control group could have had an impact on the sign and symptom assessments in our Phase 1b/2a trial. If such assessments improved because of the use of artificial tears, we believe these improvements would have occurred disproportionately in the vehicle control group because we observed that patients in the vehicle control group used more artificial tears and a higher percentage of patients in the vehicle control group used large amounts of artificial tears compared to the combined EBI-005 treatment groups. As a result, we believe that the differences in our Phase 1b/2a trial in the sign and symptom assessment scores between the vehicle control group and the combined EBI-005 treatment groups might have been greater if the use of artificial tears had been restricted.
Dose of EBI—005. Overall in our Phase 1b/2a trial, we did not observe any significant differences between administration of EBI-005 three times per day at a concentration of 5 mg/ml and at a concentration of 20 mg/ml. Based on our understanding of the mechanism of action and potency of EBI-005, we did not expect to observe any such differences. In our Phase 3 trials, we will be evaluating topical administration of EBI-005 three times per day at a concentration of 5 mg/ml.

Efficacy Endpoint—CFS Score. In a retrospective analysis of the results of our Phase 1b/2a trial, we observed a trend of greater improvement of CFS scores from baseline at week six in the combined EBI-005 treatment groups relative to the improvement from baseline in the vehicle control group when we excluded the seven patients who had major protocol deviations and included only patients who had baseline OSDI scores less than 50. We believe this trend is consistent with the results of the anakinra trial. In our first Phase 3 trial, we have pre-specified the change in CFS scores from baseline at week 12 as a co-primary efficacy endpoint.

Efficacy Endpoint—OSDI Pain. In a retrospective analysis of the results of our Phase 1b/2a trial, we observed a trend of greater improvement of the scores on the OSDI question regarding painful or sore eyes from baseline at week six in the combined EBI-005 treatment groups relative to the improvement from baseline in the vehicle control group when we excluded the seven patients who had major protocol deviations and included only patients who had baseline OSDI scores less than 50. We believe this trend is consistent with our understanding of the mechanism of action of EBI-005 and the trends we observed in our retrospective analysis of the results of the anakinra trial. In our first Phase 3 trial, we have pre-specified the change in scores from baseline on the OSDI question regarding painful or sore eyes from baseline at week 12 as a co-primary efficacy endpoint.

Number of Patients. Based on the results of our Phase 1b/2a trial, we believe that each of our Phase 3 trials will be adequately powered with approximately 650 patients to detect a difference between the EBI-005 treatment group and vehicle control on our proposed co-primary efficacy endpoints. We plan to perform a sample size reassessment on a masked basis of all randomized patients after the first one-third of the randomized patients complete 12 weeks of treatment with EBI-005 in our first Phase 3 trial to determine whether we need to increase the number of patients we randomize in this trial. We plan to conduct this sample size reassessment to determine whether the observed variability of the clinical response is greater than the variability we expected based on the results of our Phase 1b/2a trial. If we need to increase the number of patients, we plan to randomize an equal number of additional patients in each treatment arm of our first Phase 3 trial. We expect to engage a contract research organization, or CRO, to conduct this sample size reassessment, and we expect not to receive any information other than whether we need to randomize additional patients. We do not believe this masked sample size reassessment will compromise our final statistical analysis. We do not expect that any increase in the number of randomized patients will have a significant impact on the costs or duration of our first Phase 3 trial.

Duration of Trial. In the anakinra trial, the investigators observed greater improvements on mean change from baseline on both CFS score and OSDI score at 12 weeks in patients treated with lower dose anakinra compared to vehicle control than was observed at six weeks. We believe that the longer treatment period in our Phase 3 trials may improve our ability to detect differences between the EBI-005 treatment group and the vehicle control group on our co-primary efficacy endpoints.

Vehicle. We have modified the vehicle in our formulation of EBI-005 for our Phase 3 trials relative to the vehicle in our formulation of EBI-005 for our Phase 1b/2a trial primarily by removing carboxymethyl cellulose, or CMC, a common ingredient in artificial tears. CMC is not included in Restasis. We made this refinement to make our formulation of EBI-005 suitable for vialing in an industry standard single-use format, to increase stability of EBI-005 and to improve ease of manufacturing. We believe our new formulation remains comfortable to patients and that the removal of CMC will not meaningfully affect patient responses.

Natural Environment. We will conduct our Phase 3 trials in a natural environment and will not use a controlled adverse environment chamber. We also conducted our Phase 1b/2a trial in a natural environment. A controlled adverse environment chamber historically has been used in trials of product candidates for the treatment of dry eye disease. A controlled adverse environment chamber allows the clinical investigator to exacerbate the signs and symptoms of dry eye in a controlled manner by regulating humidity, temperature, airflow, lighting conditions and visual tasking. However, we believe that the controlled adverse environment chamber introduces differences in the presentation and manifestation of dry eye disease and in patients’ perceptions of their disease. We believe that the controlled adverse environment chamber does not reflect the environment in which patients experience their dry eye disease on a daily basis and in which patients and physicians ultimately will judge the benefits of any dry eye disease drug. As a result, we believe that a natural environment is a better setting for the evaluation of EBI-005.
In addition to the two Phase 3 trials required to support marketing approval of EBI-005 for the treatment of dry eye disease in the United States, we will be required to demonstrate the long-term safety of EBI-005 treatment in a safety trial. To meet this requirement, we plan to conduct a safety trial with no fewer than 100 patients who will be treated with EBI-005 for one year. We expect that patients in this safety trial will be treated three times a day with EBI-005 at a concentration of 5 mg/ml. During this study, the safety and tolerability of longer term exposure to EBI-005 will be evaluated, along with immunogenicity and potentially other endpoints that may support the application for marketing approval of EBI-005.

We began randomizing and treating patients in our first Phase 3 trial in our pivotal Phase 3 clinical program in January 2014. Based on our estimates regarding patient enrollment, we expect to have top-line data from our first Phase 3 trial available in early 2015. If the results of our first Phase 3 trial are favorable, we plan to conduct a second Phase 3 trial that will be designed to evaluate co-primary endpoints that met the criteria of acceptability in our first Phase 3 trial as co-primary endpoints or as one co-primary endpoint and one secondary endpoint. We expect that our second Phase 3 trial will be designed similarly to the first trial. We currently intend to initiate our second Phase 3 trial after reviewing top-line data from our first Phase 3 trial. If the results of both Phase 3 trials in our pivotal Phase 3 clinical program and our separate safety trial are favorable, we plan to submit a BLA seeking approval in the United States of EBI-005 for the treatment of dry eye disease in the second half of 2016.

**Completed Phase 1b/2a Clinical Trial in Dry Eye Disease**

In the second quarter of 2013, we completed a multicenter, double masked, randomized, placebo controlled Phase 1b/2a clinical trial evaluating the safety and biological activity of EBI-005 in patients with moderate to severe dry eye disease. We conducted this trial in 74 patients at eight centers in the United States. We conducted this trial in a natural environment. We did not use a controlled adverse environment chamber.

We screened patients against eligibility criteria at a first visit. Patients who qualified for enrollment received topical administration in each eye three times per day for one week of vehicle. At the conclusion of the one-week run-in period, we reassessed patients again against eligibility criteria. Those patients who qualified under these additional criteria were randomized to one of three treatment groups. We refer to the CFS score, OSDI score and other measures taken at randomization as baseline.

Eligible subjects were at least 18 years of age, with moderate to severe dry eye disease. Additional eligibility criteria included the following:

- OSDI score greater than or equal to 23 and less than 90 at the time of screening;
- OSDI score greater than or equal to 19 at randomization;
- CFS score greater than or equal to six and less than 15 on the NEI scale at the time of screening; and
- CFS score greater than or equal to five at randomization.

Patients who were randomized to a treatment group were treated in both eyes three times per day for six weeks beginning at randomization. Treatments for the three groups in this trial were as follows:

- In the first group, 22 patients received topical administration in each eye three times per day of EBI-005 at a concentration of 20 mg/ml.
- In the second group, 22 patients received topical administration in each eye three times per day of EBI-005 at a concentration of 5 mg/ml.
- In the third group, 30 patients received topical administration in each eye three times per day of vehicle.

We assessed patients at screening, at randomization, at evaluation visits on weeks two, four and six following randomization, and at a follow up visit one week after the completion of treatment.
The principal objective of our Phase 1b/2a trial was to evaluate the safety and tolerability of six weeks of dosing three times a day with EBI-005 as compared to vehicle control in patients with moderate to severe dry eye disease. The protocol also included other objectives and pre-specified primary and secondary efficacy endpoints to assist us in the evaluation of the biological and clinical response of patients to EBI-005.

The primary safety endpoints included adverse event reporting, complete ophthalmic examination, testing for corneal health and assessment of clinical laboratory markers. The primary efficacy endpoint of our Phase 1b/2a trial was the absolute change of OSDI score, a symptom of dry eye disease, at week six from baseline. The secondary efficacy endpoints of this trial were changes at week six from baseline in the following sign and symptom scores:

- CFS score, a sign of dry eye disease.
- Symptom assessment in dry eye, or modified SANDE, questionnaire score. The modified SANDE questionnaire is a short questionnaire completed by the patient that quantifies the frequency and severity of symptoms of dry eye disease using a visual analog scale.
- Subject-rated and investigator-rated global symptom assessment, or GSA. The GSA is a short questionnaire that assesses degrees of relief or worsening of specified signs and symptoms of dry eye disease.
- Subject-rated individual ocular symptom assessments of the severity of eyelid itching, the sensation of having a foreign body in the eye and ocular burning or pain.

**Statistical Analysis and Significance**

In accordance with the protocol and the statistical analysis plan, the primary analysis population was the intent-to-treat, or ITT, population, which is all patients enrolled in the trial. There were major protocol deviations with respect to seven of the 74 enrolled patients in the intent-to-treat population. Five of these deviations occurred in the EBI-005 treatment groups, and two occurred in the vehicle control group. These deviations included two patients, one in each of the EBI-005 treatment groups, who were inadvertently enrolled despite having met an exclusion criteria of no history of corneal surgery and five patients in the vehicle control group who missed at least one entire day’s dosing. In accordance with the protocol and the statistical analysis plan, we also conducted analyses on the 67 enrolled patients in the efficacy evaluable, or EE, population, which excludes those patients with major protocol deviations.

We analyzed efficacy data by first combining both the 5 mg/ml and 20 mg/ml EBI-005 dose groups, as specified in the statistical analysis plan, and by individual dose groups. Overall, we did not see a meaningful difference in response between the two EBI-005 dose groups on any efficacy measure when we analyzed the data for each separate drug treatment group in either the intent-to-treat or efficacy evaluable population.
In our Phase 1b/2a trial, the median baseline OSDI score was 50 for all patients at randomization, meaning that 50% of the intent-to-treat population had baseline OSDI scores of less than 50. During our Phase 1b/2a trial of EBI-005, we observed greater variability in clinical response in patients who had an OSDI score greater than or equal to 50. We believe that increased variability in clinical response made it more difficult to detect differences between the combined EBI-005 treatment groups and the vehicle control group on the primary and secondary efficacy endpoints. Therefore, we performed additional retrospective analyses that were not pre-specified primary or secondary endpoints in our Phase 1b/2a trial. In these analyses, we assessed whether patients with OSDI scores of less than 50 at baseline responded differently to EBI-005 treatment than patients with OSDI scores greater than or equal to 50 at baseline. The results of these analyses are described below. Although a retrospective analysis performed after trial results are unmasked can result in the introduction of bias, we believe that the various retrospective analyses that we performed will assist us in the assessment of the population of patients with the most robust separation between the treatment and vehicle control groups for both signs and symptoms to inform the design of our Phase 3 trials.

We designed this Phase 1b/2a trial to measure trends of efficacy, and we did not power the trial to measure with statistical significance the differences in any efficacy endpoints. Therefore, the improvements we observed with respect to pre-specified primary, secondary and exploratory endpoints and retrospective analyses in the intent-to-treat and efficacy evaluable populations that are described below were not statistically significant when compared to vehicle, except as specifically noted.

**Primary and Secondary Efficacy Endpoints—Intent-to-Treat Population**

We observed in the combined EBI-005 treatment groups in the intent-to-treat population an improvement from baseline in both CFS, a sign of dry eye disease, and OSDI, a symptom of dry eye disease, after six weeks of treatment with EBI-005. We believe that the magnitudes of these responses were clinically relevant.

The table below sets forth for the combined EBI-005 treatment groups and the vehicle control group, in each case assessing the intent-to-treat population, the mean score at baseline, mean change from baseline at week six, and the percentage change from baseline at week six on the following primary and secondary efficacy endpoints:

- the primary efficacy endpoint of change from baseline in OSDI score; and
- the secondary efficacy endpoint of change from baseline in CFS.

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<tbody>
<tr>
<td>Mean Score at Baseline</td>
<td>OSDI 49.8 Points</td>
<td>OSDI 52.6 Points</td>
</tr>
<tr>
<td></td>
<td>CFS 9.1 Points</td>
<td>CFS 8.8 Points</td>
</tr>
<tr>
<td>Mean Change from Baseline at Week Six</td>
<td>OSDI 18.9 Points</td>
<td>OSDI 19.0 Points</td>
</tr>
<tr>
<td></td>
<td>CFS 3.0 Points</td>
<td>CFS 2.7 Points</td>
</tr>
<tr>
<td>Percentage Change from Baseline at Week Six</td>
<td>OSDI 38%</td>
<td>OSDI 36%</td>
</tr>
<tr>
<td></td>
<td>CFS 33%</td>
<td>CFS 31%</td>
</tr>
</tbody>
</table>

We observed improvements in the combined EBI-005 treatment groups in the intent-to-treat population from baseline through week six on each of the secondary efficacy endpoints of modified SANDE questionnaire score, subject-rated and investigator-rated GSA and subject-rated individual ocular symptom assessments of the severity of eyelid itching, the sensation of having a foreign body in the eye and ocular burning or pain. However, the differences between the improvements we observed in the combined EBI-005 treatment groups from baseline at week six and the improvements we observed in the vehicle control group from baseline at week six were not statistically significant for any of these measures. We do not plan to use any of these measures as primary or secondary endpoints in our Phase 3 trials.

**Analyses of Efficacy Endpoints—Efficacy Evaluable Population**

As noted above, there were major protocol deviations with respect to seven of the 74 enrolled patients in the intent-to-treat population. As a result, we believe the efficacy evaluable population, which excludes those patients with major protocol deviations, is a more appropriate population on which to conduct further analyses. The results of our additional retrospective analyses are presented below only with respect to the efficacy evaluable population. The results of pre-specified analyses of the corresponding primary and secondary efficacy endpoints with respect to the efficacy evaluable population also are presented below.
We observed in patients with OSDI scores less than 50 at randomization less variability in clinical response than we observed in patients with OSDI scores greater than or equal to 50 at randomization. We believe that increased variability in clinical response in the total efficacy evaluable population made it more difficult to detect differences between the EBI-005 treatment groups and vehicle control. We refer to the efficacy evaluable population with OSDI scores of less than 50 at randomization as the EE50 population.

Retrospective Analysis—OSDI Score. In the total efficacy evaluable population and in patients in the EE50 population, we observed an improvement of OSDI scores from baseline at week six in the combined EBI-005 treatment groups. We believe the magnitude of the response was clinically relevant. We also observed that the trend in the improvement in OSDI scores from baseline at week six favoring the combined EBI-005 treatment groups compared to the improvement in OSDI scores from baseline at week six in vehicle control was greater in the EE50 population than in the total efficacy evaluable population.

The table below sets forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population:

- the mean OSDI score at baseline;
- the mean change in OSDI score from baseline to week six; and
- the percentage change in OSDI score from baseline to week six.

<table>
<thead>
<tr>
<th></th>
<th>Combined EBI-005 treatment groups</th>
<th>Vehicle control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OSDI score</strong></td>
<td>EE population (n = 41)</td>
<td>EE50 population (n = 20)</td>
</tr>
<tr>
<td>Mean OSDI Score at Baseline</td>
<td>50.0 Points</td>
<td>31.1 Points</td>
</tr>
<tr>
<td>Mean Change in OSDI from Baseline to Week Six</td>
<td>18.0 Points</td>
<td>12.7 Points</td>
</tr>
<tr>
<td>Percentage Change in OSDI Score from Baseline to Week Six</td>
<td>36%</td>
<td>41%</td>
</tr>
</tbody>
</table>

The graphs below set forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population, the mean change in OSDI scores from baseline at each evaluation visit following randomization during the treatment period.
Retrospective Analysis—Painful or Sore Eyes Question on OSDI. In the total efficacy evaluable population and in patients in the EE50 population, we observed an improvement on the OSDI question regarding painful or sore eyes at week six from baseline in the combined EBI-005 treatment groups. We also observed that the trend in the improvement in the score on the OSDI question regarding painful or sore eyes from baseline at week six favoring the combined EBI-005 treatment groups compared to the improvement in the score on the OSDI question regarding painful or sore eyes from baseline at week six in the vehicle control group was greater in the EE50 population than in the total efficacy evaluable population.

The table below sets forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population:

- the mean score on the OSDI question regarding painful or sore eyes at baseline;
- the mean change in score on the OSDI question regarding painful or sore eyes from baseline at week six; and
- the percentage change in score on the OSDI question regarding painful or sore eyes from baseline at week six.

<table>
<thead>
<tr>
<th>Painful or sore eyes question</th>
<th>Combined EBI-005 treatment groups</th>
<th>Vehicle control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EE population (n = 41)</td>
<td>EE50 population (n = 20)</td>
</tr>
<tr>
<td>Mean Score on OSDI Question at Baseline</td>
<td>1.8 Points</td>
<td>1.4 Points</td>
</tr>
<tr>
<td>Mean Change in Score on OSDI Question from Baseline to Week Six</td>
<td>0.9 Points</td>
<td>0.9 Points</td>
</tr>
<tr>
<td>Percentage Change in Score on OSDI Question from Baseline to Week Six</td>
<td>46% Points</td>
<td>61% Points</td>
</tr>
</tbody>
</table>

The graphs below set forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population, the mean change in scores on the OSDI question regarding painful or sore eyes from baseline at each evaluation visit following randomization during the treatment period.

On most of the other individual OSDI questions, we observed trends in changes in scores at week six from baseline that favored patients treated with EBI-005 compared to patients treated with vehicle control in an analysis of the efficacy evaluable population. On eight of the other OSDI questions, we observed trends in changes in scores at week six from baseline that favored patients treated with EBI-005 compared to vehicle control in an analysis of the efficacy evaluable population. On the other three OSDI questions, we observed trends in changes in scores at week six from baseline that favored vehicle control compared to patients treated with EBI-005 in an analysis of the efficacy evaluable population. However, none of these trends were statistically significant.
Retrospective Analysis—CFS. In the total efficacy evaluable population and in patients in the EE50 population, we observed an improvement in CFS at week six from baseline in the combined EBI-005 treatment groups. We also observed in the EE50 population a strong trend in the improvement in the CFS score from baseline at week six favoring the combined EBI-005 treatment groups compared to improvement in the CFS score from baseline at week six in the vehicle control group. We did not observe this trend in the total efficacy evaluable population.

The table below sets forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population:

- the mean total CFS score at baseline;
- the mean change in total CFS score from baseline at week six; and
- the percentage change in total CFS score from baseline at week six.

<table>
<thead>
<tr>
<th></th>
<th>Combined EBI-005 treatment groups</th>
<th>Vehicle control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EE population (n = 41)</td>
<td>EE50 population (n = 20)</td>
</tr>
<tr>
<td>Mean Total CFS Score at Baseline</td>
<td>9.0 Points</td>
<td>8.9 Points</td>
</tr>
<tr>
<td>Mean Change in Total CFS Score from Baseline at Week Six</td>
<td>3.0 Points</td>
<td>3.5 Points</td>
</tr>
<tr>
<td>Percent Change in Total CFS Score from Baseline at Week Six</td>
<td>33%</td>
<td>39%</td>
</tr>
</tbody>
</table>

The graphs below set forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population, the mean change in total CFS scores from baseline at each evaluation visit following randomization during the treatment period.

Pre-Specified Exploratory Endpoint—Artificial Tear Use

We distributed artificial tears to patients in this trial with one dose per vial. Patients were permitted to use up to four vials of these artificial tears daily. Patients were instructed not to use any other artificial tears during this trial. At the end of the trial,
we counted the number of vials used by each patient. We excluded from our assessment of artificial tear use in the combined EBI-005 treatment groups one patient for whom there were no records of use of artificial tears. In addition, we performed a statistical outlier assessment of artificial tear use and excluded from our assessment of the combined EBI-005 treatment groups one patient whose use of artificial tears was many times greater than any other patient and whose inclusion could distort any statistical analysis. All of the results presented on the use of artificial tears excluded these two patients from the combined EBI-005 treatment groups.

The use of artificial tears was similar at baseline for patients in the combined EBI-005 treatment groups and vehicle control groups. However, over the course of the six-week treatment period of this trial, we observed the following differences, which were statistically significant only with respect to the efficacy evaluable population:

- the mean artificial tear usage was greater in the vehicle control group than in the combined EBI-005 treatment groups in the total efficacy evaluable population (p=0.005) and in the EE50 population (p=0.190);
- the median artificial tear usage was higher in the vehicle control group than in the combined EBI-005 treatment groups in the total efficacy evaluable population and in the EE50 population; and
- a greater percentage of patients in the vehicle control group used large amounts of artificial tears, which we defined as the use of more than 50 vials during this trial, than in the combined EBI-005 treatment groups in the total efficacy evaluable population (p=0.005) and in the EE50 population (p=0.267).

The table below sets forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population:

- the mean number of vials of artificial tears used;
- the median number of vials of artificial tears used; and
- the percentage of patients who used large amounts of artificial tears.

<table>
<thead>
<tr>
<th>Artificial tear use</th>
<th>Combined EBI-005 treatment groups</th>
<th>Vehicle control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EE population (n = 39)</td>
<td>EE50 population (n = 19)</td>
</tr>
<tr>
<td>Mean Number of Vials of Artificial Tears Used</td>
<td>11.1</td>
<td>9.8</td>
</tr>
<tr>
<td>Median Number of Vials of Artificial Tears Used</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Percentage of Patients Who Used Large Amounts of Artificial</td>
<td>5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

The graphs below set forth with respect to each of the combined EBI-005 treatment groups and the vehicle control group in the total efficacy evaluable population and in the EE50 population:

- the mean number of vials of artificial tear usage; and
- the percentage of patients who used large amounts of artificial tears.
Safety, Pharmacokinetics and Immunogenicity

Both doses of EBI-005 were generally well tolerated in our Phase 1b/2a trial. No patients discontinued their participation in this trial due to adverse events. We did not observe any significant imbalances between the combined EBI-005 treatment groups and the vehicle control group in the incidence of ocular adverse events or systemic adverse events. There were no serious adverse events reported during this trial, and no patients discontinued the trial due to adverse events or for any other reason. The reporting of ocular and non-ocular adverse events was similar between the treatment and vehicle control groups. The number of ocular adverse events reported during this trial and the number of patients in our Phase 1b/2a trial with one or more ocular adverse events as coded using MedDRA Version 12.1, a standard method of reporting adverse events, are set forth in the table below.

<table>
<thead>
<tr>
<th></th>
<th>Vehicle Control</th>
<th>EBI-005 (5 mg/ml N=22)</th>
<th>EBI-005 (20 mg/ml N=22)</th>
<th>EBI-005 (5+20 mg/ml N=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with one or more ocular adverse events</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
<td>2 (9%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Eye disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye irritation</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Eye pain</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Foreign body sensation in eyes</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Increased tearing</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Ocular redness</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>
In addition to the ocular adverse events noted above, two patients reported application site pain during the one-week run-in period of this trial when all patients received only vehicle and one patient in the vehicle control group reported application site pain during the treatment period of this trial. Application site pain is coded under general disorders and administrative site conditions, and not eye disorders, under MedDRA Version 12.1.

There was no measurable EBI-005 in the systemic circulation following topical administration. We observed low titer, anti-EBI-005 antibodies in three of 44 treated patients. The presence of these antibodies was not associated with any clinically relevant observations.

We have used an assay that generates a signal in the presence of IL-1\(\beta\) and EBI-005, but cannot distinguish between them, to assess the amount of EBI-005 remaining on the surface of the eye. Using this assay, we observed in tears of patients treated with EBI-005 a 20-fold increase in signal compared to signal prior to dosing with EBI-005. We believe this increase is due to the high concentration of EBI-005 on the surface of the eye. We have correlated the levels of this signal with the time since the last dose of EBI-005 and believe this correlation indicates EBI-005 is present on the eye for almost 10 hours after dosing.

**Completed Phase 1 Clinical Trial in Healthy Volunteers**

In 2012, we completed a double masked, placebo controlled, single dose Phase 1 clinical trial evaluating the safety and tolerability of EBI-005 in healthy volunteers. We conducted our Phase 1 trial in 16 healthy volunteers at a single center in the United States. We conducted this trial in a natural environment. We did not use a controlled adverse environment chamber.

The principal objective of our Phase 1 trial was to evaluate the safety and tolerability of topical ocular administration of EBI-005 in healthy volunteers. Other objectives of this trial were to evaluate the pharmacokinetics and immunogenicity of EBI-005.

Subjects were randomized to receive EBI-005 or vehicle on three occasions, every six hours, on day one. Subjects randomized to the EBI-005 treatment groups received EBI-005 in the right eye and vehicle in the left eye. Subjects randomized to the vehicle control groups received vehicle in each eye. Subjects were randomized in two groups as follows:

- **Group 1**
  - Six subjects: 5 mg/ml EBI-005, one dose at six-hour intervals
  - Two subjects: vehicle, one dose at six-hour intervals

- **Group 2**
  - Six subjects: 20 mg/ml EBI-005, one dose at six-hour intervals
  - Two subjects: vehicle, one dose at six-hour intervals

We assessed the subjects for safety and tolerability for four days following the one day of dosing and at a final follow up visit seven days following dosing.

EBI-005 was generally well tolerated in this Phase 1 trial. There were no serious adverse events reported during this trial, and no subjects discontinued their participation in this trial due to adverse events. The reporting of mild ocular and non-ocular adverse events was similar between the treatment and vehicle control groups. There were no detectable systemic levels of EBI-005 and no specific anti-EBI-005 antibody formation in any of the subjects exposed to EBI-005.

**Expand the Use of EBI-005 for Additional Ocular Indications**

We are evaluating other ocular surface diseases for which we believe EBI-005 treatment may be beneficial. In March 2014, we began randomizing and treating subjects in our Phase 2 clinical trial of EBI-005 for the treatment of allergic conjunctivitis in patients who have not responded adequately to antihistamines and mast cell stabilizers, which are the current standard of care. Based on our estimates regarding patient enrollment, we expect that top-line data from the trial could be available before the end of 2014.
**Allergic conjunctivitis**

Allergic conjunctivitis is an inflammatory disease of the conjunctiva, the membrane covering the inside of the eyelids and white part of the eye, primarily from a reaction to allergy-causing substances such as pollen or pet dander. This inflammation results in the primary sign of redness and primary symptom of acute itch. According to a study on the management of seasonal allergic conjunctivitis published in 2012 in the peer reviewed journal *Acta Ophthalmologica*, allergic conjunctivitis affects 15% to 40% of the United States population. Allergic conjunctivitis ranges in clinical severity from relatively mild, common forms to more severe forms that can cause impaired vision and even, in the most severe cases, blindness. The mild to moderate manifestations of allergic conjunctivitis tend to fall into the seasonal, or SAC, and perennial, or PAC, allergic conjunctivitis classes. The more severe forms of allergic conjunctivitis include vernal keratoconjunctivitis, or VKC, and atopic keratoconjunctivitis, or AKC.

VKC involves severe inflammation of the conjunctiva and cornea. VKC appears most often in young males and can have significant effects on children, including photophobia, or abnormal sensitivity to light, and pain and foreign body sensation in patients with inflammation of the cornea. Although VKC often resolves spontaneously following puberty, visual impairment can be severe if the cornea is extensively involved. According to a study on vernal keratoconjunctivitis published in 2004 in the peer reviewed journal *Eye-Nature*, approximately 6% of VKC patients show reduced visual acuity. VKC is rare in the United States and is classified by the FDA as a distinct disease, which is a necessary precondition for a product to qualify for orphan drug designation.

AKC, while more common than VKC, is also rare in the United States. AKC involves severe, chronic external ocular inflammation associated with asthma and eczema that may first appear in teenagers and continue for decades. It is often associated with severe photophobia and extreme discomfort and pain. Patients with AKC often have difficulty opening their eyelids in the morning as a result of a combination of ocular discharges and discomfort. AKC also commonly impairs the vision of patients due to a combination of corneal surface disease and frequent scarring. In severe cases of AKC, ulceration of the cornea can result in blindness.

We believe that prolonged and more severe cases of allergic conjunctivitis, including VKC and AKC, are characterized by an inflammatory process that is mediated by IL-1. IL-1 stimulates the maturation and recruitment of antigen presenting cells, or dendritic cells, that perpetuate or exacerbate the allergic response. IL-1 also mediates the turning on and off of genes that code for key chemokines that activate and direct pathogenic white blood cells to the ocular surface.

**Treatment of Allergic Conjunctivitis**

For many patients with chronic or more severe forms of allergic conjunctivitis, antihistamines and mast cell stabilizers are not sufficient to treat their signs and symptoms. These refractive patients often are treated with topical corticosteroids, which have been associated with a higher risk of developing glaucoma and cataracts and an increased risk of ocular infection. We believe there remains a significant unmet medical need for new treatments for patients suffering from VKC and AKC and for patients with SAC and PAC that have severe enough disease that they are not satisfactorily treated by antihistamines and mast cell stabilizers.

**Phase 2 Clinical Trial of EBI-005 for the Treatment of Allergic Conjunctivitis**

We are conducting our Phase 2 clinical trial of EBI-005 for the treatment of allergic conjunctivitis in controlled exposure models commonly used to assess anti-allergy medications. In these models, subjects are tested following exposure to specific allergens. The conjunctival allergen challenge model, or CAC, is an allergen challenge model that achieves a very high transient dose exposure by placing allergen directly into the space between the eyelid and the surface of the eye of the study subject. The allergen environmental exposure chamber, or EEC, is another clinical model that exposes patients to allergen in the circulated air of a sealed room. We believe the CAC and the EEC models will mimic the exacerbation of disease typically observed in those patients with prolonged and more severe cases of allergic conjunctivitis.

We currently expect to conduct our Phase 2 trial in approximately 150 subjects at a single center in Canada. We will enroll ragweed-allergic volunteers whose allergy has been confirmed with a positive skin prick test to ragweed within one year prior to enrollment. Inclusion and exclusion criteria will require that subjects have a history of chronic ocular allergy and resistance to treatment with antihistamines and mast cell stabilizers. We will enroll subjects in EEC and CAC arms. Subjects will be randomized to each arm and to receive either EBI-005 at 5 mg/ml or vehicle. Treatment will be applied in each of the subject’s eyes three times per day for two weeks. The subjects will undergo study evaluations one day following randomization and then return to the clinic 14 days later to undergo daily allergen exposure for 3 consecutive days in either the EEC or CAC model. Subjects will then return one day following last allergen exposure. The last study visit will occur at study day 45 which is 25 days after last allergen exposure.
The design of our Phase 2 trial of EBI-005 is depicted in the graphic below.

The primary endpoint in both the EEC and CAC arms is an assessment of symptoms of allergic conjunctivitis as measured by subject reported ocular itching. The secondary endpoints in our Phase 2 trial include redness, swelling and other measures of the signs of ocular allergy. We also will assess general ocular safety and tolerability. If the results of this Phase 2 trial are favorable, we will use these results to help determine whether to proceed with, and how to design, subsequent pivotal studies for allergic conjunctivitis in the United States, Canada, Europe and other countries. We expect that the FDA will require that any pivotal clinical trials evaluate EBI-005 against standard-of-care antihistamines. We also may study the response of VKC populations to treatment with EBI-005 separately to determine whether to proceed with further development and whether an orphan drug designation might be available for EBI-005 for such use.

Our Other Product Candidates

In addition to EBI-005, we have two proprietary product candidates in early preclinical development, EBI-029 and EBI-028. We plan to further evaluate these product candidates for potential use in humans as follows:

- EBI-029, a novel inhibitor of the cytokine IL-6, which we are developing as an intravitreal injection for the treatment of certain retinal diseases, such as DME; and
- EBI-028, a novel inhibitor of the cytokine IL-17, which we are developing as an intravitreal injection for the treatment of uveitis and other diseases of the back of the eye, such as dry AMD.

If results of our preclinical studies are favorable, we will consider further development of these product candidates either directly by us or in collaboration with one or more strategic collaborators. We are continuing to apply our AMP-Rx platform to further enhance our current product candidates and generate new product candidates.

**EBI-029 – a Novel Inhibitor of the Cytokine IL-6**

DME is characterized by abnormal new blood vessel formation and growth, referred to as neovascularization, in the layer of tissue beneath the retina called the choroid. 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 the current standard of care for the treatment of DME.

We designed and engineered EBI-029 using our AMP-Rx platform to block two forms of IL-6: free IL-6 and IL-6 bound to IL-6 receptor, or IL-6R. We believe the ability of EBI-029 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 unable to test EBI-029 in animal models because EBI-029 only blocks human IL-6. In a live animal, or *in vivo*, study in a mouse model of choroidal neovascularization, we used a commercially available anti-IL-6 antibody that blocks mouse IL-6. In this study, we observed a significant reduction in abnormal neovascularization in animals treated with this anti-IL-6 antibody compared to animals that received placebo.
The graphs below illustrate the blocking of IL-6 signaling in an \textit{in vitro} cell-based assay by increasing concentrations of the fragment of EBI-029 that blocked IL-6 and of a reference anti-IL-6-receptor antibody, or anti-IL-6R, that also blocked IL-6. EBI-029 blocked signaling of free IL-6 (left panel) and also IL-6 bound to soluble IL-6R (right panel). In contrast, the anti-IL-6R antibody blocked signaling of free IL-6 (left panel) but did not block signaling of IL-6 bound to soluble IL-6R (right panel). We believe the ability of EBI-029 to block signaling of free IL-6 and IL-6 bound to IL-6R could lead to improved biological effect.

**EBI-029 – a Novel Inhibitor of the Cytokine IL-17**

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 \textit{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 \textit{British Journal of Ophthalmology}, uveitis also accounts for approximately 10% to 15% of cases of blindness in the United States. In a study published in the peer reviewed journal \textit{Basic and Clinical Immunology}, patients with uveitis had elevated serum levels of IL-17. In addition, in a published study in the peer reviewed \textit{Journal of Translational Medicine}, patients with dry AMD and geographic atrophy, a serious disease of the retina, had increased serum concentrations of IL-17 compared to healthy individuals.

The two most common forms of the inflammatory cytokine IL-17 are IL-17A and IL-17F. We believe that blocking both of these two forms of IL-17 may be important to inhibit the harmful effects of IL-17 in certain diseases of the eye such as uveitis and dry AMD.

We designed and engineered EBI-028 using our AMP-Rx platform to block IL-17A and IL-17F. We are unable to test EBI-028 in animal models because EBI-028 only blocks human IL-17. In an \textit{in vivo} study in a mouse model of uveitis of the retina and choroid, we used a commercially available anti-IL-17 antibody that blocks mouse IL-17. In this study, we observed a significant reduction in inflammation in the eyes of animals treated with this anti-IL-17 antibody compared to animals that received placebo.
The graphs below illustrate the blocking of IL-17A and IL-17F signaling in an in vitro cell-based assay by increasing concentrations of EBI-028 and of a reference IL-17 receptor fusion protein, comprised of the natural, human IL-17 receptor fused to a carrier protein, or H17RA-Fc. EBI-028 blocked signaling of IL-17A (left panel) and also IL-17F (right panel). In contrast, H17RA-Fc blocked signaling of IL-17A (left panel) but did not effectively block signaling of IL-17F (right panel). We believe the ability of EBI-028 to block both IL-17A and IL-17F could lead to improved biological effect.

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 31, 2014, we owned or exclusively in-licensed a total of 19 U.S. patent applications, as well as numerous foreign counterparts of some of these patent applications. Our patent portfolio includes the following patent applications that we own or, where noted below, license:

- composition-of-matter patent applications covering EBI-005 filed in the United States, Australia, Brazil, Canada, China, Europe, India, Israel, Japan, Korea, Mexico, New Zealand, Russia, Singapore, South Africa and Taiwan, which, if granted, are expected to expire in 2031;
- a Patent Cooperation Treaty, or PCT, patent application and a U.S. patent application covering the formulation of EBI-005, which, if granted, is expected to expire in 2034;
- patent applications covering methods of manufacturing EBI-005 filed in the United States, Australia, Brazil, Canada, China, Europe, India, Japan, Russia and Singapore, which, if granted are expected to expire in 2033;
- two patent applications that are licensed from The Schepens Eye Research Institute, Inc., or Schepens, that are each pending in the United States, Australia, Canada, Europe and Japan covering the use of IL-1 inhibitors to treat certain ocular disease, one of which, if granted, is expected to expire in 2028 and the other of which, if granted, is expected to expire in 2030;
- a PCT patent application covering EBI-029, which, if granted, is expected to expire in 2033;
- a provisional U.S. patent application covering a candidate IL-17 inhibitor, which, if granted, is expected to expire in 2034; and
- two provisional U.S. patent applications and a PCT patent application related to our technologies, including methods and compositions for improving the serum half-life of proteins which, if granted, are expected to expire beginning in 2032.
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-005, 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.

License and Collaboration Agreements

We are a party to a number of license agreements under which we license patents, patent applications and other intellectual property from third parties. We enter into these agreements to augment our proprietary intellectual property portfolio. The licensed intellectual property covers some of the compounds that we are researching and developing and some of the scientific processes that we use. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. The only existing license that we consider to be material to our current product portfolio is our agreement with Schepens, which is described below.

The Schepens Eye Research Institute, Inc.

In July 2010, we entered into a license agreement with Schepens, under which we hold 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 EBI-005. Schepens has retained rights to practice the patents and technology licensed to us under the agreement for internal research and educational purposes.

Financial Terms. In connection with the agreement, we paid Schepens an upfront licensing fee, are obligated to make a milestone payment to Schepens as a result of the initiation of our first Phase 3 clinical trial of EBI-005 and are obligated to make future milestone payments to Schepens with respect to the first covered anti-IL-1 product to achieve each milestone, which we expect will be EBI-005, of up to an aggregate of $1,600,000 if we achieve specified clinical and regulatory milestones and an additional $1,000,000 if we achieve a specified commercial milestone. We also are obligated to make additional future payments to Schepens of up to an aggregate of $1,600,000 if we achieve specified clinical and regulatory milestones with respect to a second covered anti-IL-1 product. We are also obligated to make additional payments to Schepens of up to an aggregate of $145,000 upon the occurrence of certain other events which we believe are unlikely to occur.

We are obligated to pay Schepens a tiered royalty ranging from low single digit to mid-single digit percentages of net sales made by us, our affiliates or our sublicensees. These royalties may be reduced in specified circumstances. Our obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the expiration of the last to expire valid claim of specified patents that cover the composition, manufacture or use of each covered product in each country.

In addition, we are obligated to pay Schepens a mid-single digit percentage of any non-royalty payments that we receive from any sublicensee of our rights under the agreement.

Diligence Obligations. We are required to use commercially reasonable efforts to research, develop and commercialize at least one covered product for the diagnosis, prophylaxis or treatment of a disease or condition in humans or animals.
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 or commercial quantities of EBI-005 or any other of our product candidates. We currently rely, and expect to continue to rely, on third parties for the manufacture of EBI-005 and our other product candidates. We have personnel with the experience to manage the third-party contract manufacturers producing EBI-005 and other products that we may develop in the future.
The process for manufacturing EBI-005 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 clinical supplies of EBI-005 and another single third-party manufacturer to provide fill-finish services for clinical supplies of EBI-005. 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 blow fill seal, single-use vial that has also been used for other topical 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 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-005 and any other products that we develop in markets outside the United States.

We hold worldwide commercialization rights to EBI-005. We believe that specialists in the United States who treat most of the moderate to severe dry eye disease patients are sufficiently concentrated that if EBI-005 receives marketing approval in the United States we could effectively promote EBI-005 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-005 in the United States. We intend to enter into strategic collaborations for the development and commercialization of EBI-005 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 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.
Allergan currently markets Restasis in the United States. If we receive marketing approval in the United States for EBI-005 for the treatment of moderate to severe dry eye disease, EBI-005 will compete with Restasis. In June 2013, the FDA issued draft bioequivalence guidance recommending that a biochemical analysis outside the body, or in vitro, alone may be sufficient for generic competitors to establish bioequivalence between their products and Restasis. In August 2013, Allergan submitted comments in response to the FDA’s draft guidance urging the agency to require comparative clinical studies to demonstrate that a proposed generic product is bioequivalent to Restasis. It is unclear when the FDA will issue final bioequivalence guidance or when, if at all, the FDA will approve generic versions of Restasis. If generic versions of Restasis are approved for marketing by the FDA, they would likely be offered at a lower price than EBI-005. As a result, healthcare professionals and third-party payors may choose to rely on such products rather than EBI-005.

There are a number of products in preclinical research and clinical development by third parties for the treatment of dry eye disease. We expect that product candidates currently in clinical development, or that could enter clinical development in the near future, may represent significant competition if approved. These product candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. Based on publicly available information, we have identified, among others, the following product candidates in clinical development for the treatment of dry eye disease:

- Shire Plc has a small molecule integrin antagonist, lifitegrast, which is formulated for topical, ophthalmic delivery and is currently in Phase 3 clinical development.
- Acucela Inc., in collaboration with Otsuka Pharmaceutical Co., Ltd., has a small molecule that stimulates prostaglandin generation, rebamipide, which is formulated for topical ophthalmic delivery and is currently in Phase 3 clinical development. Rebamipide has been approved for sale for the treatment of dry eye disease in Japan.
- Mimetogen Pharmaceuticals Inc., in collaboration with Bausch + Lomb Corporation, has a small molecule TrkA agonist, MIM-D3, which is formulated for topical, ophthalmic delivery and is currently in Phase 3 clinical development.
- OphthaliX Inc. has a small molecule A3 adenosine receptor agonist, CF101, which is designed to be administered orally and is currently in Phase 3 clinical development.
- Rigel Pharmaceuticals, Inc. has a small molecule Jak/Syk inhibitor, R9348, which is being formulated for topical ophthalmic delivery and is currently in Phase 2 clinical development.
- Allergan, Inc. has a molecule, AGN-195263, which is being formulated for topical ophthalmic delivery and is currently in Phase 2 clinical development.

In December 2013, the results of the first Phase 3 clinical trial of twice daily lifitegrast in patients with dry eye disease were published in *JAMA Ophthalmology*. In this trial, referred to by Shire as the OPUS-1 trial, there was an improvement of 3% in the pre-specified co-primary endpoint of CFS of the lower quadrant, or inferior CFS, a sign of dry eye disease, in patients treated with lifitegrast from baseline at 84 days, which was statistically significant when compared to the differences from baseline at 84 days in patients who received vehicle control. Improvements on other signs of dry eye disease were observed as early as 14 days after treatment began. In addition, patients treated with lifitegrast showed a statistically significant improvement in ocular discomfort and eye dryness, symptoms of dry eye disease, as reported by patients on a visual analogue scale from baseline at 84 days when compared to the differences from baseline at 84 days in patients who received vehicle control. In December 2013, Shire announced top-line results of the second Phase 3 trial of twice daily lifitegrast in patients with dry eye disease. In this trial, referred to by Shire as the OPUS-2 trial, patients treated with lifitegrast showed a statistically significant improvement on the pre-specified co-primary symptom endpoint of eye dryness, as reported by patients on a visual analogue scale, from baseline at 84 days when compared to the differences from baseline at 84 days in patients who received vehicle control. Shire reported that lifitegrast did not meet the pre-specified co-primary endpoint of inferior CFS in the OPUS-2 trial. In both the OPUS-1 and OPUS-2 trials, Shire reported that one of the most commonly reported treatment-emergent adverse events in patients treated with lifitegrast was dysgeusia, or altered sense of taste, which was reported in approximately 13% of patients in the OPUS-1 trial and approximately 16% of patients in the OPUS-2 trial.

Because there are a variety of means to block the activity and signaling of IL-1, our patents and other proprietary protections for EBI-005 will not prevent development or commercialization of product candidates that are different from EBI-005.
Government Regulation

Government authorities in the United States and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, and import and export of pharmaceutical products. 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, requires 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 process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant 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 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;
- 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 risk evaluation and mitigation strategies, 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 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. An IND sponsor must submit 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, 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. 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.
**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, 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.

In addition, 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.

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.

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. 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 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.

Sponsors of clinical trials for investigational products must publicly disclose certain clinical trial information, including detailed trial design and trial results in public databases maintained by the National Institutes of Health, or NIH, at ClinicalTrials.gov. These requirements are subject to specific timelines and apply to most controlled clinical trials of FDA-regulated products.

**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.

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 at least $2.1 million, and the sponsor of an approved BLA is also subject to annual product and establishment user fees, currently at least $104,000 per product and $554,600 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of a BLA within 60 days of its receipt and informs the sponsor by the 74th 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.

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, 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, including 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, no biosimilar or interchangeable biosimilar has been licensed under the BPCIA, although biosimilars have been approved in Europe. The FDA has issued several draft guidance documents outlining an approach to review and approval of biosimilars. Those guidances are expected to be finalized sometime in 2014.

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 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 convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product will be entitled to orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications 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 a type of non-patent exclusivity in the United States and, if granted, provides for an additional six months of marketing protection beyond 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.

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.

**Pharmaceutical Coverage, Pricing and Reimbursement**

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may receive regulatory approval by the FDA and other government authorities. In the United States and in other countries, sales of any products for which we receive regulatory approval for commercial sales will depend, in part, on the availability of coverage and adequate reimbursement from third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. 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 may limit coverage to specific products on an approved list, or 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 regulatory approvals. A payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

The containment of healthcare costs has become a priority of federal and state and foreign governments, and the prices of pharmaceuticals have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The federal government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription products. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

As a result, the marketability of any of our product candidates that receive regulatory approval for commercial sale may suffer if the government or other third-party payors fail to provide coverage and adequate reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will likely continue to increase the pressure on product pricing. Coverage policies, third-party reimbursement rates and product pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.
Federal and State Fraud and Abuse and Data Privacy and Security Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state fraud and abuse laws restrict business practices in the pharmaceutical industry. These laws include anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations. The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively PPACA, which, among other things, amended the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. PPACA also created new federal requirements for reporting, by applicable manufacturers of covered drugs, payments and other transfers of value to physicians and teaching hospitals.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes “any request or demand” for money or property presented to the United States government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, and thus non-reimbursable, uses. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH and the omnibus rule make HIPAA’s privacy and security standards directly applicable to “business associates,” defined as independent
contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctive relief in federal courts to enforce the federal HIPAA laws and seek attorney’s fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that 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 healthcare programs, and the curtailment or restructuring of our operations. To the extent that any of our product candidates receive approval and are sold in a foreign country, we may be subject to foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Impact of Healthcare Reform on Coverage, Reimbursement, and Pricing

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 prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and/or affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program and provided authority for limiting the number of drugs that will be covered in any therapeutic class thereunder. The MMA, including, without limitation, its cost reduction initiatives, could limit the coverage of and reduce the reimbursement rate that we receive for any of our approved products. Furthermore, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

PPACA, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription drug products. It also contains substantial new provisions intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare industry, impose new taxes and fees on pharmaceutical manufacturers, and impose additional health policy reforms, any or all of which may affect our business. A significant number of provisions are not yet, or have only recently become, effective, but PPACA is likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Other legislative changes have also been proposed and adopted since PPACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of up to 2% per fiscal year, starting in 2013, and the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of 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.

We expect that PPACA, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria 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.

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, 2013, we had 15 employees, including a total of eight with M.D. or Ph.D. degrees. Of these full-time employees, 10 employees are engaged in research and development activities and five employees are engaged in finance, 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 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 $18.0 million for the year ended December 31, 2013 and $19.7 million for the year ended December 31, 2012. As of December 31, 2013, we had an accumulated deficit of $57.6 million. To date, we have financed our operations primarily through private placements of our preferred stock and convertible bridge notes, venture debt borrowings and an initial public offering, or IPO, of our common stock 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, including preclinical studies and, beginning in 2012, clinical trials. 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 our expenses will increase substantially as compared to prior periods in connection with conducting our pivotal Phase 3 clinical program, consisting of two Phase 3 clinical trials evaluating the safety and efficacy of EBI-005, our most advanced product candidate, for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year, and seeking marketing approval for EBI-005 for this indication in the United States. We began randomizing and treating patients in our first Phase 3 trial in January 2014.

We received scientific advice from the European Medicine Agency’s, or EMA, Committee for Medicinal Products for Human Use, or CHMP, that indicates that the requirements for European registration in dry eye disease will differ from the requirements for registration in the United States and our pivotal Phase 3 clinical program is not consistent with the advice of the CHMP. We will continue to evaluate the scientific advice received from the EMA and plan to further discuss with the EMA a registration plan for EBI-005 in moderate to severe dry eye disease for the European Union. We may be required to conduct additional clinical trials to support an application for marketing approval of EBI-005 in the European Union. We anticipate that our expenses will increase...
substantially if we pursue, alone or in collaboration with third parties, the development of and seek marketing approval for, EBI-005 for the treatment of moderate to severe dry eye disease in the European Union.

Our expenses will also increase if and as we:

- pursue the development of EBI-005 for the treatment of allergic conjunctivitis or additional indications or for use in other patient populations or, if it is approved, seek to broaden the label for EBI-005;
- continue the research and development of our other 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 expand our clinical trials and commence commercialization of EBI-005.

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 EMA to perform studies in addition to those currently expected; or
- if there are any delays in enrollment of patients in, continuing or completing our clinical trials or the development of EBI-005 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-005, which we do not expect will occur before 2017, if ever. This will require us to be successful in a range of challenging activities, including:

- completing and obtaining favorable results from our pivotal Phase 3 clinical program for EBI-005 for the treatment of moderate to severe dry eye disease;
- subject to obtaining favorable results from our pivotal Phase 3 clinical program for EBI-005, applying for and obtaining marketing approval for EBI-005 in the United States;
- establishing sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties, to effectively market and sell EBI-005 in the United States;
- initiating and obtaining favorable results from registration trials of EBI-005 for the treatment of moderate to severe dry eye disease in the European Union;
- subject to obtaining favorable results from our registration trials for EBI-005 in the European Union, applying for and obtaining marketing approval for EBI-005 in the European Union;
- establishing collaboration, distribution or other marketing arrangements with third parties to commercialize EBI-005 in markets outside the United States;
- achieving an adequate level of market acceptance of EBI-005;
- protecting our rights to our intellectual property portfolio related to EBI-005; and
- ensuring the manufacture of commercial quantities of EBI-005.
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 completing our pivotal Phase 3 clinical program evaluating EBI-005 for the treatment of moderate to severe dry eye disease and, if successful, seeking marketing approval for EBI-005. We expect to devote additional financial resources to the clinical development of EBI-005 as we initiate and conduct additional clinical trials of EBI-005 for the treatment of dry eye disease in the European Union and for the treatment of allergic conjunctivitis or other diseases and to functions associated with operating as a public company. We also expect to 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 our pivotal Phase 3 clinical program for EBI-005 and of any clinical activities for regulatory review of EBI-005 outside of the United States;
- the costs and timing of process development and manufacturing scale up and validation activities associated with EBI-005;
- the costs, timing and outcome of regulatory review of EBI-005 in the United States, the European Union and in other jurisdictions;
- the costs and timing of commercialization activities for EBI-005 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-005;
- the progress, costs and outcome of developing EBI-005 for the treatment of additional indications or for use in other patient populations, including our Phase 2 clinical trial to assess the potential therapeutic benefit of EBI-005 for the treatment of allergic conjunctivitis in patients who do not respond adequately to antihistamines and mast cell stabilizers;
- 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 success of our collaboration with ThromboGenics N.V., or ThromboGenics;
- 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, 2013, we had cash and cash equivalents of $7.9 million. We believe that our cash and cash equivalents as of December 31, 2013 and the approximately $50.2 million in net proceeds from our IPO that we completed in February 2014, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into the second half of 2016, without giving effect to any potential milestone payments we may receive under our existing collaboration and license agreement with ThromboGenics. 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 complete our Phase 3 clinical program.
evaluating EBI-005 and to submit a Biologics License Application, or BLA, to the FDA seeking approval of EBI-005 for the treatment of dry eye disease in the United States in the second half of 2016. At this time we cannot reasonably estimate the remaining costs necessary to commercialize EBI-005 for the treatment of dry eye disease, including commercial manufacturing of EBI-005, or the nature, timing or costs of the efforts necessary 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-005 or any other products that we successfully develop, none of which we expect to be commercially available for several years, if at all. In addition, if approved, EBI-005 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.

**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 other than funding under our existing collaboration and license agreement with ThromboGenics in the form of research funding. Under this collaboration, we also may receive potential milestone payments upon the achievement of specified development, regulatory and other milestones and royalties with respect to future sales of collaboration products by ThromboGenics. ThromboGenics may terminate our existing collaboration for convenience on short notice. 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 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 loan and security agreement with our venture debt lender, 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, beginning in 2012, conducting clinical trials of EBI-005. All of our product candidates, other than EBI-005, are still in preclinical development. We have not yet demonstrated our ability to successfully complete a pivotal Phase 3 clinical trial, 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 depend heavily on the success of EBI-005, our most advanced product candidate, which we are developing for the treatment of moderate to severe dry eye disease. If we are unable to successfully complete our pivotal Phase 3 clinical program and obtain marketing approvals for EBI-005, or experience significant delays in doing so, or if after obtaining marketing approvals, we fail to commercialize EBI-005, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of EBI-005 for the treatment of patients with moderate to severe dry eye disease and for other disease indications. There remains a significant risk that we will fail to successfully develop EBI-005. In 2013, we completed a Phase 1b/2a clinical trial to evaluate the safety, tolerability and biological activity of EBI-005 in patients with moderate to severe dry eye disease. Our pivotal Phase 3 clinical program will consist of two Phase 3 clinical trials evaluating EBI-005 for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year. We began randomizing and treating patients in our first Phase 3 trial in January 2014. We do not expect to have initial, top-line data from our first Phase 3 trial available until early in 2015. The timing of the availability of such top-line data and the completion of our pivotal Phase 3 clinical program is dependent, in part, on our ability to locate and enroll a sufficient number of eligible patients in our pivotal Phase 3 clinical program on a timely basis. Even if the results of both of our Phase 3 clinical trials evaluating EBI-005 for the treatment of moderate to severe dry eye disease and our separate safety trial are favorable, we do not plan to submit a BLA to the FDA seeking approval of EBI-005 for the treatment of dry eye disease in the United States before the second half of 2016. We cannot accurately predict when or if EBI-005 will prove effective or safe in humans or whether it will receive marketing approval. Our ability to generate product revenues, which we do not expect will occur before 2017, if ever, will depend heavily on our obtaining marketing approval for and commercializing EBI-005.

The success of EBI-005 will depend on several factors, including the following:

- completing and obtaining favorable results from our pivotal Phase 3 clinical program for EBI-005;
- initiating and obtaining favorable results from registration trials of EBI-005 for the treatment of moderate to severe dry eye disease in the European Union;
- applying for and receiving marketing approvals from applicable regulatory authorities for EBI-005;
- making arrangements with third-party manufacturers for commercial quantities of EBI-005 and receiving regulatory approval of our manufacturing processes and our third-party manufacturers’ facilities from applicable regulatory authorities;
- establishing sales, marketing and distribution capabilities and launching commercial sales of EBI-005, if and when approved, whether alone or in collaboration with others;
- acceptance of EBI-005, 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-005 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-005.

Successful development of EBI-005 for additional indications, if any, or for use in broader patient populations and our ability, if it is approved, to broaden the label for EBI-005 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-005, which would materially harm our business.

If clinical trials of EBI-005 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-005 or any other product candidate.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, including EBI-005, 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.

We will be required to demonstrate the safety of treatment with EBI-005 for one year in a separate safety trial in order to support marketing approval of EBI-005 for the treatment of dry eye disease in the United States. To meet this requirement, we plan to conduct a safety trial with no fewer than 100 patients who will be treated with EBI-005 for one year. We cannot predict the results of this safety trial because we have no clinical data on the safety of EBI-005 when administered for a period longer than six weeks and no clinical safety data on the effects of EBI-005 when formulated with the vehicle we intend to use in our pivotal Phase 3 clinical program.

In general, the FDA requires two adequate and well controlled clinical trials demonstrating effectiveness on two primary endpoints for marketing approval of a dry eye disease drug. One of these co-primary endpoints must be a sign of dry eye disease and the other must be a symptom of dry eye disease. We are not aware of any investigational dry eye disease drug in development that has met these criteria. Regulatory authorities outside the United States, in particular in the European Union, have not issued public guidance on the requirements for approval of a dry eye drug. We have received scientific advice from the CHMP regarding European registration requirements for EBI-005 for the treatment of moderate to severe dry eye disease. The scientific advice indicates that the requirements for registration in the European Union will differ from the requirements for registration in the United States and our pivotal Phase 3 clinical program is not consistent with the advice of the CHMP. Our pivotal Phase 3 clinical program also may not be sufficient to support an application for marketing approval in other jurisdictions outside the United States.

Our Phase 1b/2a trial evaluated EBI-005 for the treatment of moderate to severe dry eye disease. In our Phase 1b/2a trial, neither of the doses of EBI-005 tested achieved statistically significant superiority compared to vehicle control based on any primary or secondary efficacy endpoints, including those we intend to use for our Phase 3 clinical trials.

Retrospective subgroup analyses that we performed on the results of our Phase 1b/2a clinical trial may not be predictive of the results of our pivotal Phase 3 clinical program. We have based many elements of the design of the protocol for our Phase 3 clinical trials on retrospective subgroup analyses, including our expected use of improvement in pain and discomfort as measured by the painful or sore eyes question of the ocular surface disease index, or OSDI, as the co-primary endpoint measuring a patient symptom. In our Phase 1b/2a trial, we used total OSDI scores as a secondary efficacy endpoint. Although we believe that the retrospective analyses support our protocol design for our Phase 3 clinical trials and our proposed mechanism of action, retrospective analyses performed after unmasking trial results can result in the introduction of bias and are given less weight by regulatory authorities than pre-specified analyses.

We may fail to achieve success in our pivotal Phase 3 clinical program evaluating EBI-005 for the treatment of moderate to severe dry eye disease for a variety of potential reasons.

- The efficacy endpoints in our Phase 1b/2a trial were measured six weeks after the first dose of EBI-005. The co-primary efficacy endpoints in our pivotal Phase 3 clinical program will be measured 12 weeks after the first dose of EBI-005. We have no clinical data on EBI-005 in any clinical trial longer than six weeks.

- We have made changes to the vehicle we use to formulate EBI-005 for topical, ophthalmic delivery in our Phase 3 clinical trials from the vehicle used in our Phase 1b/2a trial. The most significant change to the vehicle is the removal of carboxymethyl cellulose, or CMC. CMC is a common ingredient in artificial tears. We have no clinical data on our new formulation. In addition, if the new formulation is not comfortable to patients, patients may discontinue their participation in our Phase 3 clinical trials. Such discontinuations would harm our ability to complete the trial on a timely basis.

- We will restrict the use of rescue artificial tears by patients in our Phase 3 clinical trials. If the restriction on the use of artificial tears causes discomfort to patients and results in patients’ discontinuing their participation in our Phase 3 clinical trials, such discontinuations would harm our ability to complete our Phase 3 clinical trials on a timely basis.

- We changed the eligibility criteria in our Phase 3 clinical trials from the criteria we used in our Phase 1b/2a trial with regard to patient scores on the OSDI. We cannot predict the impact these changes will have on the rate at which patients will be enrolled or randomized in our Phase 3 clinical trials. If these changes slow the rate at which patients are enrolled or randomized compared to the rate we anticipate, the availability of top-line clinical data from our first Phase 3 clinical trial and our completion of our pivotal Phase 3 clinical program will be delayed.

- We plan to conduct our Phase 3 clinical trials at many clinical centers that were not included in our Phase 1b/2a trial. The introduction of new centers, and the resulting involvement of new treating physicians, can introduce additional variability into the conduct of the trials in accordance with their protocols and may result in greater variability of patient outcomes, which could adversely affect our ability to detect statistically significant differences between patients treated with EBI-005 and vehicle control.
If, in our first Phase 3 clinical trial, we do not demonstrate a statistically significant improvement from baseline in the EBI-005 treatment group on a pre-specified co-primary endpoint, but we do demonstrate a statistically significant improvement from baseline in the EBI-005 treatment group on one of our secondary endpoints, we may decide to substitute that secondary endpoint for the co-primary endpoint in our second Phase 3 clinical trial prior to initiation of our second Phase 3 clinical trial. Whether this substitution and combination of results would be an acceptable means of meeting the FDA’s requirement that we duplicate in two adequate and well controlled clinical trials a statistically significant improvement on a clinically relevant sign and symptom would be a review issue at the time of our application for marketing approval. If the FDA does not find this to be an acceptable means of meeting the requirements for marketing approval, we will not receive marketing approval for EBI-005, and we will have to conduct another Phase 3 clinical trial if we wish to seek marketing approval for EBI-005 in the future. Additionally, if we initiate our second Phase 3 clinical trial of EBI-005 before we have completed our first Phase 3 clinical trial, the option to substitute a secondary endpoint from the first Phase 3 clinical trial for a co-primary endpoint in the second Phase 3 clinical trial would not be available to us.

The protocols for our pivotal Phase 3 clinical program and other supporting information are subject to review by the FDA and regulatory authorities outside the United States. The FDA or other regulatory authorities may request additional information, require us to conduct additional non-clinical trials or require us to modify our pivotal Phase 3 clinical program, including its endpoints or patient enrollment criteria, to receive clearance to initiate such program or to continue such program once initiated.

In November 2013, we submitted to the FDA the protocol for our first pivotal Phase 3 clinical trial of EBI-005 and data supporting our change to a larger-scale manufacturing process for the production of EBI-005 to be used in this Phase 3 clinical trial. We intend to submit the protocols for our second pivotal Phase 3 clinical trial and our separate safety study of EBI-005 to the FDA prior to initiation of those trials. The FDA is not obligated to comment on our submissions within any specified time period or at all or to affirmatively clear or approve any clinical trial, and we are not obligated to wait for clearance or approval of the FDA to commence any clinical trial. We initiated our first pivotal Phase 3 clinical trial in the United States in January 2014 without waiting for comments from the FDA. On March 24, 2014, we received a letter from the FDA requesting additional information regarding the characterization of EBI-005 produced using our larger-scale manufacturing process based on the FDA’s product quality review of our November 2013 submission. We have responded to the FDA with the information the FDA requested. If the FDA is not satisfied with our responses, the FDA may delay our continuing our first Phase 3 clinical trial. If our Phase 3 program is placed on clinical hold by the FDA, we may be significantly delayed and incur significantly greater expense in our proposed development program. For example, our Phase 1b/2a trial of EBI-005 was placed on clinical hold between September 6, 2012 and October 29, 2012 until we provided particular manufacturing stability information regarding the drug product lots intended to be used in our clinical studies.

We submitted to the EMA a draft protocol for our Phase 3 clinical program of EBI-005 for the treatment of moderate to severe dry eye disease and sought and received scientific advice from the CHMP regarding European registration requirements for EBI-005. The scientific advice received indicates that the requirements for European registration in dry eye disease will differ from the requirements for registration in the United States and our pivotal Phase 3 clinical program is not consistent with the advice of the CHMP. We will continue to evaluate the scientific advice received from the EMA and plan to further discuss with the EMA a registration plan for EBI-005 in moderate to severe dry eye disease for the European Union. The EMA may require us to conduct other clinical trials, in addition to those included in our Phase 3 clinical program, in order to support an application for marketing approval of EBI-005.

We also are required to submit our plans for clinical trials to each national regulatory authority in the European Union having jurisdiction over a country in which we wish to conduct these clinical trials. These national regulatory authorities are not obligated to follow the scientific advice of the EMA and may impose additional requirements on our conduct of clinical trials of EBI-005 in order to initiate clinical trials and support our application for marketing approval of EBI-005. If we are required by the EMA or a national regulatory authority in the European Union to conduct other clinical trials, in addition to those included in our Phase 3 clinical program, our expenses will increase substantially, and we may experience delays in completing the development and commercialization of EBI-005 in the European Union.

We have not received guidance from other regulatory authorities outside the United States regarding the design of our pivotal Phase 3 clinical program. We may not receive clearance from the EMA or other national regulatory authorities in the European Union or other regulatory authorities outside the European Union to initiate our pivotal Phase 3 clinical trials on a timely basis, if at all.

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-005 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-005 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-005, 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-005 or any other product candidates that we may develop, we may need to abandon or limit our development of EBI-005 or such other product candidates.

If EBI-005 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. Although EBI-005 was generally well tolerated in our Phase 1b/2a trial, we have no clinical safety data on or patient exposure to EBI-005 for longer than six weeks. We have no clinical safety data on patient exposure to EBI-005 formulated with the vehicle we intend to use in our Phase 3 clinical trials. 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 is 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. Other than EBI-005, our product candidates all 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.

**We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.**

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 commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through 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.

**Risks Related to the Commercialization of Our Product Candidates**

**Even if EBI-005 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-005 may be smaller than we estimate.**

If EBI-005 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 moderate to severe dry eye disease include low cost artificial tears, Restasis 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-005, if and when it is approved for marketing by the FDA. In addition, it is possible that the FDA may approve generic versions of Restasis in the foreseeable future. If generic versions of Restasis are approved for marketing by the FDA, they would likely be offered at a substantially lower price than EBI-005. As a result, healthcare professionals and third-party payors may choose to rely on such products rather than EBI-005. If EBI-005 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-005 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, particularly by Medicare in light of the prevalence of dry eye disease in persons over age 55;

- 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-005 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-005 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-005 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-005 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-005 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-005 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-005 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-005 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-005 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-005 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-005 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 dry eye disease includes artificial tears and topical anti-inflammatory and immune-modulating drugs. The anti-inflammatory and immune-modulating drug market for the treatment of moderate to severe dry eye disease consists primarily of Restasis, which is approved for use in the United States, and off-label use of corticosteroids. Some patients with moderate to severe dry eye disease are effectively treated by the current standard of care therapies, some of which are available in generic form or offered at relatively low prices. There are also a number of products and therapies in preclinical research and clinical development by third parties to treat dry eye disease. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. These companies include pharmaceutical companies, biotechnology organizations, and specialty pharmaceutical and generic drug companies of various sizes, such as Shire Plc (lifitegrast), Acucela Inc., in collaboration with Otsuka Pharmaceutical Co., Ltd. (rebamipide), Mimetogen Pharmaceuticals Inc., in collaboration with Bausch + Lomb Corporation (MIM-D3), OphthaliX Inc. (CF101), Rigel Pharmaceuticals, Inc. (R9348) and Allergan, Inc. (AGN-195263). See “Business—Competition” for additional information regarding our competitors.

In 2013, the peer-reviewed journal *JAMA Ophthalmology* published the results of an exploratory clinical trial in 75 patients conducted by one of our scientific co-founders, Dr. Reza Dana, at the Massachusetts Eye and Ear Infirmary using anakinra to treat patients with moderate to severe dry eye disease. Interleukin-1, or IL-1, is the therapeutic target of both anakinra and EBI-005, and the mechanisms of action of anakinra and EBI-005 are very similar. For this proof-of-concept study, the investigators compounded, or reformulated, anakinra in eye drops at two different concentrations for topical administration. The investigators reported positive results from this trial. We believe that the investigators continue to treat dry eye patients using reformulated anakinra. We would face competition with respect to EBI-005 if reformulated anakinra was available commercially through compounding pharmacies or if a third party successfully completed pivotal clinical trials of, and received marketing approval for, reformulated anakinra for the treatment of dry eye disease.

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-005 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. For example, the FDA’s Office of Generic Drugs recently released guidance for the development of generic versions of Restasis. If EBI-005 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-005 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-005 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-005 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-005 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-licences 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-005 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-005 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-005. 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-005 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, which 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 potential litigation;

• 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. 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 contract research organizations, or CROs, to conduct our completed Phase 1 and Phase 1b/2a trials of EBI-005 and do not plan to independently conduct clinical trials of EBI-005 or our other product candidates, including our Phase 3 clinical trials of EBI-005. We 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. 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 contract with third parties for the manufacture of EBI-005 for clinical trials and expect to continue to do so in connection with the commercialization of EBI-005 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-005 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-005, 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-005 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-005 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-005 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-005 or for fill-finish services. The prices at which we are able to obtain supplies of EBI-005 drug substance and fill-finish services may vary substantially over time and adversely affect our financial results.

If our third-party manufacturer for EBI-005 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-005 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-005 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.

We are the exclusive licensee of patent applications owned by The Schepens Eye Research Institute, Inc., or Schepens, that cover methods of treating diseases of the eye using an inhibitor of the inflammatory cytokine IL-1. Even if these applications issue as patents, method-of-treatment patents are more difficult to enforce than composition-of-matter patents because of the risk of off-label sale or use of a drug for the subject method. In addition, European patent law generally makes the enforcement of patents that cover methods of treatment of the human body difficult. In the United States, the FDA does not prohibit physicians from prescribing an approved product for uses that are not described in the product’s labeling. Although use of a product directed by off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties, particularly in the United States, and such infringement is difficult to detect, prevent or prosecute. For example, anakinra is an IL-1 inhibitor that is approved for marketing in the United States and other countries for the treatment of rheumatoid arthritis and is formulated for subcutaneous administration. Anakinra can be re-formulated, or compounded, for topical ophthalmic application. Off-label sales of anakinra or other products comprising an IL-1 inhibitor could limit our ability to generate revenue from the sale of EBI-005.

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-005 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 Approval of Our Product Candidates and Other Legal Compliance Matters**

**If we are not able to obtain required regulatory approvals, we will not be able to commercialize EBI-005 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-005 or any other product candidate.**

The activities associated with the development and commercialization of our product candidates, including EBI-005, 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. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market EBI-005 or any other product candidate from regulatory authorities in any jurisdiction. 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 or other regulatory authorities may determine that EBI-005 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. There are no drugs approved in the European Union and no drugs, other than Restasis, approved in the United States for the treatment of a sign or symptom of moderate to severe dry eye disease. The EMA has not issued any public guidance on the clinical trials that would be sufficient to support an application for marketing approval of a drug to treat dry eye disease. The lack of a defined regulatory pathway in the European Union, the different requirements of the EMA compared with the FDA and the lack of successful development of therapies to treat dry eye disease in both the United States and the European Union 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.

Our therapeutic 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 biosimilar biologics 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 international jurisdictions would prevent our product candidates from being marketed abroad.**

In order to market and sell EBI-005 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-005 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-005 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 costly post-marketing studies or 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.

**We may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products.**

Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion or manufacturing of prescription products may lead to investigations by the FDA, Department of Justice and state Attorneys General alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- 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;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
Non-compliance with European Union 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.

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-005, 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 of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false 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 imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act 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, 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.

Recently enacted and future legislation may affect our ability to commercialize and the prices we obtain for any products that are approved in the United States or foreign jurisdictions.

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 affect our ability to profitably sell or commercialize any product candidate, including EBI-005, for which we obtain marketing approval or that we may in-license. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. 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 receive for any approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of this legislation could limit coverage of and reduce the price that we receive for any approved products. While the MMA applies only to product benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA or other healthcare reform measures may result in a similar reduction in payments from private payors.

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 PPACA. Among the provisions of PPACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates and that are approved for sale, are the following:

• an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
• an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
• a new Medicare Part D coverage gap discount program, in which participating manufacturers must agree to offer 50% point-of-sale discounts off negotiated drug prices during the coverage gap period as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;
• expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, and the addition of new government investigative powers, and enhanced penalties for noncompliance;
• extension of manufacturers’ Medicaid rebate liability;
• expansion of eligibility criteria for Medicaid programs; and
• expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of 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.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. 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. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.
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 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.
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, Gregory D. Perry, our Chief Financial and Business Officer, Eric Furfine, Ph.D., our Chief Scientific Officer, and Karen L. Tubridy, our Chief Development 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. 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.

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 21, 2014, 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 72.1% 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 effectuated 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 may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price is likely to be volatile. 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-005 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-005. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources.

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

As of December 31, 2013, we had federal net operating loss, or NOL, carryforwards of $53.8 million, state NOL carryforwards of $53.0 million and aggregate federal and state research and development tax credit carryforwards of $1.8 million available to reduce future taxable income. These federal and state NOL carryforwards and federal and state tax credit carryforwards will begin to expire at various dates beginning in 2014, 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, our most recent private placement of our series B preferred 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 restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

While a significant portion of our total outstanding shares are restricted from immediate resale, they may be sold into the market in the near future, 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 21, 2014, we had outstanding 16,240,985 shares of common stock. Of these shares, 10,726,869 shares are restricted securities under Rule 144 under the Securities Act, substantially all of which are subject to lock-up agreements entered into in connection with our IPO, a description of which, including certain exceptions thereto, is available in the registration statement filed in connection with such offering. These shares will be able to be sold beginning on August 4, 2014. Any of our remaining shares that are not restricted securities under Rule 144 under the Securities Act or subject to lock-up agreements, including, for example, shares sold in our IPO, may be resold in the public market without restriction unless purchased by our affiliates. Moreover, holders of an aggregate of 8,699,135 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or, along with holders of an additional 30,708 shares of our common stock issued upon exercise of warrants issued to our venture debt lender, to include their shares in registration statements that we may file for ourselves or other stockholders. We intend to file a registration statement registering all shares of common stock that we may issue under our equity compensation plans. As of March 21, 2014, we had outstanding options to purchase an aggregate of approximately 1,414,355 shares of our common stock, of which options to purchase approximately 390,624 shares were vested. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates and the applicable lock-up agreements entered into in connection with our public offering.
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:

• being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
• 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 for the foreseeable future.

**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 January 31, 2016.

**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:

<table>
<thead>
<tr>
<th>Market Price</th>
<th>High</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>First quarter (February 6, 2014 to March 28, 2014)</td>
<td>$19.33</td>
<td>$10.11</td>
</tr>
</tbody>
</table>

As of March 21, 2014, we had approximately 53 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. 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.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of our common stock, shares of our preferred stock, warrants to purchase shares of our common stock and convertible promissory notes issued, and stock options granted, by us since January 1, 2013 that were not registered under the Securities Act. Also included is the consideration, if any, received by us for such shares, warrants and options and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuances of Securities

In June 2013, we issued and sold 7% convertible promissory notes in the aggregate principal amount of $3,500,000 to four investors.

In December 2013, we issued and sold 7,203,845 shares of our series B preferred stock to five investors at a price per share of $1.75 for an aggregate purchase price of $12.6 million.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 5 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All purchasers of shares of our preferred stock and convertible promissory notes described above...
represented to us in connection with their purchase that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

(b) Stock Option Grants

Between January 1, 2013 and December 31, 2013, we granted options to purchase an aggregate of 882,835 shares of common stock, with exercise prices ranging from $0.83 to $9.59 per share, to our employees, directors, advisors and consultants pursuant to our 2009 Stock Incentive Plan. Between January 1, 2013 and December 31, 2013, we issued an aggregate of 87,182 shares of common stock upon the exercise of options for aggregate consideration of $21,957 and options to purchase 276,321 shares had been forfeited. We intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and options and other awards issuable pursuant to our equity compensation plans.

The stock options and the common stock issuable upon the exercise of such options as described in this section (b) of Item 5 were issued pursuant to written compensatory plans or arrangements with the Registrant’s employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about the Registrant or had access, through employment or other relationships, to such information.

(c) Issuance of Warrants

In connection with our June 2013 convertible note financing, we issued to four investors in June 2013, warrants to purchase up to 275,589 shares of our common stock, at an exercise price of $0.06 per share.

In connection with our series B preferred stock financing, in December 2013, we issued to five investors warrants to purchase up to 202,472 shares of our common stock, at an exercise price of $0.06 per share.

The issuance of these warrants was made in reliance on the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All acquirers of warrants described above represented to us that they were accredited investors and were acquiring the warrants for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the warrants for an indefinite period of time, and appropriate legends were affixed to the instruments representing such warrants issued in such transactions. Such recipients either received adequate information about us or had, through their relationships with us, access to such information.

All of the foregoing securities described in sections (a), (b) and (c) of Item 5 are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued shares of capital stock described in this Item 5 included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

Use of Proceeds

In February 2014, we completed our IPO pursuant to a registration statement on Form S-1 (File No. 333-193131), which the SEC declared effective on February 5, 2014. In the IPO, we issued and sold 5,750,000 shares of 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 public offering price of $10.00 per share, for aggregate offering proceeds of $57.5 million. The managing underwriters for the IPO were Citigroup Global Markets Inc., Cowen and Company, LLC and Leerink Partners LLC. The IPO commenced on February 6, 2014 and did not terminate until the sale of all of the shares offered.

The aggregate proceeds received by the Company from the IPO were $50.2 million, net of underwriting discounts and commissions and estimated offering expenses payable by the Company. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

There has been no material change in the use of proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on February 6, 2014. Because the closing of our IPO occurred on February 11, 2014, as of December 31, 2013, we had not yet received the net proceeds from the sale of shares of common stock in our IPO and therefore had used none of the proceeds as of December 31, 2013.
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.


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, 2013, 2012 and 2011 and the balance sheet data as of December 31, 2013 and 2012 from our audited financial statements included in this Annual Report on Form 10-K, which have been audited by Ernst & Young LLP, an independent registered public accounting firm. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands, except per share data)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Statement of Operations Data:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collaboration revenue</td>
<td>$1,334</td>
<td>$—</td>
<td>$—</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>13,788</td>
<td>15,263</td>
<td>9,411</td>
</tr>
<tr>
<td>General and administrative</td>
<td>4,024</td>
<td>4,213</td>
<td>3,267</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>17,812</td>
<td>19,476</td>
<td>12,678</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(16,478)</td>
<td>(19,476)</td>
<td>(12,678)</td>
</tr>
<tr>
<td>Other income (expense):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (expense) income, net</td>
<td>(147)</td>
<td>(13)</td>
<td>3</td>
</tr>
<tr>
<td>Interest expense</td>
<td>(1,400)</td>
<td>(168)</td>
<td>(151)</td>
</tr>
<tr>
<td>Total other expense, net</td>
<td>(1,547)</td>
<td>(181)</td>
<td>(148)</td>
</tr>
<tr>
<td>Net loss and comprehensive loss</td>
<td>$(18,025)</td>
<td>$(19,657)</td>
<td>$(12,826)</td>
</tr>
<tr>
<td>Cumulative preferred stock dividends and accretion of preferred stock discount</td>
<td>(3,857)</td>
<td>(3,111)</td>
<td>(1,452)</td>
</tr>
<tr>
<td>Net loss applicable to common stockholders</td>
<td>$(21,882)</td>
<td>$(22,768)</td>
<td>$(14,278)</td>
</tr>
<tr>
<td>Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted</td>
<td>1,352</td>
<td>993</td>
<td>802</td>
</tr>
</tbody>
</table>

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 and unaudited pro forma basic and diluted net loss per share.

<table>
<thead>
<tr>
<th>As of December 31,</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Balance Sheet Data:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$7,942</td>
<td>$7,882</td>
<td>$700</td>
</tr>
<tr>
<td>Working capital</td>
<td>2,677</td>
<td>6,446</td>
<td>(1,229)</td>
</tr>
<tr>
<td>Total assets</td>
<td>11,237</td>
<td>9,503</td>
<td>2,665</td>
</tr>
<tr>
<td>Notes payable, net of current portion</td>
<td>2,876</td>
<td>1,769</td>
<td>325</td>
</tr>
<tr>
<td>Warrant liability</td>
<td>297</td>
<td>147</td>
<td>26</td>
</tr>
<tr>
<td>Convertible preferred stock</td>
<td>56,678</td>
<td>45,035</td>
<td>19,644</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>(57,594)</td>
<td>(39,569)</td>
<td>(19,912)</td>
</tr>
<tr>
<td>Total stockholders’ deficit</td>
<td>(54,332)</td>
<td>(39,296)</td>
<td>(19,791)</td>
</tr>
</tbody>
</table>
Overview

We are a clinical-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 is EBI-005, which we designed, engineered and generated using our AMP-Rx platform and are developing as a topical treatment for dry eye disease and allergic conjunctivitis. In 2013, we completed a Phase 1b/2a clinical trial of EBI-005 in patients with moderate to severe dry eye disease. In early 2014, we initiated a pivotal Phase 3 clinical program evaluating EBI-005 for the treatment of moderate to severe dry eye disease. We also initiated a Phase 2 clinical trial to evaluate the use of EBI-005 in patients with allergic conjunctivitis in early 2014. We hold worldwide commercialization rights to EBI-005.

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, beginning in 2012, conducting clinical trials. To date, we have financed our operations primarily through private placements of our preferred stock and convertible bridge notes, venture debt borrowings, the initial public offering of our common stock, or IPO, 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 recognized collaboration revenue of $1.3 million for the year ended December 31, 2013. Since inception, we have incurred significant operating losses. As of December 31, 2013, we had an accumulated deficit of $57.6 million. Our net loss was $18.0 million for the year ended December 31, 2013, $19.7 million for the year ended December 31, 2012 and $12.8 million for the year ended December 31, 2011. In February 2014, we closed our IPO. 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.

We anticipate that our expenses will increase substantially as compared to prior periods in connection with conducting our pivotal Phase 3 clinical program, consisting of two Phase 3 clinical trials evaluating the safety and efficacy of EBI-005, our most advanced product candidate, for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year, and seeking marketing approval for EBI-005 for this indication in the United States.

We also expect our expenses to increase as we conduct our Phase 2 clinical trial of EBI-005 for the treatment of allergic conjunctivitis, as we conduct additional clinical trials of EBI-005 for the treatment of additional indications or for use in other patient populations, as we seek marketing approval of EBI-005 for the treatment of allergic conjunctivitis or other indications or for use in other patient populations, and as we continue research and development and initiate additional clinical trials of, and seek marketing approval for, our other product candidates. In addition, if we obtain marketing approval for EBI-005 or any other product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, with the closing of our IPO, we have begun to incur additional costs associated with operating as a public company. 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.

Financial Operations Overview

Revenue

To date, we have not generated any revenues from the sale of products. All of our revenue to date has been derived from a collaboration. We do not expect to generate significant product revenue unless and until we obtain marketing approval for, and commercialize, EBI-005, which we do not expect will occur before 2017, if ever.
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 extends for 30 months from the date we entered into the agreement, but may be extended on mutual agreement. 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 $1.3 million in connection with this collaboration for the year ended December 31, 2013. We expect that any revenue we generate from our collaboration with Thrombogenics will fluctuate from quarter to quarter as a result of the uncertain timing and amount of payments for research services, milestone payments and royalties.

**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 contract 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.

In April 2013, we implemented a strategic restructuring designed to conserve resources and improve our financial position. As part of this strategic restructuring, we reduced spending on early stage research programs and implemented a reduction in force of 15 positions, or 50% of our workforce, primarily in the research area. We expect our research and development expenses to increase substantially as compared to prior periods in connection with conducting our pivotal Phase 3 clinical program for EBI-005, seeking marketing approval for EBI-005 in the United States and, whether alone or in collaboration with third parties, in the European Union and other jurisdictions, initiating and conducting additional clinical trials of EBI-005 for the treatment of allergic conjunctivitis or additional indications or for use in other patient populations, and continuing the research and development and initiating clinical trials of our other product candidates.

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-005 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-005 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 EBI-005 product program and other expenses by category. We did not allocate research and development expenses to any other specific product program during the periods presented:

<table>
<thead>
<tr>
<th></th>
<th>Year ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>EBI-005</td>
<td>$7,366</td>
</tr>
<tr>
<td>Personnel and other expenses:</td>
<td></td>
</tr>
<tr>
<td>Employee and contractor-related expenses</td>
<td>4,409</td>
</tr>
<tr>
<td>Platform-related lab expenses</td>
<td>997</td>
</tr>
<tr>
<td>Facility expenses</td>
<td>773</td>
</tr>
<tr>
<td>Other expenses</td>
<td>243</td>
</tr>
<tr>
<td>Total personnel and other expenses</td>
<td>6,422</td>
</tr>
<tr>
<td>Total research and development expenses</td>
<td>$13,788</td>
</tr>
</tbody>
</table>

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 and human resource functions. Other general and administrative expenses include facility-related costs and professional fees for legal, patent, consulting and accounting services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also anticipate increased accounting, audit, legal, regulatory, compliance, insurance and investor and public relations expenses associated with being a public company.

Other Income (Expense), Net

Other income and expense consists primarily of interest income earned on cash and cash equivalents, interest expense on outstanding debt and the gain or loss associated with the change in the fair value of our preferred stock warrant liability and the convertible notes that are carried 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. 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 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 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 is estimated on the date of grant using the Black-Scholes option pricing model based on the assumptions noted in the following table:

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>1.09-2.07%</td>
<td>0.57-0.95%</td>
<td>1.16-2.69%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Expected term (in years)</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>72.13-77.80%</td>
<td>70.48-70.80%</td>
<td>70.61%</td>
</tr>
</tbody>
</table>

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, 2013, actual forfeitures have not been material.

Stock-based compensation expense was $1.3 million for the year ended December 31, 2013, $0.1 million for the year ended December 31, 2012 and $38,000 for the year ended December 31, 2011. As of December 31, 2013, we had $3.4 million of total unrecognized stock-based compensation expense related to service-based vesting awards, which we expect to recognize over a weighted-average remaining vesting period of approximately 2.77 years. In addition, as of December 31, 2013, we had unrecognized compensation expense related to performance-based awards of $2.3 million, which will be recorded when the vesting conditions become probable of achievement. Our stock-based compensation expense is expected to increase as a result of recognizing our existing unrecognized stock-based compensation for awards that will vest and as we issue additional stock-based awards to attract and retain our employees.

We allocated stock-based compensation expense as follows:

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and development</td>
<td>$ 1,150</td>
<td>$ 117</td>
<td>$ 37</td>
</tr>
<tr>
<td>General and administrative</td>
<td>110</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Total stock-based compensation expense</td>
<td>$ 1,260</td>
<td>$ 130</td>
<td>$ 38</td>
</tr>
</tbody>
</table>

**Fair Value of Common Stock**

Prior to the completion of our IPO, we were required to estimate the fair value of our common stock underlying our stock-based awards when performing the fair value calculations using the Black-Scholes option pricing model. The fair value of our common stock underlying our stock-based awards was determined on each grant date by our board of directors, with input from management. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant. In the absence of a public trading market for our common stock, on each grant date, we developed an estimate of the fair value of our common stock in order to determine an exercise price for the option grants. We determined the fair value of stock options using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants, or AICPA, *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the AICPA Practice Guide. In addition, we considered various objective and subjective factors, along with input from management and contemporaneous valuations, to determine the fair value of our common stock, including:

- external market conditions affecting the biotechnology industry;
The per share estimated fair value of common stock in the table below represents the determination by our board of directors of the fair value of our common stock as of the date of grant, taking into consideration the various objective and subjective factors described above, including the conclusions, if applicable, of contemporaneous valuations of our common stock as discussed below. The following table sets forth information about our stock option grants since January 1, 2012:

<table>
<thead>
<tr>
<th>Date of Grant</th>
<th>Number of shares underlying option grants</th>
<th>Exercise price per share</th>
<th>Per share estimated fair value of common stock</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 16, 2012</td>
<td>23,622</td>
<td>$ 0.76</td>
<td>$ 0.76</td>
</tr>
<tr>
<td>May 17, 2012</td>
<td>103,811</td>
<td>0.76</td>
<td>0.76</td>
</tr>
<tr>
<td>August 9, 2012</td>
<td>18,268</td>
<td>0.76</td>
<td>0.76</td>
</tr>
<tr>
<td>February 14, 2013</td>
<td>84,646</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>February 22, 2013</td>
<td>173,228</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>March 15, 2013</td>
<td>90,551</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>May 16, 2013</td>
<td>25,197</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>August 15, 2013</td>
<td>92,913</td>
<td>6.22</td>
<td>6.22</td>
</tr>
<tr>
<td>October 31, 2013</td>
<td>160,315</td>
<td>7.37</td>
<td>7.37</td>
</tr>
<tr>
<td>November 5, 2013</td>
<td>15,748</td>
<td>7.37</td>
<td>7.37</td>
</tr>
<tr>
<td>December 19, 2013</td>
<td>145,748</td>
<td>9.59</td>
<td>9.59</td>
</tr>
<tr>
<td>December 26, 2013</td>
<td>94,488</td>
<td>9.59</td>
<td>9.59</td>
</tr>
</tbody>
</table>

In determining the exercise prices of the options set forth in the table above granted since January 1, 2012, our board of directors considered the most recent valuations of our common stock, which were prepared as of November 1, 2011, November 1, 2012, June 30, 2013, August 15, 2013, September 30, 2013 and December 17, 2013.

The intrinsic value of all outstanding vested and unvested options as of December 31, 2013 was $9.5 million based on a per share price of $10.41 for our common stock, and based on 1,346,238 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2013 and a weighted average exercise price of $3.39 per share.

**Valuations**

*Common stock valuation methodologies.* These valuations of our common stock were prepared in accordance with the guidelines in the AICPA Practice Guide, which prescribes several valuation approaches for determining the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its capital structure and specifically the common stock.

We generally used the market approach, in particular the guideline company and precedent transaction methodologies, based on inputs from comparable public companies’ equity valuations and comparable acquisition transactions, to estimate the equity value of our company. Additionally, if applicable, we considered company valuations implied by arm’s length transactions involving sale of our securities to independent investors, taking into consideration the various rights and preferences of the equity securities transacted.
Methods used to allocate our enterprise value to classes of securities. In accordance with the AICPA Practice Guide, we considered the following methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date.

- **Option pricing method, or OPM.** The OPM treats common stock and preferred stock as call options on the enterprise’s value, with exercise prices based on the liquidation preference and conversion terms of the preferred stock. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the liquidation preference at the time of a liquidity event (for example, merger or sale).

- **Probability-weighted expected return method, or PWERM.** Under a PWERM, the value of the various equity securities are estimated based upon an analysis of future values for the enterprise assuming various future outcomes. Share value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise, as well as the rights of each share class, discounted for a lack of marketability.

For each of the valuations of our common stock, we used either the OPM or the PWERM to determine the estimated fair value of our common stock. The method selected was based on availability and the quality of information to develop the assumptions for the methodology.

There is inherent uncertainty in the estimates, forecasts and projections we used in determining the fair value of our common stock, and if we had made different assumptions and estimates than those described above, the amount of our share-based compensation expense, net loss and net loss per share amounts could have been materially different.

**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 Year Ended December 31, 2013 and 2012**

<table>
<thead>
<tr>
<th></th>
<th>Year ended December 31,</th>
<th></th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013 (in thousands)</td>
<td>2012</td>
<td></td>
</tr>
<tr>
<td>Collaboration revenue</td>
<td>$1,334</td>
<td>$—</td>
<td>$1,334</td>
</tr>
<tr>
<td>Research and development</td>
<td>13,788</td>
<td>15,263</td>
<td>(1,475)</td>
</tr>
<tr>
<td>General and administrative</td>
<td>4,024</td>
<td>4,213</td>
<td>(189)</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>17,812</td>
<td>19,476</td>
<td>(1,664)</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(16,478)</td>
<td>(19,476)</td>
<td>2,998</td>
</tr>
<tr>
<td>Other income (expense), net</td>
<td>(1,547)</td>
<td>(181)</td>
<td>(1,366)</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(18,025)</td>
<td>$(19,657)</td>
<td>$1,632</td>
</tr>
</tbody>
</table>

**Revenue.** Revenue was $1.3 million for the year ended December 31, 2013 compared to $0 for the year ended December 31, 2012. The increase of $1.3 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 $13.8 million for the year ended December 31, 2013 compared to $15.3 million for the year ended December 31, 2012. The decrease of $1.5 million was primarily due to a decrease of $1.3 million of EBI-005 related development expenses and a decrease in platform-related laboratory expenses of $0.7 million. In April 2013, we implemented a strategic restructuring to focus more of our research and development expenses on the development of EBI-005. As a result, we reduced headcount from 30 to 15, including 13 positions in our research and development function. These decreases in research and development expenses were partially offset by an increase in employee and contractor-related expenses of $0.5 million to support the increased development activities of the Phase 1b/2a clinical trial of EBI-005.
General and administrative expenses. General and administrative expenses were $4.0 million for the year ended December 31, 2013 compared to $4.2 million for the year ended December 31, 2012. The decrease of $0.2 million was primarily due to our strategic restructuring, which focused more of our resources on the development of EBI-005. As a result of the restructuring in April 2013, we reduced total headcount from 30 to 15, including two positions in our general and administrative function.

Other income (expense), net. Other income (expense), net was $(1.5) million for the year ended December 31 2013 compared to $(0.2) million for the year ended December 31, 2012. The increase was primarily due to the change in the fair value of the warrant liability, which increased from $0.1 million to $0.3 million, the change in the fair value of convertible notes payable of $1.0 million, and an increase in interest expense due to additional borrowings under our debt facility during the year ended December 31, 2013.

Comparison of the Years Ended December 31, 2011 and 2012

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2011</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(in thousands)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>$15,263</td>
<td>$9,411</td>
<td>$5,852</td>
</tr>
<tr>
<td>General and administrative</td>
<td>4,213</td>
<td>3,267</td>
<td>946</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>19,476</td>
<td>12,678</td>
<td>6,798</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(19,476)</td>
<td>(12,678)</td>
<td>(6,798)</td>
</tr>
<tr>
<td>Other income (expense), net</td>
<td>(181)</td>
<td>(148)</td>
<td>(33)</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(19,657)</td>
<td>$(12,826)</td>
<td>$(6,831)</td>
</tr>
</tbody>
</table>

Revenue. We did not recognize any revenue during the years ended December 31, 2012 and 2011.

Research and development expenses. Research and development expenses were $15.3 million for the year ended December 31, 2012 compared to $9.4 million for the year ended December 31, 2011. The increase of $5.9 million was primarily due to an increase in costs associated with EBI-005, including clinical supply manufacturing and drug product process development activities in preparation for initiating our Phase 1b/2a trial of EBI-005.

General and administrative expenses. General and administrative expenses were $4.2 million for the year ended December 31, 2012 compared to $3.3 million for the year ended December 31, 2011. The increase of $0.9 million was primarily due to an increase in employee and contractor related expenses in support of our development efforts.

Other income (expense), net. Other income (expense), net was $(0.2) million for the year ended December 31, 2012 compared to $(0.1) million for the year ended December 31, 2011.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have incurred significant operating losses. All of our revenue to date has been collaboration revenue. To date, we have financed our operations primarily through private placements of our preferred stock and bridge notes convertible into our preferred stock, venture debt borrowings, our IPO, which we closed in February 2014, and, to a lesser extent, from a collaboration.

In May 2013, we entered into the collaboration and license agreement with ThromboGenics. Under this collaboration, ThromboGenics made a $1.75 million up-front, non-refundable cash payment to us and will fund the research services that we provide under the agreement.

In June 2013, we issued and sold 7% convertible promissory notes in the aggregate principal amount of $3.5 million and accompanying warrants to purchase shares of our common stock to four of the holders of our series A preferred stock. These warrants were exercised in connection with our IPO for an aggregate of 275,200 shares of our common stock. We refer to these convertible promissory notes as the June 2013 convertible notes.

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In December 2013, we issued and sold an aggregate of 7,203,845 shares of our series B preferred stock and accompanying warrants to purchase shares of our common stock to four of the holders of our series A preferred stock and one additional investor, at a price per share of $1.75, for an aggregate purchase price of $12.6 million, consisting of $9.0 million in cash and $3.6 million for the conversion of the June 2013 convertible notes, including accrued interest. These warrants were exercised in connection with our IPO for an aggregate of 202,218 shares of our common stock.

Cash Flows

As of December 31, 2013, we had cash and cash equivalents of $7.9 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:

<table>
<thead>
<tr>
<th>Year ended December 31</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net cash provided by (used in):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operating activities</td>
<td>$(13,494)</td>
<td>$(19,092)</td>
<td>$(10,869)</td>
</tr>
<tr>
<td>Investing activities</td>
<td>—</td>
<td>(110)</td>
<td>(805)</td>
</tr>
<tr>
<td>Financing activities</td>
<td>13,554</td>
<td>26,384</td>
<td>10,448</td>
</tr>
<tr>
<td>Net increase (decrease) in cash and cash equivalents</td>
<td>$60</td>
<td>$7,182</td>
<td>$(1,226)</td>
</tr>
</tbody>
</table>

Operating activities. 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 upfront payment related to the ThromboGenics collaboration.

Net cash used in operating activities was $19.1 million for the year ended December 31, 2012, and consisted primarily of a net loss of $19.7 million adjusted for non-cash items, including depreciation expense of $0.4 million, stock-based compensation expense of $0.1 million and a net change in operating assets and liabilities of $(0.1) million.

Net cash used in operating activities was $10.9 million for the year ended December 31, 2011, and consisted primarily of a net loss of $12.8 million adjusted for non-cash items, including depreciation expense of $0.4 million and a net change in operating assets and liabilities of $(1.5) million. The significant items in the change in operating assets and liabilities include decreases in other receivables of $(0.8) million and increases in accounts payable and accrued expenses of $(0.9) million offset by an increase in prepaid expenses and other current assets of $0.2 million.

Investing activities. Net cash used in investing activities consists of purchases of property and equipment. We made no such purchases during the year ended December 31, 2013. For the years ended December 31, 2012 and 2011, we purchased $0.1 million and $0.8 million, respectively, of property and equipment, primarily laboratory equipment.

Financing activities. 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.

Net cash provided by financing activities for the year ended December 31, 2012 was $26.4 million and consisted primarily of proceeds of $25.4 million from the issuance of series A preferred stock and additional borrowings under our debt facility of $2.0 million offset by $1.0 million in payments on equipment financing and notes payable.

Net cash provided by financing activities for the year ended December 31, 2011 was $10.4 million and consisted primarily of proceeds of $11.0 million from the issuance of series A preferred stock offset by $0.6 million in payments on equipment financing and notes payable.
Funding Requirements

We anticipate that our expenses will increase substantially as compared to prior periods in connection with conducting our pivotal Phase 3 clinical program, consisting of two Phase 3 clinical trials evaluating the safety and efficacy of EBI-005, our most advanced product candidate, for the treatment of moderate to severe dry eye disease and a separate clinical trial evaluating the safety of treatment with EBI-005 for one year, and seeking marketing approval for EBI-005 for this indication in the United States.

We received scientific advice from the European Medicine Agency’s, or EMA, Committee for Medicinal Products for Human Use, or CHMP, that indicates that the requirements for European registration in dry eye disease will differ from the requirements for registration in the United States and our pivotal Phase 3 clinical program is not consistent with the advice of the CHMP. We will continue to evaluate the scientific advice received from the EMA and plan to further discuss with the EMA a registration plan for EBI-005 in moderate to severe dry eye disease for the European Union. We may be required to conduct additional clinical trials to support an application for marketing approval of EBI-005 in the European Union. We anticipate that our expenses will increase substantially if we pursue, alone or in collaboration with third parties, the development of and seek marketing approval for, EBI-005 for the treatment of moderate to severe dry eye disease in the European Union.

Furthermore, with the closing of our IPO, we have begun to incur additional costs associated with operating as a public company. Accordingly, we may 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 expenses will also increase if and as we:

• pursue the development of EBI-005 for the treatment of allergic conjunctivitis or additional indications or for use in other patient populations or, if it is approved, seek to broaden the label for EBI-005;
• continue the research and development of our other 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 expand our clinical trials and commence commercialization of EBI-005.

As of December 31, 2013, we had cash and cash equivalents of 7.9 million. We believe that our cash and cash equivalents as of December 31, 2013 and the approximately $50.2 million in net proceeds from our IPO, after deducting underwriting discounts and commissions and other offering expenses payable by us, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into the second half of 2016, without giving effect to any potential milestone payments we may receive under our collaboration and license agreement with ThromboGenics. 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 our pivotal Phase 3 clinical program for EBI-005 and of any clinical activities for regulatory review of EBI-005 outside of the United States;
• the costs and timing of process development and manufacturing scale up and validation activities associated with EBI-005;
• the costs, timing and outcome of regulatory review of EBI-005 in the United States, the European Union and in other jurisdictions;
• the costs and timing of commercialization activities for EBI-005 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-005;

• the progress, costs and outcome of developing EBI-005 for the treatment of additional indications or for use in other patient populations, including
our Phase 2 clinical trial to assess the potential therapeutic benefit of EBI-005 for the treatment of allergic conjunctivitis in patients who do not
respond adequately to antihistamines and mast cell stabilizers;

• 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 success of our collaboration with ThromboGenics;

• 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 other than funding under our existing collaboration and license agreement with ThromboGenics in the
form of research funding. Under this collaboration, we also may receive potential milestone payments upon the achievement of specified development,
regulatory and other milestones and royalties with respect to future sales of collaboration products by ThromboGenics. ThromboGenics may terminate our
existing collaboration for convenience on short notice. 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. Our pledge of
specified assets as collateral to secure our obligations under our loan and security agreement with our venture debt lender, 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.

**Contractual Obligations and Commitments**

The following table summarizes our contractual obligations at December 31, 2013:

<table>
<thead>
<tr>
<th>Description</th>
<th>Total (in thousands)</th>
<th>Less than 1 year</th>
<th>1 to 3 years</th>
<th>3 to 5 years</th>
<th>More than 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating lease obligations(1)</td>
<td>$873</td>
<td>$416</td>
<td>$457</td>
<td>—</td>
<td>$—</td>
</tr>
<tr>
<td>Debt obligations(2)</td>
<td>5,162</td>
<td>1,889</td>
<td>3,273</td>
<td>—</td>
<td>$—</td>
</tr>
<tr>
<td><strong>Total fixed contractual obligations</strong></td>
<td><strong>$6,035</strong></td>
<td><strong>$2,305</strong></td>
<td><strong>$3,730</strong></td>
<td><strong>$—</strong></td>
<td><strong>$—</strong></td>
</tr>
</tbody>
</table>

(1) We lease office space at 215 First Street in Cambridge, Massachusetts under a non-cancelable operating lease that expires on January 31, 2016, with an
option to extend the lease term through 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 Silicon Valley Bank. We borrowed an aggregate of $1.5 million under the debt facility in June and July 2010 and issued Silicon Valley Bank promissory notes. In September 2012, we modified the terms of our secured debt facility with Silicon Valley Bank 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. The debt facility is secured by substantially all of our assets except for our intellectual property. The debt facility carries a fixed interest rate of 5.75%. In addition, on the date that the debt facility is paid in full we are required to make a payment in an amount equal to 4% of total borrowings during the term of the debt facility. As of December 31, 2013, the outstanding principal balance on the notes was $4.6 million. The debt facility provides for the repayment of the outstanding principal balance in equal monthly amounts beginning in October 2013 through September 2016. The debt facility contains negative covenants restricting our activities, including limitations on dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and certain other business transactions. There are no financial covenants associated with the debt facility. The obligations under the debt facility are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition.

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 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 EBI-005. See “Business—License and Collaboration Agreements” for additional information regarding our agreement with Schepens.

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, 2013, we had $53.8 million of federal NOL carryforwards, state NOL carryforwards of $53.0 million and aggregate federal and state research and development tax credit carryforwards of $1.8 million 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 reduce by a valuation allowance. These federal and state NOL carryforwards and federal and state tax credit carryforwards will begin to expire at various dates beginning in 2014, 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 on our NOL carryforwards under Section 382 of the Code. If we experienced a Section 382 ownership change in connection with our IPO 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 Securities and Exchange Commission.

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, 2013, we had cash and cash equivalents of $7.9 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, 2013, 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-25 of this Annual Report on Form 10-K.

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 and Business Officer, evaluated the effectiveness of the Company’s disclosure controls and procedures as of December 31, 2013. 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, 2013, the Company’s Chief Executive Officer and Chief Financial and Business 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
This Annual Report on Form 10-K does not include a report of management’s assessment regarding our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control over Financial Reporting
There was no change in our internal control over financial reporting that occurred during the period covered by this Annual Report on Form 10-K 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.

Executive Officers and Directors

The following table sets forth the name, age as of December 31, 2013 and position of each of our executive officers and directors.

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbie C. Celniker, Ph.D.</td>
<td>54</td>
<td>President and Chief Executive Officer and Director</td>
</tr>
<tr>
<td>Gregory D. Perry</td>
<td>53</td>
<td>Chief Financial and Business Officer</td>
</tr>
<tr>
<td>Eric S. Furfine, Ph.D.</td>
<td>54</td>
<td>Chief Scientific Officer</td>
</tr>
<tr>
<td>Karen L. Tubridy, Pharm.D.</td>
<td>51</td>
<td>Chief Development Officer</td>
</tr>
<tr>
<td>Daniel S. Lynch(1)(2)(3)</td>
<td>55</td>
<td>Chairman of the Board of Directors</td>
</tr>
<tr>
<td>Noubar B. Afeyan, Ph.D.</td>
<td>51</td>
<td>Director</td>
</tr>
<tr>
<td>David A. Berry, M.D., Ph.D.(1)(2)</td>
<td>35</td>
<td>Director</td>
</tr>
<tr>
<td>Paul G. Chanev</td>
<td>56</td>
<td>Director</td>
</tr>
<tr>
<td>Jane V. Henderson(1)(3)</td>
<td>48</td>
<td>Director</td>
</tr>
<tr>
<td>Mark J. Levin</td>
<td>63</td>
<td>Director</td>
</tr>
<tr>
<td>Cary G. Pfeffer, M.D.(2)(3)</td>
<td>51</td>
<td>Director</td>
</tr>
</tbody>
</table>

(1) Member of the Audit Committee.
(2) Member of the Compensation Committee.
(3) Member of the Nominating and Corporate Governance Committee.

Abbie C. Celniker, Ph.D. has served as our President and Chief Executive Officer and as a member of our board of directors since September 2011. Prior to joining Eleven Biotherapeutics, Dr. Celniker served as the Executive Vice President, Translational Medicine of Alexion Pharmaceuticals, Inc., a biopharmaceutical company, from January 2011 to August 2011. Prior to joining Alexion Pharmaceuticals, Dr. Celniker served as the President and Chief Executive Officer and as a member of the board of directors of Taligen Therapeutics, Inc., a biotechnology company, from July 2008 to January 2011, when Taligen Therapeutics was acquired by Alexion Pharmaceuticals. Previously, Dr. Celniker served as the Global Head of Biologics of Novartis AG, the Senior Vice President of Research and Development Strategy and Operations of Millennium Pharmaceuticals, Inc. and the Vice President Protein Technologies of the Wyeth Research facilities in Cambridge, Massachusetts. Dr. Celniker received a B.A. in Biology from the University of California, San Diego, and a Ph.D. in Molecular Biology from the University of Arizona. We believe that Dr. Celniker is qualified to serve on our board of directors because of her extensive executive leadership experience in the life sciences industry and her extensive knowledge of our company based on her position as President and Chief Executive Officer.

Gregory D. Perry has served as our Chief Financial and Business Officer since December 2013. Prior to joining Eleven Biotherapeutics, Mr. Perry served as the Interim Chief Financial Officer of InVivo Therapeutics Holdings Corp., a drug delivery company, from September 2013 to December 2013. Prior to joining InVivo Therapeutics, Mr. Perry served as the Executive Vice President and Chief Financial Officer of ImmunoGen, Inc., a biopharmaceutical company, from April 2011 to September 2013 and as the Senior Vice President and Chief Financial Officer of ImmunoGen from January 2009 to April 2011. Prior to that, Mr. Perry served as the Chief Financial Officer of Elixir Pharmaceuticals, Inc., a pharmaceutical company, from 2007 to 2008. Mr. Perry has served on the board of directors of Advanced Cell Technology, Inc. since 2011. Mr. Perry received a B.A. in Economics and Political Science from Amherst College.

Eric S. Furfine, Ph.D. has served as our Chief Scientific Officer since June 2013 and served as our President of Research and Development from December 2010 to June 2013. Prior to joining Eleven Biotherapeutics, Dr. Furfine served as the Senior Vice President of Research and Preclinical Development of Adnexus Therapeutics, Inc., a Bristol-Myers Squibb research and development company, from August 2006 to December 2010. Previously, Dr. Furfine served as the Vice President of Preclinical Development of Regeneron Pharmaceuticals, Inc., and in various senior level research positions at GlaxoSmithKline plc. Dr. Furfine received an A.B. from Washington University in St. Louis and a Ph.D. in Biochemistry from Brandeis University.

Karen L. Tubridy, Pharm.D. has served as our Chief Development Officer since June 2013. Prior to joining Eleven Biotherapeutics, Ms. Tubridy served as the Senior Vice President, Clinical Development and Medical Affairs of Inspiration Biopharmaceuticals, Inc., a biopharmaceutical company, from December 2011 to March 2013. Inspiration Biopharmaceuticals filed a bankruptcy petition under Chapter 11 of the U.S. Bankruptcy Code in October 2012. Prior to joining Inspiration Biopharmaceuticals, Ms. Tubridy served as the
Executive Director, Clinical Operations and Regulatory Affairs, Translational Medicine of Alexion Pharmaceuticals from January 2011 to November 2011, when Taligen Therapeutics was acquired by Alexion Pharmaceuticals, and as Vice President of Clinical Operations and Regulatory Affairs of Taligen Therapeutics from April 2010 to January 2011. Prior to that, Ms. Tubridy served as Vice President of Clinical Operations Hemophilia of Biogen Idec, Inc., a biotechnology company, from January 2007 through March 2010. Ms. Tubridy received a B.S. and a Pharm.D. from the Massachusetts College of Pharmacy and Allied Health Sciences.

Daniel S. Lynch has served as the Chairman of our board of directors since December 2013. Mr. Lynch has served as a venture partner at Third Rock Ventures, a venture capital firm, since May 2013 and as an entrepreneur-in-residence from May 2011 to May 2013. Since 2005, Mr. Lynch has served on the boards of directors of several life sciences companies, including on the board of directors of BIND Therapeutics, Inc. since 2012, on the board of directors of bluebird bio, Inc. since 2011, and on the board of directors of U.S. Oncology, Inc. from 2005 to 2010. Prior to that, Mr. Lynch served as the Chief Financial Officer and then the Chief Executive Officer of ImClone Systems Inc. Mr. Lynch received a B.A. in Mathematics from Wesleyan University and a M.B.A. from the Darden Graduate School of Business Administration at the University of Virginia. We believe that Mr. Lynch is qualified to serve on our board of directors because of his extensive experience as a senior executive and service on the boards of directors of other life sciences companies.

Noubar B. Afeyan, Ph.D. has served as a member of our board of directors since February 2008. Since 1999, Dr. Afeyan has served as the Managing Partner and Chief Executive Officer of Flagship Ventures, an early stage venture capital firm that he co-founded. Dr. Afeyan has served on the board of directors of BG Medicine, Inc. since 2000 and on the board of directors of BIND Therapeutics since 2007. Dr. Afeyan received a B.S. in Chemical Engineering from McGill University and a Ph.D. in Biochemical Engineering from the Massachusetts Institute of Technology. We believe that Dr. Afeyan is qualified to serve on our board of directors because of his extensive experience as an entrepreneur and venture capital investor in the life sciences industry and his service on the boards of directors of other life sciences companies.

David A. Berry, M.D., Ph.D. has served as a member of our board of directors since August 2009. Dr. Berry has been with Flagship Ventures since 2005, where he has served as a Partner since 2008. Dr. Berry received a B.S. from the Massachusetts Institute of Technology, a M.D. from Harvard Medical School and a Ph.D. from the Massachusetts Institute of Technology. We believe that Dr. Berry is qualified to serve on our board of directors because of his extensive experience as a venture capital investor in the life sciences industry and his service on the boards of directors of other life sciences companies.

Paul G. Chaney has served as a member of our board of directors since February 2014. Mr. Chaney is a co-founder of PanOptica, Inc., a private biopharmaceutical company focused on developing innovative ophthalmic therapeutics and has served as its President and Chief Executive Officer since 2009. Prior to co-founding PanOptica, Mr. Chaney was executive vice president of OSI Pharmaceuticals, Inc. and president of (OSI) Eyetech, Inc., OSI Pharmaceutical’s wholly-owned eyecare subsidiary. Mr. Chaney joined Eyetech Pharmaceuticals as Chief Operating Officer in 2003. Prior to joining Eyetech, Mr. Chaney held a variety of senior management positions at Pharmacia Corporation, including Vice President of the Global Ophthalmology Business and Vice President of Global Pharmaceutical Ophthalmology. He began his career as a sales representative for The Upjohn Company in 1980. Mr. Chaney earned a dual degree in Biological Sciences and English from the University of Delaware. We believe that Mr. Chaney is qualified to serve on our board of directors because of his extensive executive leadership experience in ophthalmology-focused biotechnology companies and pharmaceutical company business units for 19 years.

Jane V. Henderson has served as a member of our board of directors since October 2013. Since February 2013, Ms. Henderson has served as the Senior Vice President, Chief Business Officer of Kolltan Pharmaceuticals, Inc., a biopharmaceutical company. Prior to joining Kolltan Pharmaceuticals, Ms. Henderson served as the Vice President, Business Development of ISTA Pharmaceuticals, Inc., an eye care company, from June 2010 to June 2012, when ISTA Pharmaceuticals was acquired by Bausch + Lomb Incorporated. Prior to joining ISTA Pharmaceuticals, Ms. Henderson served as the Executive Vice President, Chief Financial Officer and Head of Business Development, Business Development of Axerion Pharmaceuticals, Inc., a pharmaceutical company, from September 2009 to June 2010, provided independent consulting services from February 2009 to September 2009 and served as the Executive Vice President, Chief Financial Officer and Chief Business Officer of Panacos Pharmaceuticals, Inc., a pharmaceutical company, from January 2008 to February 2009. Prior to that, Ms. Henderson served in a variety of senior investment banking roles at HSBC Holdings plc, Canadian Imperial Bank of Commerce, Lehman Brothers and Salomon Brothers. Ms. Henderson received a B.S. in Psychology from Duke University. We believe that Ms. Henderson is qualified to serve on our board of directors because of her extensive executive leadership experience in and knowledge of the life sciences industry and her extensive finance background as an investment banker for over 19 years.

Mark J. Levin has served as a member of our board of directors since September 2008. Since 2007, Mr. Levin has served as a partner of Third Rock Ventures, an early stage life sciences venture capital firm that he co-founded. While at Third Rock Ventures, Mr. Levin also served as our President and Chief Executive Officer from August 2009 to September 2011. Mr. Levin has served on the board of directors of Foundation Medicine, Inc. since 2010. Mr. Levin received a B.S. and M.S., each in Chemical and Biomedical Engineering,
from Washington University. We believe Mr. Levin is qualified to serve on our board of directors because of his extensive experience as a venture capital investor in the life sciences industry, his service on the boards of directors of other life sciences companies, his prior service as our Chief Executive Officer and his extensive executive leadership experience at other life science companies for over 20 years.

Cary G. Pfeffer, M.D. has served as a member of our board of directors since August 2009. Since 2007, Dr. Pfeffer has served as a Partner of Third Rock Ventures. While at Third Rock Ventures, Dr. Pfeffer also served as our Chief Business Officer from February 2010 to September 2011. Dr. Pfeffer received a B.A. in Biochemistry from Columbia University, a M.B.A. from the Wharton School and a M.D. from the University of Pennsylvania School of Medicine. We believe that Dr. Pfeffer is qualified to serve on our board of directors because of his extensive experience as a venture capital investor in the life sciences industry, his service on the boards of directors of other life sciences companies, his prior service as our Chief Business Officer and his extensive executive leadership experience at other life science companies for over 10 years.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors, executive officers and beneficial owners of more than 10% of our equity securities to file reports of holdings and transactions in securities of the Company with the SEC. Our directors, executive officers and beneficial owners of more than 10% of our equity securities did not become subject to such Section 16(a) reporting requirements until February 5, 2014, after the completion of our fiscal year ended December 31, 2013.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the Corporate Governance section of our website, which is located at http://www.elevenbio.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a Current Report on Form 8-K to the extent required by applicable law, the rules of the Securities and Exchange Commission or the rules of the NASDAQ Global Market.

Audit Committee

The members of our audit committee are Ms. Henderson, Mr. Lynch and Dr. Berry. Ms. Henderson is the chair of the audit committee. Our board of directors has determined that each of Ms. Henderson and Mr. Lynch is an “audit committee financial expert” as defined in applicable SEC rules and that each qualifies as independent as defined under the applicable NASDAQ rules.

Item 11. Executive Compensation.

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers in 2013. Our named executive officers for 2013 are Abbie C. Celniker, Ph.D., our President and Chief Executive Officer, Eric S. Furfine, Ph.D., our Chief Scientific Officer and Karen L. Tubridy, Pharm.D., our Chief Development Officer. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers and is intended to place in perspective the data presented in the tables and narrative that follow.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers for the year ended December 31, 2013.

<table>
<thead>
<tr>
<th>Name and Principal Position</th>
<th>Year</th>
<th>Salary ($)</th>
<th>Bonus ($)</th>
<th>Option awards ($)</th>
<th>All other compensation ($)</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbie C. Celniker, Ph.D.</td>
<td>2013</td>
<td>375,000</td>
<td>84,375</td>
<td>273,372</td>
<td>—</td>
<td>732,747</td>
</tr>
<tr>
<td>President and Chief Executive Officer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eric S. Furfine, Ph.D.</td>
<td>2013</td>
<td>309,000</td>
<td>35,500</td>
<td>91,876</td>
<td>—</td>
<td>436,376</td>
</tr>
<tr>
<td>Chief Scientific Officer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karen L. Tubridy, Pharm.D.</td>
<td>2013</td>
<td>158,654(3)</td>
<td>39,300(4)</td>
<td>364,808</td>
<td>—</td>
<td>562,762</td>
</tr>
<tr>
<td>Chief Development Officer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

87
Except where noted, the amounts reported in the “Bonus” column reflect discretionary annual cash bonuses payable to our executive officers for their 2013 performance.

The amounts reported in the “Option awards” column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification, or ASC, Topic 718. See Note 11 to our financial statements appearing at the end of this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.

Ms. Tubridy joined our company on June 3, 2013. Ms. Tubridy’s annual base salary is $275,000.

The bonus amount for Ms. Tubridy also includes the first installment of a signing bonus in the amount of $7,500 that was paid in 2013 upon the commencement of her employment with us. Ms. Tubridy is eligible to receive the second installment of her signing bonus in the amount of $7,500 upon the one-year anniversary of the commencement of her employment with us.

Narrative to Summary Compensation Table

In 2013, we paid annual base salaries of $375,000 to Dr. Celniker, $309,000 to Dr. Furfine and $275,000 to Ms. Tubridy. Base salaries are used to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

We do not have a formal performance-based bonus plan. From time to time, our board of directors has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance. During the first quarter of 2013, we paid discretionary annual cash bonuses of $25,875 to Dr. Celniker and $20,700 to Dr. Furfine for their 2012 performance. In January 2014, our board of directors approved discretionary cash bonuses of $84,375 for Dr. Celniker, $35,500 for Dr. Furfine and $31,800 for Ms. Tubridy for their 2013 performance. In 2013, we paid Ms. Tubridy the first installment of a signing bonus in the amount of $7,500 upon the commencement of her employment with us. Ms. Tubridy is eligible to receive the second installment of her signing bonus in the amount of $7,500 upon the one-year anniversary of the commencement of her employment with us.

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options. In 2013, based upon our overall performance, we granted to Dr. Celniker options to purchase 137,795 shares of our common stock, to Dr. Furfine options to purchase 47,244 shares of our common stock and to Ms. Tubridy options to purchase 85,827 shares of our common stock.

Outstanding Equity Awards at December 31, 2013

The following table sets forth information regarding all outstanding stock options and restricted stock held by each of our named executive officers as of December 31, 2013.

<table>
<thead>
<tr>
<th>Name</th>
<th>Number of securities underlying exercisable options (#)</th>
<th>Number of securities underlying unexercisable options (#)</th>
<th>Option exercise price ($)</th>
<th>Option expiration date</th>
<th>Number of shares of stock that have not vested (#)</th>
<th>Market value of shares that have not vested ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbie C. Celniker, Ph.D.</td>
<td>16,978</td>
<td>73,573(1)</td>
<td>0.83</td>
<td>3/14/2023</td>
<td>155,020(2)</td>
<td>1,550,200(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>47,244(1)</td>
<td>7.37</td>
<td>10/30/2023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eric S. Furfine, Ph.D.</td>
<td>88,583</td>
<td>29,527(4)</td>
<td>0.06</td>
<td>2/16/2021</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5,906</td>
<td>25,590(4)</td>
<td>0.83</td>
<td>2/13/2023</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>15,748(4)</td>
<td>7.37</td>
<td>10/30/2023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karen L. Tubridy, Pharm.D.</td>
<td></td>
<td>74,016(5)</td>
<td>6.22</td>
<td>8/14/2023</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>11,811(5)</td>
<td>7.37</td>
<td>10/30/2023</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Dr. Celniker’s option to purchase 90,551 shares of common stock vests over four years, with 6.25% of the shares underlying the option vesting quarterly after January 1, 2013. Dr. Celniker’s option to purchase 47,244 shares of common stock vests over four years in equal quarterly installments, with the first installment vesting on January 1, 2014.

Dr. Celniker’s shares of restricted stock vest over four years, with 25% of the shares vested on September 12, 2012 and 6.25% of the shares vesting quarterly thereafter.

The market value of these shares is based on the initial public offering price of $10.00 per share.

Dr. Furfine’s option to purchase 118,110 shares of common stock vests over four years, with 25% of the shares underlying the option vested on December 20, 2011 and 6.25% of the shares underlying the option vesting quarterly thereafter. Dr. Furfine’s option to purchase 31,496 shares of common stock vest over four years, with 6.25% of the shares underlying the option vesting quarterly after January 1, 2013. Dr. Furfine’s option to purchase 15,748 shares of common stock vests over four years in equal quarterly installments, with the first installment vesting on January 1, 2014.

Ms. Tubridy’s option to purchase 74,016 shares of common stock vests over four years, with 25% of the shares underlying the option vesting on June 3, 2014 and 6.25% of the shares underlying the option vesting quarterly thereafter. Ms. Tubridy’s option to purchase 11,811 shares of common stock vests over four years in equal quarterly installments, with the first installment vesting on January 1, 2014.

In connection with the hiring of Gregory D. Perry as our Chief Financial and Business Officer, in December 2013, our board of directors granted Mr. Perry an option to purchase 145,748 shares of our common stock at an exercise price of $9.59 per share. Mr. Perry’s stock option vests over four years, with 25% of the shares underlying the option vesting on December 9, 2014 and 6.25% of the shares underlying the option vesting quarterly thereafter.

Employment Agreements with Executive Officers

In December 2013, we entered into amended and restated employment agreements with Dr. Celniker, Ms. Tubridy and Dr. Furfine. In addition, in December 2013, we entered into an employment agreement with Mr. Perry in connection with the commencement of his employment. Each of these agreements provides that employment will continue until either we or the executive officer provides notice of termination in accordance with the terms of the agreement. In addition, we have entered into non-competition, non-solicitation, confidentiality and assignment agreements with each of our executive officers which prohibit them from competing with us, soliciting our employees and customers and disclosing confidential information during the term of their employment and for a specified time thereafter.

Pursuant to their respective employment agreements, each of our executive officers is entitled to receive an annual base salary as follows: Dr. Celniker: $375,000; Mr. Perry: $340,000; Dr. Furfine: $309,000; and Ms. Tubridy: $275,000. In January 2014, our board of directors approved merit based salary increases retroactively effective to January 1, 2014 for Dr. Celniker, whose annual base salary was increased to $393,750, Dr. Furfine, whose annual base salary was increased to $318,300, and Ms. Tubridy, whose annual base salary was increased to $283,000.

In addition, each of our executive officers is eligible to receive an annual cash bonus, which is based on the achievement of individual and corporate performance objectives, calculated as a percentage of the executive’s annual base salary, and which will be determined by our board of directors, in its sole discretion. Dr. Celniker’s target annual bonus is 50% of her annual base salary, and the target bonus for each of our other executive officers is 30% of his or her annual base salary.

Potential Payments Upon Termination or Change in Control Transaction

Upon execution and effectiveness of a release of claims, each of our executive officers will be entitled to severance payments if his or her employment is terminated under specified circumstances.

Dr. Celniker: If we terminate Dr. Celniker’s employment without cause, as defined in her employment agreement, or if Dr. Celniker terminates her employment with us for good reason, as defined in her employment agreement, absent a change in control transaction, as defined in her employment agreement, we are obligated to pay Dr. Celniker’s base salary for a period of 12 months, to pay Dr. Celniker an amount equal to her target bonus payment for the year in which the termination of employment occurs, prorated for the portion of the year in which she was employed, and, to the extent allowed by applicable law and the applicable plan documents, to continue to pay Dr. Celniker and certain of her dependents with group health and dental insurance for a period of 12 months.

If we terminate Dr. Celniker’s employment without cause or if Dr. Celniker terminates her employment with us for good reason, in each case within 18 months following a change in control transaction, we are obligated to pay Dr. Celniker an amount equal to her base salary for 12 months, paid in accordance with our then-current payroll practices, to pay Dr. Celniker an amount equal to her target bonus payment for the year in which the termination of employment occurs, to accelerate in full the vesting of all of Dr. Celniker’s outstanding equity awards and, to the extent allowed by applicable law and the applicable plan documents, to continue to provide Dr. Celniker and certain of her dependents with group health and dental insurance for a period of 12 months.

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In addition, we have agreed to indemnify Dr. Celniker in any action or proceeding arising out of her service to us, unless she initiates such action or proceeding. These indemnification obligations may require us, among other things, to indemnify Dr. Celniker for certain expenses, including attorneys’ fees, that are incurred by her, and to advance to Dr. Celniker such expenses upon request.

Other executive officers. For each of Dr. Furfine and Ms. Tubridy, if we terminate such executive officer’s employment without cause, as defined in such executive officer’s employment agreement, or if the executive officer terminates his or her employment with us for good reason, as defined in such executive officer’s employment agreement, absent a change in control transaction, as defined in such executive officer’s employment agreement, we are obligated to pay such executive officer’s base salary for a period of 12 months and, to the extent allowed by applicable law and the applicable plan documents, to continue to provide such executive officer and certain of his or her dependents with group health and dental insurance for a period of 12 months.

If we terminate either Dr. Furfine or Ms. Tubridy without cause or if such executive officer terminates his or her employment with us for good reason, in each case within 12 months following a change in control transaction, we are obligated to pay such executive officer’s base salary for a period of 12 months, to accelerate in full the vesting of all outstanding equity awards held by such executive officer and, to the extent allowed by applicable law and the applicable plan documents, to continue to provide such executive officer and certain of his or her dependents with group health and dental insurance for a period of 12 months.

If we terminate Mr. Perry’s employment without cause, as defined in Mr. Perry’s employment agreement, or if he terminates his employment with us for good reason, as defined in his employment agreement, absent a change in control, as defined in his employment agreement, we are obligated to pay Mr. Perry’s base salary for a period of 12 months, to accelerate the vesting of Mr. Perry’s unvested equity awards, if any, such that he is credited with an additional 12 months of vesting as of the termination date with respect to such unvested equity awards and, to the extent allowed by applicable law and the applicable plan documents, to continue to provide Mr. Perry and certain of his dependents with group health and dental insurance for a period of 12 months.

If we terminate Mr. Perry’s employment without cause or if he terminates his employment with us for good reason, in each case within 12 months following a change in control, we are obligated to pay Mr. Perry’s base salary for a period of 12 months, to pay Mr. Perry an amount equal to his target bonus for the year in which the termination of employment occurs, pro-rated for the portion of the year during which he was employed, to accelerate in full the vesting of Mr. Perry’s unvested equity awards, if any, and, to the extent allowed by applicable law and the applicable plan documents, to continue to provide Mr. Perry and certain of his dependents with group health and dental insurance for a period of 12 months. Notwithstanding the foregoing, Mr. Perry will not be entitled to the benefits in the preceding sentence and will instead be entitled to the benefits in the preceding paragraph to the extent that the change in control occurs within 6 months of his employment commencement date and a specified entity is involved in the change in control.

Taxation. To the extent that any severance or other compensation payment to any of Dr. Celniker, Dr. Furfine or Ms. Tubridy pursuant to his or her employment agreement or any other agreement constitutes an “excess parachute payment” within the meaning of Sections 280G and 4999 of the Internal Revenue Code of 1986, as amended, then such executive officer will receive the full amount of such severance and other payments, or a reduced amount intended to avoid the application of Sections 280G and 4999, whichever provides the executive with the highest amount on an after-tax basis.

Equity Incentive Plans

2009 Stock Incentive Plan

Our 2009 Stock Incentive Plan, or 2009 Plan, is administered by our board of directors and provides for the grant of incentive stock options within the meaning of Section 422 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, non-statutory stock options and restricted stock. Our employees, officers, directors, consultants and advisors are eligible to receive awards under our 2009 Plan. However, incentive stock options may only be granted to our employees. The terms of awards are set forth in the applicable award agreements. Our board of directors may amend, suspend or terminate our 2009 Plan at any time. Awards under our 2009 Plan are subject to adjustment in the event of certain corporate transactions affecting our common stock such as reorganizations, recapitalization, stock splits or similar transactions.

Upon a change in control transaction (as defined in our 2009 Plan), our board of directors, may, in its sole discretion, take any one or more of the following actions pursuant to the 2009 Plan, as to some or all outstanding options:

• provide that all outstanding options will be assumed, or substantially equivalent options shall be substituted, by the acquiring or successor corporation or an affiliate thereof;
• upon written notice to a participant, provide that the participant’s unexercised options will terminate immediately prior to the consummation of the transaction unless exercised by the participant;
• make or provide for a cash payment to an optionee equal to the difference between (1) the fair market value of the per share consideration (whether cash, securities or other property or any combination of the above) the holder of a share of common stock will receive upon consummation of the Change in Control Transaction, or the Per Share Transaction Price, times the number of shares of common stock subject to outstanding vested options (to the extent then exercisable at prices not equal to or in excess of the Per Share Transaction Price) and (2) the aggregate exercise price of such outstanding vested options, in exchange for the termination of such options; and

• provide that all or any outstanding options shall become exercisable immediately prior to such event.

Upon the occurrence of a change in control transaction, our board of directors, may, in its sole discretion, take any one or more of the following actions pursuant to the 2009 Plan, as to some or all outstanding restricted stock awards:

• upon written notice to a grantee, provide that all unvested shares of restricted stock held by the grantee shall be repurchased at cost immediately prior to the consummation of the transaction; and

• provide that all or any outstanding restricted stock awards shall vest in part or in full immediately prior to such event.

In the case of a business combination or other reorganization event, any securities, cash or other property received in exchange for shares of restricted stock shall continue to be governed by the provisions of any restricted stock agreement pursuant to which they were issued including any provision regarding vesting, and such securities, cash or other property may be held in escrow on such terms as the board of directors may direct, to insure compliance with the terms of any such restricted stock agreement. At any time, our board of directors may, in its sole discretion, accelerate the date or dates on which any award under the 2009 Plan may be exercised or extend the period or periods of time during which any award may be exercised.

As of January 21, 2014, under our 2009 Plan, there were options to purchase an aggregate of 1,346,235 shares of common stock outstanding at a weighted average exercise price of $3.39 per share, and we had granted 588,583 shares of restricted stock, of which 119,521 shares of restricted stock were repurchased by us, and all but 159,941 shares were vested as of January 21, 2014. There were 1,586 shares remaining and available for issuance under the 2009 Plan as of that date. Following the closing our IPO, no further stock options or other awards will be granted under our 2009 Plan. However, any shares of common stock subject to awards under our 2009 Plan that expire, terminate, or are otherwise surrendered, canceled, forfeited or repurchased without having been fully exercised or resulting in any common stock being issued will become available for issuance under our 2014 Stock Incentive Plan, or the 2014 Plan, up to a specified number of shares.

**2014 Stock Incentive Plan**

Our 2014 Plan was adopted by our board of directors in December 2013 and was approved by our stockholders in January 2014. The 2014 Plan may be administered by our board of directors or by a committee appointed by our board of directors. 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 our 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 (x) 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 (y) the number of shares of our common stock subject to outstanding awards under our 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 our common stock, 4% of the number of shares of our common stock outstanding on the first day of the applicable fiscal year and an amount determined by our board of directors.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2014 Plan. However, incentive stock options may only be granted to our employees. The maximum number of shares of common stock with respect to which awards may be granted to any participant under the 2014 Plan is per calendar year. For purposes of this limit on the maximum number of shares that may be awarded to any participant, the combination of an option in tandem with a stock appreciation right will be treated as a single award.

Subject to any limitation in the 2014 Plan, our board of directors or any committee or officer to which our board of directors has delegated authority will select the recipients of awards and determine:

• the number of shares of common stock covered by options and stock appreciation rights and the dates upon which those awards become exercisable;
the type of options to be granted;

• the exercise price of options and measurement price of stock appreciation rights, neither of which may be less than 100% of the fair market value of our common stock on the grant date;

• the duration of options and stock appreciation rights which may not be in excess of ten years;

• the methods of payment of the exercise price of options; and

• the number of shares of common stock subject to any restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including the issue price, conditions for repurchase, repurchase price and performance conditions, if any.

If our board of directors delegates authority to an executive officer to grant awards other than restricted stock under the 2014 Plan, the executive officer will have the power to make awards to all of our employees, other than executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards, and the maximum number of shares subject to awards that such executive officer may make.

Upon a merger or other reorganization event, our board of directors, may, in its sole discretion, take any one or more of the following actions pursuant to the 2014 Plan, as to some or all outstanding awards, other than restricted stock:

• provide that all outstanding awards will be assumed, or substantially equivalent awards shall be substituted, by the acquiring or successor corporation or an affiliate thereof;

• upon written notice to a participant, provide that the participant’s unexercised options or awards will terminate immediately prior to the consummation of such transaction unless exercised by the participant;

• provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;

• in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by the participant equal to (1) the number of shares of our common stock subject to the vested portion of the award, after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event, multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such awards; and

• provide that, in connection with a liquidation or dissolution, awards convert into the right to receive liquidation proceeds.

In the case of specified restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights under each outstanding restricted stock award will continue for the benefit of the successor company and will, unless our board of directors may otherwise determine, apply to the cash, securities or other property into which our common stock is converted pursuant to the reorganization event. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award.

At any time, our board of directors may, in its sole discretion, provide that any award under the 2014 Plan will become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part.

No award may be granted under the 2014 Plan after the tenth anniversary of the closing of our IPO. Our board of directors may amend, suspend or terminate the 2014 Plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

2014 Employee Stock Purchase Plan

Our 2014 Employee Stock Purchase Plan, or the 2014 ESPP, was adopted by our board of directors in December 2013 and approved by our stockholders in January 2014. The 2014 ESPP may be administered by our board of directors or by a committee appointed by our board of directors. The 2014 ESPP initially provided participating employees with the opportunity to purchase an aggregate of 157,480 shares of our common stock.
All of our employees and employees of any of our designated subsidiaries, as defined in the 2014 ESPP, are eligible to participate in the 2014 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least six months prior to enrolling in the 2014 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2014 ESPP.

No employee may purchase shares of our common stock under the 2014 ESPP and any of our other employee stock purchase plans in excess of $25,000 of the fair market value of our common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of our common stock under the 2014 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2014 ESPP beginning at such time as our board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% percent of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2014 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2014 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may for any reason withdraw from participation in an offering prior to the end of an offering period and permanently draw out the balance accumulated in the employee’s account. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee’s employment ends before the last business day of an offering period, no additional payroll deductions will be made and the balance in the employee’s account will be paid to the employee.

We will be required to make equitable adjustments to the number and class of securities available under the 2014 ESPP, the share limitations under the 2014 ESPP and the purchase price for an offering period under the 2014 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event (as defined in the 2014 ESPP), our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2014 ESPP on such terms as our board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee’s accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2014 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or

• provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2014 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board of directors may not make any amendment that would cause the 2014 ESPP to fail to comply with Section 423 of the Code. The 2014 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) Plan

We maintain a defined contribution employee retirement plan for our employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Code so that contributions to our 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan. Our 401(k) plan provides that each participant may contribute up to 90% of his or her pre-tax compensation, up to a statutory limit, which is $17,500 for 2013 and 2014. Participants who are at least 50 years old can also make “catch-up” contributions, which in 2013 may be up to an additional $5,500 above the statutory limit. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan’s trustee, subject to participants’ ability to give investment directions by following certain procedures. We do not currently make discretionary contributions or matching contributions to our 401(k) plan.

Limitation of Liability and Indemnification

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law, or the DGCL, and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

• for any breach of the director’s duty of loyalty to us or our stockholders;
• for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
• for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
• for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the DGCL is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys’ fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with all of our directors and executive officers. These indemnification agreements may require us, among other things, to indemnify each such director and executive officer for some expenses, including attorneys’ fees, judgments, fines and settlement amounts incurred by him in any action or proceeding arising out of his or her service as one of our directors or executive officers.
Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, or the Securities Act, may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

**Director Compensation**

During and prior to 2013, we did not pay cash compensation to any non-employee director for his or her service as a director. We reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending board of director and committee meetings or otherwise in direct service of our company.

The table below shows all compensation to our non-employee directors during 2013.

<table>
<thead>
<tr>
<th>Name</th>
<th>Option awards ($)</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daniel S. Lynch(2)</td>
<td>561,143</td>
<td>561,143</td>
</tr>
<tr>
<td>Noubar B. Afeyan, Ph.D.</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>David A. Berry, M.D., Ph.D.</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mark J. Levin</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cary G. Pfeffer, M.D.</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Jane V. Henderson(3)</td>
<td>143,502</td>
<td>143,502</td>
</tr>
</tbody>
</table>

(1) The amounts reported in the “Option awards” column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board ASC Topic 718.

(2) In connection with the election of Mr. Lynch as the Chairman of our board of directors, in December 2013, our board of directors granted Mr. Lynch an option to purchase 90,551 shares of our common stock, at an exercise price of $9.59 per share. Mr. Lynch’s stock option vests over one year, with 1/12th of the shares underlying the option vesting at the end of each one-month period following December 26, 2013.

(3) In connection with the election of Ms. Henderson as a member of our board of directors, in October 2013, our board of directors granted Ms. Henderson an option to purchase 25,197 shares of our common stock at an exercise price of $7.37 per share. The October 2013 stock option vests over four years, with 1/48th of the shares underlying the option vesting at the end of each one-month period following November 1, 2013. In December 2013, our board of directors granted Ms. Henderson an additional option to purchase 3,937 shares of our common stock, at an exercise price of $9.59 per share. The December 2013 stock option vests over three years, with 1/36th of the option shares vesting at the end of each one-month period following December 26, 2013.

During 2013, we did not provide any additional compensation to Dr. Celniker, our President and Chief Executive Officer, for her service as a director. Dr. Celniker’s compensation as an executive officer is set forth above under “Executive Compensation—Summary Compensation Table.”

Our non-employee directors are compensated for their services on our board of directors as follows:

- non-employee directors will receive initial stock option grants as follows:
  - upon his or her initial election or appointment to our board of directors, each newly elected or appointed non-employee director will receive an option to purchase 16,143 shares of common stock, representing a number of shares of common stock equal to 0.1% of the total number of shares of common stock issued and outstanding as of immediately following our IPO;
  - effective as of the 30th trading day of our common stock on The NASDAQ Global Market, each currently-serving non-employee director, other than Mr. Lynch and Ms. Henderson, also received an option to purchase 16,143 shares of common stock, representing a number of shares of common stock equal to 0.1% of the total number of shares of common stock issued and outstanding as of immediately following our IPO; and
immediately following the closing of our IPO, Mr. Lynch received a grant of restricted stock for 70,879 shares of common stock, representing a number of shares of common stock equal to 1.0% of the total number of shares of common stock issued and outstanding as of immediately following our IPO less 90,551 shares;

- on the date of each annual meeting of our stockholders, each non-employee director who has served on our board of directors for at least six months will receive an annual grant of an option to purchase 8,072 shares of common stock, representing a number of shares equal to 0.05% of the total number of shares of common stock issued and outstanding as of immediately following our IPO;

- each non-employee director will receive an annual cash fee of $35,000;

- the chairman of the board of directors will receive an additional annual cash fee of $47,500;

- each member of the audit committee will receive an additional annual cash fee of $7,500 ($15,000 for the audit committee chair);

- each member of the compensation committee will receive an additional annual cash fee of $6,000 ($10,000 for the compensation committee chair);

- each member of the nominating and corporate governance committee will receive an additional annual cash fee of $3,750 ($7,500 for the nominating and corporate governance committee chair).

The stock options granted to our non-employee directors will have an exercise price equal to the fair market value of our common stock on the date of grant and will expire ten years after the date of grant. The initial stock options granted to our non-employee directors will, subject to the director’s continued service on our board, vest monthly in equal amounts over a three-year period following the grant date. The annual stock options granted to our non-employee directors will, subject to the director’s continued service on our board, vest monthly in equal amounts over a one-year period following the grant date.

The restricted stock granted to the chairman of our board of directors will, subject to his continued service on our board, vest quarterly in equal amounts over a four-year period following closing of our IPO.

Each annual cash fee will be payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of each payment will be prorated for any portion of a quarter that a director is not serving on our board and no fee will be payable in respect of any period prior to February 5, 2014, the effective date of the registration statement for our IPO.

Each member of our board of directors will also be entitled to reimbursement for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors and any committee on which he or she serves.

**Compensation Committee Interlocks and Insider Participation**

None of our executive officers serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company.

Securities Authorized for Issuance under Equity Compensation Plans

The following table shows information relating to our equity compensation plan as of December 31, 2013. Under this plan, we can issue stock options and restricted stock.

<table>
<thead>
<tr>
<th>Plan Category</th>
<th>Number of securities to be issued upon exercise of outstanding options, warrants and rights</th>
<th>Weighted average exercise price of outstanding options, warrants and rights</th>
<th>Number of securities remaining available for future issuance under equity compensation plans (excluding securities in first column)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equity compensation plans approved by security holders</td>
<td>1,346,238</td>
<td>$ 3.39</td>
<td>1,586</td>
</tr>
<tr>
<td>Equity compensation plans not approved by security holders</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>1,346,238</td>
<td>$ 3.39</td>
<td>1,586</td>
</tr>
</tbody>
</table>

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information with respect to the beneficial ownership of our common stock as of March 21, 2014 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock based on currently available Schedules 13D and 13G filed with the Securities and Exchange Commission.

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The column entitled “Percentage of Shares Beneficially Owned” is based on a total of 16,240,985 shares of our common stock outstanding as of March 21, 2014.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options and warrants that are currently exercisable or exercisable within 60 days after March 21, 2014 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of each beneficial owner is c/o Eleven Biotherapeutics, Inc., 215 First Street, Suite 400, Cambridge, Massachusetts 02142.

<table>
<thead>
<tr>
<th>Name and Address of Beneficial Owner</th>
<th>Number of shares beneficially owned</th>
<th>Percentage of shares beneficially owned</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>5% Stockholders:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entities affiliated with Flagship Ventures Management, Inc.(1)</td>
<td>3,373,425</td>
<td>20.8%</td>
</tr>
<tr>
<td>JAFCO Super V3 Investment Limited Partnership(2)</td>
<td>2,127,291</td>
<td>13.1</td>
</tr>
<tr>
<td>Third Rock Ventures, L.P.(3)</td>
<td>4,841,591</td>
<td>29.8</td>
</tr>
<tr>
<td>Broadfin Capital, LLC(4)</td>
<td>896,100</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>Directors and Named Executive Officers:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daniel S. Lynch(5)</td>
<td>101,062</td>
<td>*</td>
</tr>
<tr>
<td>Mark J. Levin(3)</td>
<td>4,842,487</td>
<td>29.8</td>
</tr>
<tr>
<td>Cary G. Pfeffer, M.D.(6)</td>
<td>4,842,487</td>
<td>29.8</td>
</tr>
<tr>
<td>Noubar B. Afeyan, Ph.D. (7)</td>
<td>3,374,320</td>
<td>20.8</td>
</tr>
<tr>
<td>David A. Berry, M.D., Ph.D.(8)</td>
<td>896</td>
<td>*</td>
</tr>
<tr>
<td>Jane V. Henderson(9)</td>
<td>4,110</td>
<td>*</td>
</tr>
<tr>
<td>Paul G. Chaney(10)</td>
<td>896</td>
<td>*</td>
</tr>
<tr>
<td>Abbie C. Celniker, Ph.D.(11)</td>
<td>388,532</td>
<td>2.4</td>
</tr>
<tr>
<td>Eric S. Furfine, Ph.D.(12)</td>
<td>107,775</td>
<td>*</td>
</tr>
<tr>
<td>Karen L. Tubridy, Pharm.D(13)</td>
<td>1,476</td>
<td>*</td>
</tr>
<tr>
<td>All current executive officers and directors as a group (10 persons)(14)</td>
<td>8,822,451</td>
<td>53.7</td>
</tr>
</tbody>
</table>

* Less than one percent.

(1) Consists of (i) 1,907,008 shares of common stock held by Flagship Ventures Fund 2007 L.P., or Flagship 2007, (ii) 1,173,149 shares of common stock held by Flagship Ventures Fund IV, L.P., or Flagship IV, and (iii) 293,268 shares of common stock held by Flagship Ventures Fund IV-Rx, L.P., or Flagship IV-Rx. Each of Flagship Ventures 2007 General Partner LLC, the general partner of Flagship 2007, and Flagship Ventures Fund IV General Partner LLC, the general partner of Flagship IV and Flagship IV-Rx, may be deemed to share voting and dispositive power with respect to the shares held by the Flagship Funds respectively. In addition, investment decisions with respect to the shares held by each of the Flagship Funds are made in part by Dr. Afeyan, a member of our board of directors, as the managing partner and chief executive officer of Flagship Ventures. Dr. Berry, a member of our board of directors, is a partner of Flagship Ventures. Each of Dr. Afeyan and Dr. Berry disclaim beneficial ownership of all shares held by the Flagship Funds, except to the extent of his pecuniary interest therein. The address for Flagship Ventures Management, Inc. is One Memorial Drive, 7th Floor, Cambridge, MA 02142. Beneficial ownership is derived from a Schedule 13D filed on February 13, 2014.

(2) All shares are held by JAFCO Super V3 Investment Limited Partnership. The address for JAFCO Super V3 Investment Limited Partnership is Otemachi First Square, West Tower, 11F, 1-5-1 Otemachi Chiyoda-ku, Tokyo 100-0004, Japan.

(3) All shares are held by Third Rock Ventures, L.P., or TRV L.P. Each of Third Rock Ventures GP L.P., or TRV GP L.P., and Third Rock Ventures GP, LLC, or TRV GP LLC, may be deemed to share voting and dispositive power with respect to all shares held by TRV L.P. In addition, investment decisions with respect to the shares held by TRV L.P. are made by an investment committee at TRV GP L.P., of which Mr. Levin and Dr. Pfeffer, each of whom is a member of our board of directors, are members. Each of Mr. Levin and Dr. Pfeffer disclaim beneficial ownership of all shares held by TRV L.P., except to the extent of his pecuniary interest therein. The address for TRV L.P. is 29 Newbury Street, Boston, MA 02116. Beneficial ownership is derived from a Schedule 13D filed on February 21, 2014.
(4) All shares are held by Broadfin Capital, LLC. Each of Broadfin Capital, LLC, Broadfin Healthcare Master Fund, Ltd. and Kevin Kotler may be deemed to have shared voting power and shared dispositive power with respect to all shares held by Broadfin Capital, LLC. The address for Broadfin Capital, LLC is 237 Park Avenue, Suite 900, New York, NY 10017. Beneficial ownership is derived from a Schedule 13G filed on February 19, 2014.

(5) Consists of (i) 70,879 shares of restricted common stock and (ii) 30,183 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(6) Consists of (1) the shares held by Third Rock Ventures, L.P. described in footnote 3 above, which Dr. Pfeffer beneficially owns, and (2) 896 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(7) Consists of (1) the shares held by the entities affiliated with Flagship Ventures Management, Inc. described in footnote 1 above, which Dr. Afeyan beneficially owns, and (2) 896 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(8) Consists of 896 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014. Mr. Berry was deemed not to beneficially own the 3,373,424 shares held by the entities affiliated with Flagship Ventures Management, Inc.

(9) Consists of 4,110 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(10) Consists of 896 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(11) Consists of (i) 354,330 shares of restricted common stock and (ii) 34,202 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(12) Consists of 107,775 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(13) Consists of 1,476 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 21, 2014.

(14) Consists of (i) 8,215,016 shares of common stock, (ii) 425,209 shares of restricted common stock, and (iii) 182,226 shares of common stock underlying options that are exercisable as of March 21, 2014 or will become exercisable within 60 days after such date.

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

Since January 1, 2013, we have engaged in the following transactions with our directors, executive officers and holders of more than 5% of our voting securities, and affiliates of our directors, executive officers and holders of more than 5% of our voting securities. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

2013 Bridge Loan Financing

In June 2013, we issued and sold 7% convertible promissory notes in the aggregate principal amount of $3.5 million and accompanying warrants to purchase shares of our common stock to four of our 5% stockholders. The warrants were exercised for an aggregate of 275,200 shares of our common stock at a price of $0.06 per share upon the closing of our IPO. We refer to these convertible promissory notes as the June 2013 convertible notes.

The following table sets forth the principal amount of June 2013 convertible notes we issued and sold to our 5% stockholders and their affiliates in this transaction and the number of shares of our common stock that were issued and sold to our 5% stockholders and their affiliates upon the exercise of the warrants issued in connection with the June 2013 convertible notes:

<table>
<thead>
<tr>
<th>Purchaser</th>
<th>Principal amount of notes</th>
<th>Warrants to purchase common stock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entities affiliated with Flagship Ventures Management, Inc.(1)</td>
<td>$1,108,334</td>
<td>87,270</td>
</tr>
<tr>
<td>JAFCO Super V3 Investment Limited Partnership</td>
<td>777,776</td>
<td>61,242</td>
</tr>
<tr>
<td>Third Rock Ventures, L.P.(2)</td>
<td>1,613,890</td>
<td>127,077</td>
</tr>
</tbody>
</table>

(1) The 2013 convertible notes and accompanying warrants to purchase shares of our common stock are held by each of Flagship IV and Flagship IV-RX LP. Flagship Ventures Fund IV General Partner LLC, the general partner of Flagship IV and Flagship IV-Rx, may be deemed to share voting and dispositive power with respect to the 2013 convertible notes and the accompanying warrants held by Flagship IV and Flagship IV-Rx. In addition, investment decisions with respect to the notes and accompanying warrants held by Flagship IV and Flagship IV-Rx are made in part by Dr. Afeyan, a member of our board of directors, as the managing partner and chief executive officer of Flagship Ventures. Dr. Berry, a member of our board of directors, is a partner of Flagship Ventures. Each of Dr. Afeyan and Dr. Berry disclaim beneficial ownership of the 2013 convertible notes and accompanying warrants to purchase shares of our common stock held by Flagship IV and Flagship IV-Rx except to the extent of his pecuniary interest therein.
The 2013 convertible notes and accompanying warrants to purchase shares of our common stock are held by TRV L.P. Each of TRV GP L.P. and TRV GP LLC, may be deemed to share voting and dispositive power with respect to the 2013 convertible notes and accompanying warrants held by TRV L.P. In addition, investment decisions with respect to the shares held by TRV L.P. are made by an investment committee at TRV GP L.P. of which Mr. Levin and Dr. Pfeffer, each of whom is a member of our board of directors, are members. Each of Mr. Levin and Dr. Pfeffer disclaim beneficial ownership of the 2013 convertible notes and accompanying warrants to purchase shares of our common stock held by TRV L.P., except to the extent of his pecuniary interest therein.

Series B Preferred Stock Financing

In December 2013, we issued and sold an aggregate of 7,203,845 shares of our series B preferred stock and accompanying warrants to purchase shares of our common stock to four of our 5% stockholders and one additional investor, at a price per share of $1.75, for an aggregate purchase price of $12.6 million, consisting of $9.0 million in cash and $3.6 million for the conversion of the June 2013 convertible notes, including accrued interest. The warrants were exercised for an aggregate of 202,218 shares of our common stock at a price of $0.06 per share upon the closing of our IPO.

The following table sets forth the aggregate number of shares of our series B preferred stock that we issued and sold to our 5% stockholders and their affiliates in these transactions, the aggregate purchase price for such shares and the number of shares of our common stock that were issued and sold to our 5% stockholders and their affiliates upon the exercise of the warrants issued in connection with our series B preferred stock financing:

<table>
<thead>
<tr>
<th>Purchaser</th>
<th>Shares of series B preferred stock</th>
<th>Cash purchase price</th>
<th>Conversion of convertible promissory notes</th>
<th>Warrants to purchase common stock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entities affiliated with Flagship Ventures Management, Inc.(1)</td>
<td>2,100,266</td>
<td>$2,533,335</td>
<td>$1,142,131</td>
<td>56,992</td>
</tr>
<tr>
<td>JAFCO Super V3 Investment Limited Partnership</td>
<td>1,473,869</td>
<td>1,777,778</td>
<td>801,493</td>
<td>39,994</td>
</tr>
<tr>
<td>Third Rock Ventures, L.P.(2)</td>
<td>3,058,281</td>
<td>3,688,889</td>
<td>1,663,103</td>
<td>82,989</td>
</tr>
</tbody>
</table>

(1) Consists of (i) 1,680,213 shares of our series B preferred stock and warrants to purchase 45,594 shares of our common stock held by Flagship IV and (ii) 420,053 shares of our series B preferred stock and warrants to purchase 11,398 shares of our common stock held by Flagship IV-Rx. Flagship Ventures Fund IV General Partner LLC, the general partner of Flagship IV and Flagship IV-Rx, may be deemed to share voting and dispositive power with respect to the shares held by Flagship IV and Flagship IV-Rx. In addition, investment decisions with respect to the shares held by Flagship IV and Flagship IV-Rx, are made in part by Dr. Afeyan, a member of our board of directors, as the managing partner and chief executive officer of Flagship Ventures. Dr. Berry, a member of our board of directors, is a partner of Flagship Ventures. Each of Dr. Afeyan and Dr. Berry disclaim beneficial ownership of all shares held by Flagship IV and Flagship IV-Rx, except to the extent of his pecuniary interest therein.

(2) All shares are held by TRV L.P. Each of TRV GP L.P. and TRV GP LLC may be deemed to share voting and dispositive power with respect to all shares held by TRV L.P. In addition, investment decisions with respect to the shares held by TRV L.P. are made by an investment committee at TRV GP L.P. of which our directors Mr. Levin and Dr. Pfeffer are members. Each of Mr. Levin and Dr. Pfeffer disclaim beneficial ownership of all shares held by TRV L.P., except to the extent of his pecuniary interest therein.

Participation in our Initial Public Offering

Our principal stockholders and their affiliated entities purchased shares in our initial public offering, or IPO, at the initial public offering price. Third Rock Ventures LP purchased a total of 551,482 shares of our common stock for a purchase price of $5,514,820; JAFCO Super V3 Investment Limited Partnership purchased a total of 219,790 shares of our common stock for a purchase price of $2,197,900; and Flagship Ventures Management, Inc., and its affiliated entities, purchased a total of 378,729 shares of our common stock for a purchase price of $3,787,290.

Indemnification Agreements

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with all of our directors and executive officers.
Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a “related person,” has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a “related person transaction,” the related person must report the proposed related person transaction to our principal accounting officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chair of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person’s interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person’s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person’s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC’s related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person’s position as an executive officer of another entity, whether or not the person is also a director of the entity, that is a participant in the transaction where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or by-laws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee’s charter.

We did not have a written policy regarding the review and approval of related person transactions prior to our IPO. Nevertheless, with respect to such transactions, it has been the practice of our board of directors to consider the nature of and business reasons for such transactions, how the terms of such transactions compared to those which might be obtained from unaffiliated third parties and whether such transactions were otherwise fair to and in the best interests of, or not contrary to, our best interests. In addition, all related person transactions required prior approval, or later ratification, by our board of directors.
Director Independence

Our board of directors has determined that each of Ms. Henderson, Mr. Lynch and Mr. Chaney are independent as independence is currently defined in applicable NASDAQ listing standards, including for purposes of Rule 10A-3 under the Exchange Act. Ms. Henderson, Mr. Lynch and Dr. Berry are the current members of our audit committee; Mr. Lynch, Dr. Berry and Dr. Pfeffer are the current members of our compensation committee; and Mr. Lynch, Dr. Pfeffer and Ms. Henderson are the current members of our nominating and corporate governance committee. Although the board of directors did not determine that Dr. Berry and Mr. Pfeffer are independent, under NASDAQ rules, we are permitted to phase in our compliance with the independent committee requirements for each committee as follows: (1) one independent member of each committee at the time of listing, (2) a majority of independent members of each committee within 90 days of listing and (3) all independent members of each committee within one year of listing. Within one year of our listing on The NASDAQ Global Market, we expect that each member of our committees will satisfy independence requirements under applicable NASDAQ rules.

Item 14. Principal Accountant Fees and Services.

Ernst & Young LLP provided audit and tax services to the Company consisting of the audit of the Company’s 2012 and 2013 financial statements and tax compliance services. The following table summarizes the fees for Ernst & Young LLP services to the Company for the last two fiscal years.

<table>
<thead>
<tr>
<th>Fee Category</th>
<th>Fiscal Year 2013 ($)</th>
<th>Fiscal Year 2012 ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audit Fees (1)</td>
<td>$800,321</td>
<td>$27,779</td>
</tr>
<tr>
<td>Audit-Related Fees (2)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tax Fees (3)</td>
<td>7,000</td>
<td>6,000</td>
</tr>
<tr>
<td>All Other Fees (4)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total Fees</strong></td>
<td><strong>$807,321</strong></td>
<td><strong>$33,779</strong></td>
</tr>
</tbody>
</table>

(1) Audit fees consist of fees for the audit of our annual financial statements and fees related to our IPO.

(2) There were no audit-related fees for fiscal years 2013 and 2012.

(3) Tax fees consist of fees for tax compliance services. Tax compliance services primarily relate to the preparation of our U.S. and Massachusetts tax returns.

(4) There were no other fees for fiscal years 2013 and 2012.

In 2014, the Audit Committee adopted a formal policy concerning approval of audit and non-audit services to be provided to the Company by its independent registered public accounting firm, Ernst & Young LLP. The policy requires that all services to be provided by Ernst & Young LLP, including audit services and permitted audit-related and non-audit services, must be preapproved by the Audit Committee, provided that de minimis non-audit services may instead be approved in accordance with applicable SEC rules. The Board of Directors preapproved all audit and non-audit services provided by Ernst & Young LLP during fiscal year 2013 and fiscal year 2012.
PART IV


(a) Financial Statements

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

- Report of Independent Registered Public Accounting Firm
- Balance Sheets
- Statements of Operations and Comprehensive Loss
- Statements of Convertible Preferred Stock and Stockholders’ (Deficit) Equity
- Statements of Cash Flows
- Notes to Financial Statements

(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 BIOThERAPUETICS, INC.

By: /s/ Abbie C. Celniker
    Abbie C. Celniker, Ph.D.
    President and Chief Executive Officer

March 31, 2014

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
    Director, President and Chief Executive Officer (Principal Executive Officer)
    March 31, 2014

/s/ Gregory D. Perry
    Chief Financial and Business Officer (Principal Financial and Accounting Officer)
    March 31, 2014

/s/ Daniel S. Lynch
    Chairman of the Board of Directors
    March 31, 2014

/s/ Noubar B. Afeyan
    Director
    March 31, 2014

/s/ David A. Berry
    Director
    March 31, 2014

/s/ Mark J. Levin
    Director
    March 31, 2014

/s/ Cary G. Pfeffer
    Director
    March 31, 2014

/s/ Jane V. Henderson
    Director
    March 31, 2014

/s/ Paul G. Chaney
    Director
    March 31, 2014
**EXHIBIT INDEX**

<table>
<thead>
<tr>
<th>Exhibit No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>Restated Certificate of Incorporation (Incorporated by reference to Exhibit 3.3 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)</td>
</tr>
<tr>
<td>3.2</td>
<td>Amended and Restated By-laws (Incorporated by reference to Exhibit 3.3 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)</td>
</tr>
<tr>
<td>10.1+</td>
<td>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)</td>
</tr>
<tr>
<td>10.2+</td>
<td>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)</td>
</tr>
<tr>
<td>10.3+</td>
<td>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)</td>
</tr>
<tr>
<td>10.4+</td>
<td>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)</td>
</tr>
<tr>
<td>10.5+</td>
<td>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)</td>
</tr>
<tr>
<td>10.6+</td>
<td>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)</td>
</tr>
<tr>
<td>10.7+</td>
<td>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)</td>
</tr>
<tr>
<td>10.8+†</td>
<td>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)</td>
</tr>
<tr>
<td>10.9+†</td>
<td>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)</td>
</tr>
<tr>
<td>10.10</td>
<td>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)</td>
</tr>
<tr>
<td>10.11</td>
<td>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)</td>
</tr>
<tr>
<td>10.12</td>
<td>Form of Indemnification Agreement by and between the Registrant and each of its directors and executive officers (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)</td>
</tr>
<tr>
<td>10.13</td>
<td>2014 Employee Stock Purchase 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)</td>
</tr>
<tr>
<td>10.14</td>
<td>Employment Agreement, dated December 23, 2013, by and between the Registrant and Abbie C. Celniker, Ph.D. (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)</td>
</tr>
<tr>
<td>10.15</td>
<td>Employment Agreement, dated December 23, 2013, by and between the Registrant and Eric S. Furfine, Ph.D. (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)</td>
</tr>
<tr>
<td>Exhibit No.</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>10.16</td>
<td>Employment Agreement, dated December 26, 2013, by and between the Registrant and Karen L. Tubridy, Pharm.D (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)</td>
</tr>
<tr>
<td>10.17†</td>
<td>Employment Agreement, dated December 8, 2013, by and between the Registrant and Gregory D. Perry (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1 filed with the SEC on December 30, 2013)</td>
</tr>
<tr>
<td>10.18+</td>
<td>Form of Director Restricted Stock 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)</td>
</tr>
<tr>
<td>10.19</td>
<td>Form of Warrant issued to Silicon Valley Bank under the Loan and Security Agreement dated May 27, 2010 by and between the Registrant and Silicon Valley Bank, as modified (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1/A filed with the SEC on January 23, 2014)</td>
</tr>
<tr>
<td>31.1</td>
<td>Rule 13a-14(a) Certification of Principal Executive Officer</td>
</tr>
<tr>
<td>31.2</td>
<td>Rule 13a-14(a) Certification of Principal Financial Officer</td>
</tr>
<tr>
<td>32.1</td>
<td>Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. §1350</td>
</tr>
</tbody>
</table>

† 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

<table>
<thead>
<tr>
<th>Financial Statement Type</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report of Independent Registered Public Accounting Firm</td>
<td>F-2</td>
</tr>
<tr>
<td>Balance Sheets</td>
<td>F-3</td>
</tr>
<tr>
<td>Statements of Operations and Comprehensive Loss</td>
<td>F-4</td>
</tr>
<tr>
<td>Statements of Convertible Preferred Stock and Stockholders’ (Deficit) Equity</td>
<td>F-5</td>
</tr>
<tr>
<td>Statements of Cash Flows</td>
<td>F-6</td>
</tr>
<tr>
<td>Notes to Financial Statements</td>
<td>F-7</td>
</tr>
</tbody>
</table>
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, 2013 and 2012, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders’ (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2013. 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, 2013 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 31, 2014

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### ELEVEN BIOTHRAPEUTICS, INC.

**BALANCE SHEETS**

(in thousands, except share and per share data)

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2013</th>
<th>December 31, 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$ 7,942</td>
<td>$ 7,882</td>
</tr>
<tr>
<td>Restricted cash</td>
<td>—</td>
<td>134</td>
</tr>
<tr>
<td>Prepaid expenses and other current assets</td>
<td>88</td>
<td>255</td>
</tr>
<tr>
<td>Total current assets</td>
<td>8,030</td>
<td>8,271</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>759</td>
<td>1,197</td>
</tr>
<tr>
<td>Restricted cash</td>
<td>94</td>
<td>—</td>
</tr>
<tr>
<td>Other assets</td>
<td>2,354</td>
<td>35</td>
</tr>
<tr>
<td>Total assets</td>
<td>$ 11,237</td>
<td>$ 9,503</td>
</tr>
<tr>
<td><strong>Liabilities, convertible preferred stock, and stockholders’ deficit</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current liabilities:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounts payable</td>
<td>$ 1,746</td>
<td>$ 1,107</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>850</td>
<td>482</td>
</tr>
<tr>
<td>Equipment loan, current portion</td>
<td>—</td>
<td>94</td>
</tr>
<tr>
<td>Notes payable, current portion</td>
<td>1,642</td>
<td>142</td>
</tr>
<tr>
<td>Deferred revenue, current portion</td>
<td>1,115</td>
<td>—</td>
</tr>
<tr>
<td>Total current liabilities</td>
<td>5,353</td>
<td>1,825</td>
</tr>
<tr>
<td>Deferred revenue, net of current portion</td>
<td>355</td>
<td>—</td>
</tr>
<tr>
<td>Restricted stock liability</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>Notes payable, net of current portion</td>
<td>2,876</td>
<td>1,769</td>
</tr>
<tr>
<td>Warrant liability</td>
<td>297</td>
<td>147</td>
</tr>
<tr>
<td><strong>Commitments and contingencies (Note 7)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series A convertible preferred stock, $0.001 par value; 45,445,000 shares authorized at December 31, 2013 and 2012; 45,250,000 shares issued and outstanding at December 31, 2013 and 2012; (aggregate liquidation preference of $53,843 and $50,223 at December 31, 2013 and 2012, respectively)</td>
<td>45,035</td>
<td>45,035</td>
</tr>
<tr>
<td>Series B convertible preferred stock, par value $0.001 per share; 7,207,297 shares authorized at December 31, 2013, 7,203,845 shares issued and outstanding at December 31, 2013, no shares authorized, issued and outstanding at December 31, 2012; (aggregate liquidation preference of $12,680 at December 31, 2013)</td>
<td>11,643</td>
<td>—</td>
</tr>
<tr>
<td><strong>Stockholders’ deficit:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common stock, $0.001 par value; 77,688,009 and 65,795,000 shares authorized at December 31, 2013 and 2012, respectively, and 1,636,137 and 1,205,038 shares issued and outstanding at December 31, 2013 and 2012, respectively</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Additional paid-in capital</td>
<td>3,260</td>
<td>272</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>(57,594)</td>
<td>(39,569)</td>
</tr>
<tr>
<td>Total stockholders’ deficit</td>
<td>(54,332)</td>
<td>(39,296)</td>
</tr>
<tr>
<td><strong>Total liabilities, convertible preferred stock, and stockholders’ deficit</strong></td>
<td>$ 11,237</td>
<td>$ 9,503</td>
</tr>
</tbody>
</table>

*See accompanying notes.*
## ELEVEN BIOThERAPEUTICS, INC.

### STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except per share data)

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaboration revenue</td>
<td>$1,334</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>13,788</td>
<td>15,263</td>
<td>9,411</td>
</tr>
<tr>
<td>General and administrative</td>
<td>4,024</td>
<td>4,213</td>
<td>3,267</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>17,812</td>
<td>19,476</td>
<td>12,678</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(16,478)</td>
<td>(19,476)</td>
<td>(12,678)</td>
</tr>
<tr>
<td>Other income (expense):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (expense) income, net</td>
<td>(147)</td>
<td>(13)</td>
<td>3</td>
</tr>
<tr>
<td>Interest expense</td>
<td>(1,400)</td>
<td>(168)</td>
<td>(151)</td>
</tr>
<tr>
<td>Total other expense, net</td>
<td>(1,547)</td>
<td>(181)</td>
<td>(148)</td>
</tr>
<tr>
<td>Net loss and comprehensive loss</td>
<td>$(18,025)</td>
<td>$(19,657)</td>
<td>$(12,826)</td>
</tr>
<tr>
<td>Cumulative preferred stock dividends and accretion of preferred stock discount</td>
<td>(3,857)</td>
<td>(3,111)</td>
<td>(1,452)</td>
</tr>
<tr>
<td>Net loss applicable to common stockholders</td>
<td>$(21,882)</td>
<td>$(22,768)</td>
<td>$(14,278)</td>
</tr>
<tr>
<td>Net loss per share applicable to common stockholders—basic and diluted</td>
<td>$(16.18)</td>
<td>$(22.93)</td>
<td>$(17.80)</td>
</tr>
<tr>
<td>Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted</td>
<td>1,352</td>
<td>993</td>
<td>802</td>
</tr>
</tbody>
</table>

See accompanying notes.
### ELEVEN BIOTHERAPEUTICS, INC.

**STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS’ (DEFICIT) EQUITY**

(in thousands, except share data)

<table>
<thead>
<tr>
<th>Series A Convertible Preferred Stock</th>
<th>Series B Convertible Preferred Stock</th>
<th>Common Stock</th>
<th>Additional Paid-in Capital</th>
<th>Accumulated Deficit</th>
<th>Stockholders’ (Deficit) Equity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Amount</td>
</tr>
<tr>
<td>8,750,000</td>
<td>$8,644</td>
<td>—</td>
<td>—</td>
<td>724,085</td>
<td>$7</td>
</tr>
<tr>
<td>Balance at December 31, 2010</td>
<td>Exercise of stock awards and vesting of restricted stock awards</td>
<td>173,395</td>
<td>—</td>
<td>11</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of series A convertible preferred stock, net of issuance costs of $109</td>
<td>11,000,000</td>
<td>11,000</td>
<td>—</td>
<td>—</td>
<td>1,428</td>
</tr>
<tr>
<td>Issuance of common stock in exchange for services</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Balance at December 31, 2011</td>
<td>19,750,000</td>
<td>19,644</td>
<td>—</td>
<td>—</td>
<td>898,908</td>
</tr>
<tr>
<td>Exercise of stock awards and vesting of restricted stock awards</td>
<td>303,374</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of series A convertible preferred stock, net of issuance costs of $109</td>
<td>25,500,000</td>
<td>25,391</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of common stock in exchange for services</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Balance at December 31, 2012</td>
<td>45,250,000</td>
<td>45,035</td>
<td>—</td>
<td>—</td>
<td>1,205,038</td>
</tr>
<tr>
<td>Exercise of stock awards and vesting of restricted stock awards</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of series B convertible preferred stock, net of issuance costs of $163</td>
<td>—</td>
<td>—</td>
<td>5,142,859</td>
<td>7,439</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of series B convertible preferred stock upon the conversion of notes payable</td>
<td>—</td>
<td>—</td>
<td>2,060,986</td>
<td>4,204</td>
<td>—</td>
</tr>
<tr>
<td>Beneficial conversion feature of Series B preferred stock</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(163)</td>
<td>—</td>
</tr>
<tr>
<td>Accretion of Series B preferred stock discount</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>163</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of warrants for the purchase of common stock</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Exercise of warrants</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Balance at December 31, 2013</td>
<td>45,250,000</td>
<td>$45,035</td>
<td>7,203,845</td>
<td>$11,643</td>
<td>1,636,137</td>
</tr>
</tbody>
</table>

See accompanying notes.

F-5
ELEVEN BIOThERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS
(in thousands)

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2015</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operating activities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(18,025)</td>
<td>$(19,657)</td>
<td>$(12,826)</td>
</tr>
<tr>
<td>Adjustments to reconcile net loss to net cash used in operating activities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depreciation and amortization</td>
<td>438</td>
<td>448</td>
<td>364</td>
</tr>
<tr>
<td>Non-cash interest expense</td>
<td>36</td>
<td>47</td>
<td>20</td>
</tr>
<tr>
<td>Change in fair value of warrant liability</td>
<td>150</td>
<td>24</td>
<td>(12)</td>
</tr>
<tr>
<td>Change in fair value of convertible notes payable, included in interest expense</td>
<td>991</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>1,260</td>
<td>130</td>
<td>38</td>
</tr>
<tr>
<td>Common stock issued for services</td>
<td>—</td>
<td>—</td>
<td>4</td>
</tr>
<tr>
<td>Changes in operating assets and liabilities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prepaid expenses and other assets</td>
<td>167</td>
<td>39</td>
<td>(169)</td>
</tr>
<tr>
<td>Other receivables</td>
<td>—</td>
<td>—</td>
<td>839</td>
</tr>
<tr>
<td>Restricted cash</td>
<td>40</td>
<td>—</td>
<td>20</td>
</tr>
<tr>
<td>Accounts payable</td>
<td>(211)</td>
<td>50</td>
<td>632</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>190</td>
<td>(173)</td>
<td>221</td>
</tr>
<tr>
<td>Deferred revenue</td>
<td>1,470</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net cash used in operating activities</strong></td>
<td>(13,494)</td>
<td>(19,092)</td>
<td>(10,869)</td>
</tr>
<tr>
<td><strong>Investing activities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purchases of property and equipment</td>
<td>—</td>
<td>(110)</td>
<td>(805)</td>
</tr>
<tr>
<td><strong>Net cash used in investing activities</strong></td>
<td>—</td>
<td>(110)</td>
<td>(805)</td>
</tr>
<tr>
<td><strong>Financing activities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proceeds from issuance of convertible notes payable</td>
<td>3,500</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from issuance of notes payable, net of debt issuance costs</td>
<td>3,000</td>
<td>1,947</td>
<td>—</td>
</tr>
<tr>
<td>Payments on equipment financing and notes payable</td>
<td>(511)</td>
<td>(955)</td>
<td>(583)</td>
</tr>
<tr>
<td>Proceeds from issuance of series A convertible preferred stock, net of issuance costs</td>
<td>—</td>
<td>25,391</td>
<td>11,000</td>
</tr>
<tr>
<td>Proceeds from issuance of series B convertible preferred stock, net of issuance costs</td>
<td>8,837</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from issuance of common stock</td>
<td>—</td>
<td>—</td>
<td>30</td>
</tr>
<tr>
<td>Repurchase of unvested restricted stock</td>
<td>—</td>
<td>(5)</td>
<td>(2)</td>
</tr>
<tr>
<td>Proceeds from exercise of common stock options</td>
<td>31</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Deferred initial public offering costs</td>
<td>(1,303)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net cash provided by financing activities</strong></td>
<td>13,554</td>
<td>26,384</td>
<td>10,448</td>
</tr>
<tr>
<td>Net increase (decrease) in cash and cash equivalents</td>
<td>60</td>
<td>7,182</td>
<td>(1,226)</td>
</tr>
<tr>
<td>Cash and cash equivalents at beginning of period</td>
<td>7,882</td>
<td>700</td>
<td>1,926</td>
</tr>
<tr>
<td><strong>Cash and cash equivalents at end of period</strong></td>
<td>$ 7,942</td>
<td>$ 7,882</td>
<td>$ 700</td>
</tr>
<tr>
<td><strong>Supplemental non-cash financing activities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conversion of notes payable and accrued interest thereon into Series B convertible preferred stock</td>
<td>$ 4,204</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of warrants for common stock</td>
<td>$ 1,685</td>
<td>$ 97</td>
<td>—</td>
</tr>
<tr>
<td><strong>Supplemental cash flow information</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash paid for interest</td>
<td>$ 264</td>
<td>$ 136</td>
<td>$ 119</td>
</tr>
</tbody>
</table>

See accompanying notes.
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 is EBI-005, which it designed, engineered and generated using its AMP-Rx platform and is developing as a topical treatment for dry eye disease and allergic conjunctivitis. In 2013, the Company completed a Phase 1b/2a clinical trial of EBI-005 in patients with moderate to severe dry eye disease. In 2014, the Company has initiated a pivotal Phase 3 clinical program evaluating EBI-005 for the treatment of moderate to severe dry eye disease. The Company also has initiated a Phase 2 clinical trial to evaluate the use of EBI-005 in patients with allergic conjunctivitis.

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 (Note 3).

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

Liquidity

The Company has generated an accumulated deficit at December 31, 2013 of $57.6 million since inception and will require substantial additional capital to fund operations. 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 drug candidates, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology and market acceptance of the Company’s products. On February 11, 2014, the Company completed its initial public offering (“IPO”) whereby the Company sold 5,750,000 shares of its common stock for aggregate net proceeds of approximately $50.2 million (see Note 2). At December 31, 2013, the Company believes that its unrestricted cash and cash equivalents, together with the proceeds from the IPO will be sufficient to fund the Company’s current operating plan through at least the next twelve months.

2. Significant Accounting Policies

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. As of December 31, 2013, the Company had incurred $2.3 million of costs related to the IPO which have been deferred and are included in other assets on the accompanying balance sheet. 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.

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.
Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles 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 convertible notes, fair value of the Company’s common stock and convertible preferred stock, liability-classified warrants and accrued expenses. Actual results could differ from those estimates.

The Company utilizes significant estimates and assumptions in determining the fair value of its common stock. The Board of Directors determined the estimated fair value of the common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which the Company sold shares of convertible preferred stock, the superior rights and preferences of securities senior to the common stock at the time and the likelihood of achieving a liquidity event, such as an IPO or sale of the Company.

The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants (“AICPA”), Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation (the “AICPA Practice Guide”), to estimate the fair value of its common stock. The methodologies include the Option Pricing Method utilizing the Black Scholes Method (a form of the market approach defined in the AICPA Practice Guide) and the Probability-Weighted Expected Return Method based upon the probability of occurrence of certain future liquidity events such as an IPO or sale of the Company. Each valuation methodology includes estimates and assumptions that require the Company’s judgment. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Revenue Recognition

To date, the Company’s only source of revenue has been the collaboration and license agreement with ThromboGenics (Note 3).

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 its lead development candidate, EBI-005, for dry eye disease and allergic conjunctivitis. 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, 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 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, 2013, 2012 and 2011, the Company recorded stock-based compensation expense for employee and non-employee stock options and restricted stock, which was allocated as follows in the statements of operations (in thousands):

<table>
<thead>
<tr>
<th>Year Ended December 31</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and development expense</td>
<td>$1,150</td>
<td>$117</td>
<td>$37</td>
</tr>
<tr>
<td>General and administrative expense</td>
<td>110</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$1,260</strong></td>
<td><strong>$130</strong></td>
<td><strong>$38</strong></td>
</tr>
</tbody>
</table>

No related tax benefits were recognized for the years ended December 31, 2013, 2012 and 2011.

**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, 2013 and 2012, 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, 2013, 2012 and 2011, comprehensive loss was equal to net loss.

**Cash and Cash Equivalents**

The Company considers highly liquid investments with a maturity of three 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 convertible notes payable (Note 6) and preferred stock warrants (Note 10) using Level 3 inputs.

The following table summarizes the assets and liabilities measured at fair value on a recurring basis at December 31, 2013 (in thousands):

<table>
<thead>
<tr>
<th>Description</th>
<th>December 31, 2013</th>
<th>Active Markets (Level 1)</th>
<th>Observable Inputs (Level 2)</th>
<th>Unobservable Inputs (Level 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assets:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$ 7,942</td>
<td>$ 7,942</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Total</td>
<td>$ 7,942</td>
<td>$ 7,942</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Liabilities:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warrant liability</td>
<td>$ 297</td>
<td></td>
<td>$ —</td>
<td>$ 297</td>
</tr>
<tr>
<td>Total</td>
<td>$ 297</td>
<td></td>
<td>$ —</td>
<td>$ 297</td>
</tr>
</tbody>
</table>

The following table summarizes the assets and liabilities measured at fair value on a recurring basis at December 31, 2012 (in thousands):

<table>
<thead>
<tr>
<th>Description</th>
<th>December 31, 2012</th>
<th>Active Markets (Level 1)</th>
<th>Observable Inputs (Level 2)</th>
<th>Unobservable Inputs (Level 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assets:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$ 7,882</td>
<td>$ 7,882</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Total</td>
<td>$ 7,882</td>
<td>$ 7,882</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Liabilities:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warrant liability</td>
<td>$ 147</td>
<td></td>
<td>$ —</td>
<td>$ 147</td>
</tr>
<tr>
<td>Total</td>
<td>$ 147</td>
<td></td>
<td>$ —</td>
<td>$ 147</td>
</tr>
</tbody>
</table>

The carrying amounts reflected in the balance sheets for restricted cash, prepaid expenses and other current assets, other assets, accounts payable and accrued expenses approximate their fair values at December 31, 2013 and 2012, due to their short-term nature.
There have been no changes to the valuation methods during the years ended December 31, 2013 and 2012. 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, 2013 and 2012.

**Fair Value Option**

Under the Fair Value Option Subsection of ASC Topic 825-10, *Financial Instruments—Overall* (“ASC 825-10”), the Company has the irrevocable option to report most financial assets and financial liabilities at fair value on an instrument by instrument basis, with changes in fair value reported in earnings. The Company has elected the fair value option for the convertible notes payable.

**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, 2013.

**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 the completion of a liquidation event, including the completion of an IPO, at which time the warrant liability may be reclassified to stockholders’ (deficit) equity if the criteria for recording the warrant as an equity instrument are met. The warrant liability totaled $297,000 and $147,000 at December 31, 2013 and 2012, respectively (Note 10).

**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**

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, and warrants are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share, as their effect would be antidilutive 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.

<table>
<thead>
<tr>
<th></th>
<th>As of December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Convertible preferred stock</td>
<td>8,260,444</td>
</tr>
<tr>
<td>Stock options</td>
<td>1,346,238</td>
</tr>
<tr>
<td>Unvested restricted stock</td>
<td>163,353</td>
</tr>
<tr>
<td>Common stock warrants</td>
<td>333,799</td>
</tr>
<tr>
<td>Preferred stock warrants</td>
<td>30,708</td>
</tr>
<tr>
<td></td>
<td>10,134,542</td>
</tr>
</tbody>
</table>

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, sublicensable, 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 will fund 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 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 $1.3 million for the year ended December 31, 2013. 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, 2013, 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):

<table>
<thead>
<tr>
<th>Estimated Useful Life (Years)</th>
<th>December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Lab equipment</td>
<td>$ 1,740</td>
</tr>
<tr>
<td>Furniture and fixtures</td>
<td>48</td>
</tr>
<tr>
<td>Computer equipment</td>
<td>206</td>
</tr>
<tr>
<td>Software</td>
<td>25</td>
</tr>
<tr>
<td>Leasehold improvements</td>
<td>Lesser of useful life or remaining lease term</td>
</tr>
<tr>
<td></td>
<td>2,096</td>
</tr>
<tr>
<td>Less accumulated depreciation and amortization</td>
<td>(1,337)</td>
</tr>
<tr>
<td>Total property and equipment, net</td>
<td>$ 759</td>
</tr>
</tbody>
</table>

Depreciation expense, including amortization expense for assets recorded under capital leases, amounted to $438,000, $448,000 and $364,000 for the years ended December 31, 2013, 2012 and 2011, respectively. Lab equipment included assets recorded under capital leases of $329,000 at December 31, 2013 and 2012. Accumulated depreciation and amortization included amortization from assets recorded under capital leases of $215,000 and $149,000 at December 31, 2013 and 2012, respectively.
5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Development costs</td>
<td>$ 62</td>
</tr>
<tr>
<td>Deferred rent</td>
<td>—</td>
</tr>
<tr>
<td>Deferred IPO costs</td>
<td>180</td>
</tr>
<tr>
<td>Employee compensation</td>
<td>346</td>
</tr>
<tr>
<td>Professional fees</td>
<td>182</td>
</tr>
<tr>
<td>Interest</td>
<td>79</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$850</td>
</tr>
</tbody>
</table>

6. Indebtedness

**Term Loan**

In May 2010, the Company entered into the Loan and Security Agreement with Silicon Valley Bank, or SVB, pursuant to which the Company could borrow up to $1.5 million. The debt facility is secured by substantially all of the Company’s assets, excluding its intellectual property. Outstanding borrowings bear interest at a fixed per annum rate equal to 8.25%. The Company borrowed the entire $1.5 million in two 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 and Security Agreement with SVB such that the Company was able to borrow up to $5.0 million. On September 4, 2012, the Company borrowed $2.0 million under the modification to the Loan and Security 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 amended Loan and Security 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 will make consecutive equal monthly payments of principal, plus accrued interest, over the remaining term through September 2016. 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 term loan. The Loan and Security Agreement contains negative covenants restricting the Company’s activities, including limitations on dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and certain other business transactions. There are no financial covenants associated with the Loan and Security Agreement. The obligations under the Loan and Security Agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in the Company’s business, operations or financial or other condition. As of December 31, 2013, the Company made payments of $2.0 million on the loans. At December 31, 2013 and 2012, $4.6 million and $2.0 million were outstanding on the term loan, respectively. At December 31, 2013, the carrying value of the debt approximates fair value, which was determined using Level 3 inputs, including a quoted rate.

**Equipment Financing**

In August 2010, the Company entered into an installment purchase agreement with a vendor for certain laboratory equipment. The Company financed $329,000 and was required to make consecutive equal monthly payments of principal, plus accrued interest at 11.75%, over 36 months through September 2013. As of December 31, 2013, the Company had made payments of $383,000. At December 31, 2013 and 2012, $0 and $94,000, respectively, were outstanding on the equipment loan.

Scheduled monthly principal payments on outstanding debt, as of December 31, 2013, are as follows (in thousands):

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>$1,667</td>
</tr>
<tr>
<td>2015</td>
<td>1,667</td>
</tr>
<tr>
<td>2016</td>
<td>1,250</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$4,584</strong></td>
</tr>
</tbody>
</table>

Less: Unamortized debt discount

<p>| |</p>
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(66)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>
Convertible Notes Payable

In June 2013, the Company sold an aggregate principal amount of $3.5 million of June 2013 Convertible Notes and issued warrants to purchase 275,589 shares of common stock (collectively the “Bridge Financing”). In the event that the Next Equity Financing, as defined, occurred prior to repayment of amounts outstanding on the June 2013 Convertible Notes, the principal and accrued interest on the June 2013 Convertible Notes was convertible into shares of the series of preferred stock issued in the Next Equity Financing, at the price at which the shares of preferred stock are issued and sold in the Next Equity Financing and on the same terms and conditions.

Unless converted earlier, principal and accrued interest on the June 2013 Convertible Notes is due and payable (i) upon demand of investors holding June 2013 Convertible Notes having an aggregate principal amount outstanding equal to at least 70% of the aggregate principal amount of all of the June 2013 Convertible Notes then outstanding (the “Requisite Holders”) at any time on or after April 1, 2014, (ii) immediately upon default, including insolvency or bankruptcy, of the Company, or (iii) upon a Deemed Liquidation Event, as defined in the Company’s charter. The outstanding amounts on the June 2013 Convertible Notes were prepayable only with the prior written consent of the Requisite Holders, and only if all of the June 2013 Convertible Notes then outstanding are prepaid in full. Rights to payment under the June 2013 Convertible Notes are subordinated to the Company’s indebtedness to the lender under the Loan and Security Agreement.

In the event that the Next Equity Financing, as defined, occurs prior to repayment of amounts outstanding on the June 2013 Convertible Notes, the principal and accrued interest on the June 2013 Convertible Notes is convertible into shares of the series of preferred stock issued in the Next Equity Financing, at the price at which the shares of preferred stock are issued and sold in the Next Equity Financing and on the same terms and conditions.

In connection with the Bridge Financing, the Company issued warrants to the June 2013 Convertible Note holders to purchase an aggregate of 275,589 shares of common stock at $0.06 per share, subject to certain limitations and adjustments. The warrants expire upon the earliest of (i) five years from the date of the closing, (ii) a Deemed Liquidation Event of the Company, or (iii) an IPO.

The Company elected to record the June 2013 Convertible Notes at fair value in accordance with ASC 825-10, in order to measure the liability at an amount that more accurately reflects the economics of that instrument. The Company recorded the debt at fair value, and the difference between the proceeds and the fair value of the June 2013 Convertible Notes of $287,000 was allocated to the warrants issued and recorded as additional paid-in capital.

The fair value of the June 2013 Convertible Notes was determined by utilizing a probability weighted discounted cash flow analysis. This analysis determined the amount to be paid on the loan in either cash or shares at the occurrence of certain events in which the June 2013 Convertible Notes would be converted into shares of the common stock or would be repaid to the lenders in cash. The probability weighted discounted cash flow analysis utilized assumptions related to the probability of the occurrence of each of the various events and appropriate discount rates for each of the scenarios.

On December 4 and December 6, 2013, the holders of the 2013 Convertible Notes converted the principal and accrued interest into 2,060,986 shares of the Company’s series B preferred stock (See Note 8). The fair value of the June 2013 Convertible Notes was remeasured to fair value on the date of conversion of $4.2 million, which resulted in $991,000 recognized as interest expense for the year ended December 31, 2013.

The Company determined that the valuation of the June 2013 Convertible Notes is based on Level 3 inputs. The following table provides a roll forward of the fair value of the June 2013 Convertible Notes (in thousands):

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance at January 1, 2013</td>
<td>$ —</td>
</tr>
<tr>
<td>Issuance of convertible notes payable at fair value</td>
<td>3,213</td>
</tr>
<tr>
<td>Change in fair value, recorded as interest expense</td>
<td>991</td>
</tr>
<tr>
<td>Conversion to series B preferred stock</td>
<td>(4,204)</td>
</tr>
<tr>
<td>Balance at December 31, 2013</td>
<td>$ —</td>
</tr>
</tbody>
</table>
7. Commitments and Contingencies

Operating Lease

The Company leases its corporate headquarters under an operating lease that was executed in January 2010, and that was scheduled to expire on November 30, 2013. Effective November 30, 2013, the Company amended its operating lease for its facility to extend the lease term to January 31, 2016, with an option to further extend the lease term through April 30, 2018. In connection with the amendment, the letter of credit required under the lease was reduced from $134,000 to $94,000, which is included in restricted cash in the accompanying balance sheets. The Company recorded $725,000, $753,000 and $755,000 in rent expense for the years ended December 31, 2013, 2012 and 2011, respectively. Rent expense is recorded on a straight-line basis. 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, 2013 is as follows (in thousands):

<table>
<thead>
<tr>
<th>Year</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>$416</td>
</tr>
<tr>
<td>2015</td>
<td>422</td>
</tr>
<tr>
<td>2016</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>$873</td>
</tr>
</tbody>
</table>

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-1 blocker for ophthalmic indications. The Company is obligated to pay Schepens up to $4.8 million 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. As of December 31, 2013, there have been no milestones achieved or sales of products licensed.

Other License Agreements

The Company has entered into various cancellable license agreements for certain technology. In consideration for the licensed rights, the Company made up-front payments totaling $240,000. The Company is obligated to pay annual maintenance payments totaling $107,000 to certain of the licensors, which are recognized as research and development expense. The Company could be required to make clinical development, regulatory and sales-based milestones of up to $1.0 million, $1.0 million and $36.0 million, respectively, to a licensor for technology not currently used by the Company. Total license expense incurred under these license agreements amounted to $105,000, $127,000, and $205,000 for the years ended December 31, 2013, 2012 and 2011, respectively.

Legal Contingencies

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

8. Preferred Stock

In February 2011, the Company issued a total of 11,000,000 shares of series A preferred stock at a price of $1.00 per share for gross proceeds of $11.0 million. In January and April 2012, the Company sold and issued 5,000,000 and 20,500,000 shares, respectively, of series A preferred stock at $1.00 per share for gross proceeds of $5.0 million and $20.5 million, respectively.

On December 4, December 6 and December 17, 2013, the Company issued and sold an aggregate of 7,203,845 shares of its series B preferred stock and accompanying warrants to purchase shares of its common stock to four of its stockholders, at a price per share of $1.75, for an aggregate purchase price of $12.6 million, consisting of $9.0 million in cash and $3.6 million for the conversion of the June 2013 Convertible Notes, including accrued interest. The warrants were initially exercisable at a price of $0.06 per share for an aggregate of 202,472 shares of Common Stock.
The Company assessed all terms and features of the series A and series B preferred stock in order to identify any potential embedded features that would require bifurcation or any beneficial conversion features. As part of this analysis, the Company assessed the economic characteristics and risks of its preferred stock, including conversion and liquidation features, as well as dividend and voting rights. The Company determined that all features of the series A preferred stock are clearly and closely associated with an equity host, and do not require bifurcation as a derivative liability. The Company determined that the features of the series B preferred stock that are clearly and closely associated with an equity host do not require bifurcation as a derivative liability.

The Company allocated $7.6 million of the proceeds received to the series B preferred stock and $1.4 million to the warrants to purchase common stock based on the relative fair values of the instruments. The series B preferred stock fair value was determined utilizing a probability weighted expected return method. The fair value of the warrants was determined using the Black-Scholes option pricing model. The allocation resulted in an effective conversion price that was deemed beneficial to the holders based on the fair value of the common stock into which it could convert, and as such the Company recorded a beneficial conversion discount of $163,000. The Company accreted this discount on December 17, 2013, the earliest date the preferred stock could be converted, which resulted in an increase in net loss attributable to common stockholders for the year ended December 31, 2013 of $163,000, or $0.12 per common share.

The rights, preferences, and privileges of series A and series B preferred stock are listed below:

**Conversion**

Shares of series A and series B preferred stock are convertible without payment of any additional consideration into such number of fully paid and non-assessable shares of common stock determined by dividing the original issuance price by the conversion price in effect at the time. The original conversion price is the original price, or $1.00 for Series A Preferred Stock, and $1.75 for Series B Preferred Stock, subject to adjustments to reflect the issuance of common stock, options, warrants, or other rights to subscribe for or to purchase common stock for a consideration per share, less than the conversion price then in effect and subsequent stock dividends, stock splits, combinations, or recapitalizations.

Conversion is at the option of the holders of series A and series B preferred stock, although conversion is automatic upon the earlier of the consummation of an IPO resulting in gross proceeds to the Company of at least $30 million and at a price of at least $5.00 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the common stock) of common stock or the vote or written consent of 80% of outstanding shares of series A preferred stock.

**Dividends**

Holders of the series A and series B preferred stock are entitled to receive, before any cash is paid out or set aside for any common stock, dividends at the annual rate of 8% of the original purchase price per share, subject to adjustment for stock splits, dividends and similar events. The dividends are cumulative and are payable only when, and if, declared by the Board of Directors. No dividends have been declared since the Company’s inception. Aggregate cumulative series A and series B preferred dividends at December 31, 2013 were $8.6 million and $74,000, respectively.

**Liquidation Preference**

Holders of the series A and series B preferred stock have preference to the assets of the Company in the event of a liquidation or dissolution or winding-up of the Company, including a change in control, on a pari passu basis, equal to $1.00 and $1.75 per share for the Series A and Series B Preferred Stock, respectively, plus any accrued but unpaid dividends, whether or not declared, plus any dividends declared but unpaid thereon. After the payment of the preference amounts to the holders of the series A and series B preferred stock, the remaining assets of the Company are to be distributed among the holders of the series A and series B preferred stock and holders of common stock on a pro rata basis. However, if the aggregate amount which the holders of series A and series B preferred stock would be entitled to receive exceeds $3.00 per share and $5.25 per share, respectively (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the common stock), each holder of series A preferred stock would receive the greater of $3.00 or $5.25 per share of series A or series B preferred stock, respectively, or the amount such holder would have received if all shares of series A and series B preferred stock had been converted into common stock immediately prior to such liquidation.

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If the assets of the Company are insufficient to pay the full preferential amounts to the holders of the series A and series B preferred stock, the assets shall be distributed ratably among such holders in proportion to their aggregate liquidation preference amounts.

**Voting Rights**

Holders of the series A and series B preferred stock are entitled to vote as a single class with the holders of common stock and have one vote for each equivalent common share into which the series A and series B preferred stock are convertible. A vote of holders of 70% of the outstanding shares of series A and series B preferred stock is required in order to, among other things, amend the Company’s Certificate of Incorporation or Bylaws; authorize, issue or reclassify any capital stock of the Company unless the same ranks junior to the series A preferred stock with respect to liquidation, payment of dividends and redemption; increase the authorized shares of the Company’s preferred stock; and subject to specified exceptions, repurchase or redeem any capital stock of the Company. A vote of holders of 80% of the outstanding shares of series A and series B preferred stock is required in order to effect a liquidation, dissolution, sale or merger of the Company; sell or grant an exclusive license with respect to EBI-005; or authorize or issue additional shares of series A and series B preferred stock.

**9. 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 common stock are entitled to one vote for each share held.

**Dividends**

The holders of common stock are not entitled to receive dividends.

**Liquidation**

After payment to the holders of shares of preferred stock of their liquidation preferences, the holders of shares of common stock, are entitled to share ratably with the holders of preferred stock based on the number of shares of common stock into which they convert, in the Company’s assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a Deemed Liquidation Event, as defined.

**Reserved for Future Issuance**

The Company has reserved the following shares of stock:

<table>
<thead>
<tr>
<th>Shares Reseved</th>
<th>2013</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series A preferred stock</td>
<td>7,125,982</td>
<td>7,125,982</td>
</tr>
<tr>
<td>Series B preferred stock</td>
<td>1,134,462</td>
<td>1,175,163</td>
</tr>
<tr>
<td>Series A preferred stock warrants</td>
<td>30,708</td>
<td>30,708</td>
</tr>
<tr>
<td>Unvested restricted stock</td>
<td>163,353</td>
<td>363,008</td>
</tr>
<tr>
<td>Options to purchase common stock</td>
<td>1,347,824</td>
<td>1,175,163</td>
</tr>
<tr>
<td>Warrants to purchase common stock</td>
<td>333,799</td>
<td>333,799</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>10,136,128</td>
<td>8,694,861</td>
</tr>
</tbody>
</table>

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10. Preferred Stock Warrants

In May 2010, the Company issued a warrant to purchase 45,000 shares of series A preferred stock at an exercise price of $1.00 per share (the “2010 Warrant”) to a third party in connection with the Loan and Security Agreement (Note 6). The 2010 Warrant was exercisable immediately and has a ten-year life. The 2010 Warrant was initially valued at $38,000 using the Black-Scholes option-pricing model. The Company recorded a debt discount of $38,000 upon issuance of the 2010 Warrant, which is being accreted as interest expense over the remaining term of the loan. The Company recorded interest expense of $0, $19,000 and $11,000 for the years ended December 31, 2013, 2012 and 2011, respectively. The offsetting credit to the debt discount was recorded as a warrant liability and is classified as a long-term liability in the accompanying balance sheets. The fair value of the 2010 Warrant is re-measured at each reporting date using then-current assumptions. As of December 31, 2013, 2012 and 2011, the 2010 Warrant was valued using the Black-Scholes option-pricing model at $64,000, $32,000 and $26,000, respectively. The following assumptions were used in valuing the 2010 Warrant:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>1.78%</td>
<td>1.26%</td>
<td>2.45%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Expected term (in years)</td>
<td>8.41</td>
<td>7.41</td>
<td>6.41</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>70.61%</td>
<td>76.60%</td>
<td>75.82%</td>
</tr>
</tbody>
</table>

The changes in fair value of $32,000, $6,000 and $(12,000) were recorded as other income (expense) in the accompanying statement of operations and comprehensive loss for the years ended December 31, 2013, 2012 and 2011, respectively. No portion of the 2010 Warrant has been exercised as of December 31, 2013.

On September 4, 2012, the Company issued a warrant to purchase 150,000 shares of series A preferred stock at an exercise price of $1.00 per share (the “2012 Warrant”) in connection with the modification to the Loan and Security Agreement (Note 6). The 2012 Warrant was exercisable immediately and has a ten-year life. The 2012 Warrant was initially valued at $97,000 using the Black-Scholes option-pricing model. The Company recorded a debt discount of $97,000 upon issuance of the 2012 Warrant, which is being accreted as interest expense over the remaining term of the loan. The Company recorded interest expense of $24,000 and $8,000 for the years ended December 31, 2013 and 2012, respectively. The offsetting credit to the debt discount was recorded as a warrant liability and is classified as a long-term liability in the accompanying balance sheets. The fair value of the 2012 Warrant is re-measured at each reporting date using then-current assumptions. As of December 31, 2013 and 2012, the 2012 Warrant was valued using the Black-Scholes option-pricing model at $233,000 and $115,000, respectively. The following assumptions were used in valuing the 2012 Warrant:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>1.67%</td>
<td>1.74%</td>
<td>2.79%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Expected term (in years)</td>
<td>10</td>
<td>9.35</td>
<td>8.68</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>76.92%</td>
<td>74.00%</td>
<td>77.90%</td>
</tr>
</tbody>
</table>

The change in fair value of $118,000 and $18,000 was recorded as other income (expense) in the accompanying statement of operations for the years ended December 31, 2013 and 2012, respectively. No portion of the 2012 Warrant had been exercised as of December 31, 2013.

The following table provides a rollforward of the fair value of the warrants determined by Level 3 inputs (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>Fair Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance at December 31, 2012</td>
<td>$ 147</td>
</tr>
<tr>
<td>Change in fair value</td>
<td>150</td>
</tr>
<tr>
<td>Balance at December 31, 2013</td>
<td>$ 297</td>
</tr>
</tbody>
</table>

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11. 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. The 2009 Plan provides for the grant of incentive and non-qualified stock options and restricted stock grants as determined by the Board of Directors. As of December 31, 2013, the Company had reserved 1,347,824 shares of common stock under the 2009 Plan, of which 1,586 shares remained available for future issuance under the 2009 Plan. Under the 2009 Plan, stock options may 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, may 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 equalled the estimated fair value of the common stock as determined by the Board of Directors on the date of grant.

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

<table>
<thead>
<tr>
<th>Shares</th>
<th>Weighted-Average Exercise Price</th>
<th>Remaining Contractual Life (in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outstanding at December 31, 2012</td>
<td>826,906</td>
<td>$0.19</td>
</tr>
<tr>
<td>Granted</td>
<td>882,835</td>
<td>5.08</td>
</tr>
<tr>
<td>Exercised</td>
<td>(87,182)</td>
<td>0.25</td>
</tr>
<tr>
<td>Cancelled or forfeited</td>
<td>(276,321)</td>
<td>0.16</td>
</tr>
<tr>
<td>Outstanding at December 31, 2013</td>
<td>1,346,238</td>
<td>$3.39</td>
</tr>
<tr>
<td>Exercisable at December 31, 2013</td>
<td>336,327</td>
<td>$0.43</td>
</tr>
<tr>
<td>Vested and expected to vest at December 31, 2013(1)</td>
<td>1,123,403</td>
<td>$3.93</td>
</tr>
</tbody>
</table>

(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 for the year ended December 31, 2013 was $7.3 million. The total intrinsic value of options exercised for the year ended December 31, 2013, 2012 and 2011 was $170,000, $29,000 and $0, respectively. The total fair value of employee options vested for the year ended December 31, 2013, 2012 and 2011 was $40,000, $9,000 and $3,000, 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’ (deficit) equity as the restricted stock vests. A summary of the status of unvested restricted stock as of December 31, 2013 and 2012, and changes during the years ended December 31, 2013 and 2012 are presented below:

| Unvested at December 31, 2012 | 363,008 | $0.06 |
| Vested | (199,655) | 0.06 |
| Unvested at December 31, 2013 | 163,353 | $0.06 |
The Company granted 2,755 shares of restricted stock to non-employees during the year ended December 31, 2012 at a purchase price of $0.06 per share. 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 no shares of non-employee unvested restricted stock outstanding at December 31, 2013. The expense related to the restricted stock granted to non-employees for the years ended December 31, 2013, 2012 and 2011 was $481,000, $71,000 and $11,000, respectively.

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. During the year ended December 31, 2013, management determined that a performance-based milestone was achieved and recorded stock-based compensation expense of $106,000. There was no expense recorded for milestone based vesting awards during the years ended December 31, 2012 or 2011. The remaining milestones were not deemed to be probable of achievement as of December 31, 2013. As of December 31, 2013, unrecognized compensation expense related to performance based awards was $2.3 million.

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

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>1.09-2.07%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>—</td>
</tr>
<tr>
<td>Expected term (in years)</td>
<td>6</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>72.13-77.80%</td>
</tr>
</tbody>
</table>

Volatility
Since the Company was privately held as of the date of these financial statements, 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 units 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 2013, 2012 and 2011 were $4.07, $0.45 and $0.06, respectively. The expense related to the options granted to employees for the years ended December 31, 2013, 2012 and 2011 were $187,000, $14,000 and $3,000, respectively.

The Company granted 231,968, 31,496 and 32,283 stock options to non-employees during the years ended December 31, 2013, 2012 and 2011, respectively, with weighted-average exercise prices of $1.77, $0.76 and $0.06 per share, respectively. 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:

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>1.82-2.99%</td>
<td>1.60-2.19%</td>
<td>2.25-2.81%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Expected option life (years)</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Expected stock price volatility</td>
<td>76.28-78.14%</td>
<td>75.51-78.29%</td>
<td>70.62%</td>
</tr>
</tbody>
</table>

The total number of non-employee stock options outstanding at December 31, 2013 was 4495,748. 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, 2013, 2012 and 2011 were $486,000, $45,000 and $24,000, respectively.

At December 31, 2013, there was $3.4 million of total unrecognized compensation cost related to non-vested stock options and unvested restricted stock with service-based vesting provisions, which is expected to be recognized over a weighted-average period of 2.77 years.

12. 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:

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income tax benefit computed at federal statutory tax rate</td>
<td>34.00%</td>
<td>34.00%</td>
<td>34.00%</td>
</tr>
<tr>
<td>State taxes, net of federal benefit</td>
<td>4.67</td>
<td>5.19</td>
<td>5.17</td>
</tr>
<tr>
<td>Change in valuation allowance</td>
<td>(39.43)</td>
<td>(39.88)</td>
<td>(42.64)</td>
</tr>
<tr>
<td>General business credits and other credits</td>
<td>4.28</td>
<td>0.86</td>
<td>3.55</td>
</tr>
<tr>
<td>Permanent differences</td>
<td>(3.52)</td>
<td>(0.17)</td>
<td>(0.08)</td>
</tr>
<tr>
<td>Total</td>
<td>— %</td>
<td>— %</td>
<td>— %</td>
</tr>
</tbody>
</table>

The Company has incurred net operating losses, or NOLs, from inception. At December 31, 2013, the Company has federal and state NOL carryforwards of $53.8 million and $53.0 million, respectively, available to reduce future taxable income, that expire beginning in 2014 through 2033. The Company also had federal and state research and development tax credit carryforwards of $1.0 million and $744,000, respectively, available to reduce future tax liabilities that expire beginning in 2025 through 2033. The Company does not have any NOL carryforwards associated with deductible stock option exercises as of December 31, 2013 and 2012.

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):

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2013</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deferred tax assets:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net operating loss carryforwards</td>
<td>$21,085</td>
<td>$14,877</td>
</tr>
<tr>
<td>Research and development credit carryforwards</td>
<td>1,511</td>
<td>739</td>
</tr>
<tr>
<td>Accruals and other</td>
<td>333</td>
<td>209</td>
</tr>
<tr>
<td>Capitalized license and organization costs</td>
<td>79</td>
<td>87</td>
</tr>
<tr>
<td>Capitalized start-up costs</td>
<td>340</td>
<td>369</td>
</tr>
<tr>
<td><strong>Total gross deferred tax asset</strong></td>
<td><strong>23,348</strong></td>
<td><strong>16,281</strong></td>
</tr>
<tr>
<td><strong>Deferred tax liability</strong></td>
<td>(77)</td>
<td>(118)</td>
</tr>
<tr>
<td><strong>Valuation allowance</strong></td>
<td>(23,271)</td>
<td>(16,163)</td>
</tr>
<tr>
<td><strong>Net deferred tax asset</strong></td>
<td>$—</td>
<td>$—</td>
</tr>
</tbody>
</table>

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 $23.3 million and $16.2 million has been established at December 31, 2013 and 2012, respectively. The change in the valuation allowance was $7.1 million for the year ended December 31, 2013. At December 31, 2013 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, 2013 and 2012, the Company had no unrecognized tax benefits. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

13. 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 (Note 7).

14. 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 did not provide any contributions to this plan during the years ended December 31, 2013, 2012 and 2011.

15. Restructuring
In April 2013, the Company implemented a strategic restructuring designed to conserve resources and improve its financial position. As part of this strategic restructuring, the Company reduced spending on early stage research programs and implemented a reduction in force of approximately 15 positions, or 50% of its workforce, primarily in the research area. The restructuring charges recorded during the year ended December 31, 2013 and the related liability balance as of December 31, 2013 for the strategic restructuring are as follows (in thousands):

<table>
<thead>
<tr>
<th>Restructuring Liability at December 31, 2013</th>
<th>Restructuring Expense</th>
<th>Cash Payments</th>
<th>Non-cash Expense</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employee severance, benefits, and related costs</td>
<td>$ 279</td>
<td>$(241)</td>
<td>$(38)</td>
</tr>
</tbody>
</table>
In connection with the termination of the aforementioned employees during the year ended December 31, 2013, the Company accelerated the vesting of certain stock options. The Company revalued the stock options as of the date of termination using the Black-Scholes option-pricing model. The expense related to the accelerated stock options for the year ended December 31, 2013, included within the table above, was $38,000. For the year ended December 31, 2013, $279,000 of restructuring expense was recorded, of which $17,000 was included within general and administrative expenses and $262,000 was included within research and development expenses in the accompanying statement of operations and comprehensive loss.

16. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for 2013 and 2012. 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.

<table>
<thead>
<tr>
<th></th>
<th>First Quarter</th>
<th>Second Quarter</th>
<th>Third Quarter</th>
<th>Fourth Quarter</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaboration revenue</td>
<td>$ —</td>
<td>$ 202</td>
<td>$ 622</td>
<td>$ 510</td>
<td>$ 1,334</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>5,435</td>
<td>3,585</td>
<td>4,162</td>
<td>4,630</td>
<td>17,812</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(5,435)</td>
<td>(3,383)</td>
<td>(3,540)</td>
<td>(4,120)</td>
<td>(16,478)</td>
</tr>
<tr>
<td>Net loss</td>
<td>(5,512)</td>
<td>(3,634)</td>
<td>(3,813)</td>
<td>(5,066)</td>
<td>(18,025)</td>
</tr>
<tr>
<td>Net loss applicable to common stockholders</td>
<td>(6,405)</td>
<td>(4,551)</td>
<td>(4,718)</td>
<td>(6,208)</td>
<td>(21,882)</td>
</tr>
<tr>
<td>Net loss per share applicable to common stockholders—basic and diluted</td>
<td>$(5.14)</td>
<td>(3.44)</td>
<td>$(3.39)</td>
<td>$(4.29)</td>
<td>$(16.18)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>First Quarter</th>
<th>Second Quarter</th>
<th>Third Quarter</th>
<th>Fourth Quarter</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaboration revenue</td>
<td>$ —</td>
<td>$ —</td>
<td>$ —</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>5,598</td>
<td>4,088</td>
<td>4,762</td>
<td>5,028</td>
<td>19,476</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(5,598)</td>
<td>(4,088)</td>
<td>(4,762)</td>
<td>(5,028)</td>
<td>(19,476)</td>
</tr>
<tr>
<td>Net loss</td>
<td>(5,629)</td>
<td>(4,111)</td>
<td>(4,823)</td>
<td>(5,094)</td>
<td>(19,657)</td>
</tr>
<tr>
<td>Net loss applicable to common stockholders</td>
<td>(6,112)</td>
<td>(4,917)</td>
<td>(5,735)</td>
<td>(6,004)</td>
<td>(22,768)</td>
</tr>
<tr>
<td>Net loss per share applicable to common stockholders—basic and diluted</td>
<td>$(6.72)</td>
<td>(5.24)</td>
<td>$(5.90)</td>
<td>$(5.22)</td>
<td>$(22.93)</td>
</tr>
</tbody>
</table>
17. Subsequent Events

In connection with the Company’s initial public offering:

(i) The Company’s board of directors adopted and the Company’s stockholders approved the 2014 stock incentive plan (“2014 Plan”), which became effective immediately prior to the closing of the Company’s initial public offering. 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 Company’s employees, officers, directors, consultants and advisors are eligible to receive awards under the 2014 Plan.

(ii) The Company’s board of directors adopted and the Company’s stockholders approved the 2014 employee stock purchase plan (“2014 ESPP”), which will become effective on a date determined by the Company’s board of directors. Once effective, the 2014 ESPP will enable eligible employees to purchase shares of the Company’s Common Stock at a discount following the date of the offering.
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 31, 2014
Rule 13a-14(a) CERTIFICATION

I, Gregory D. Perry, 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/ Gregory D. Perry
Gregory D. Perry
Chief Financial and Business Officer
(Principal Financial Officer)

Dated: March 31, 2014
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, 2013 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 31, 2014

/s/  Gregory D. Perry
Gregory D. Perry
Chief Financial and Business Officer
(Principal Financial Officer)

Dated: March 31, 2014