

2,285,714 Shares



**COMMON STOCK**

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Ophthotech Corporation is offering 1,900,000 shares of common stock and the selling stockholders identified in this prospectus are offering 385,714 shares of our common stock. We will not receive any proceeds from the sale of any shares by the selling stockholders.

Our common stock is listed on The NASDAQ Global Select Market under the symbol "OPHT". The last reported sale price of our common stock on The NASDAQ Global Select Market on February 11, 2014 was \$32.65 per share.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

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**Investing in our common stock involves risks. See "Risk Factors" beginning on page 13.**

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**PRICE \$31.50 A SHARE**

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	<u>Price to Public</u>	<u>Underwriting Discounts and Commissions(1)</u>	<u>Proceeds to Ophthotech</u>	<u>Proceeds to Selling Stockholders</u>
Per Share	\$31.50	\$1.89	\$29.61	\$29.61
Total	\$71,999,991	\$4,319,999	\$56,259,000	\$11,420,992

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(1) The underwriters will receive compensation in addition to underwriting discounts and commissions. See "Underwriters."

The selling stockholders have granted the underwriters an option to purchase up to 342,857 additional shares of our common stock. The underwriters can exercise this option at any time within 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on February 18, 2014.

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**Morgan Stanley**

**J.P. Morgan**

**Leerink Partners**

**Stifel**

## TABLE OF CONTENTS

	<u>Page</u>
<a href="#">Prospectus Summary</a>	<a href="#">1</a>
<a href="#">Risk Factors</a>	<a href="#">13</a>
<a href="#">Special Note Regarding Forward-Looking Statements</a>	<a href="#">56</a>
<a href="#">Use of Proceeds</a>	<a href="#">58</a>
<a href="#">Price Range of Common Stock</a>	<a href="#">59</a>
<a href="#">Dividend Policy</a>	<a href="#">60</a>
<a href="#">Capitalization</a>	<a href="#">61</a>
<a href="#">Dilution</a>	<a href="#">62</a>
<a href="#">Selected Financial Data</a>	<a href="#">63</a>
<a href="#">Management's Discussion and Analysis of Financial Condition and Results of Operations</a>	<a href="#">65</a>
<a href="#">Business</a>	<a href="#">84</a>
<a href="#">Management</a>	<a href="#">143</a>
<a href="#">Executive Compensation</a>	<a href="#">148</a>
<a href="#">Transactions with Related Persons</a>	<a href="#">162</a>
<a href="#">Principal and Selling Stockholders</a>	<a href="#">168</a>
<a href="#">Description of Capital Stock</a>	<a href="#">172</a>
<a href="#">Shares Eligible for Future Sale</a>	<a href="#">176</a>
<a href="#">Material U.S. Federal Tax Considerations for Non-U.S. Holders of Common Stock</a>	<a href="#">179</a>
<a href="#">Underwriters</a>	<a href="#">183</a>
<a href="#">Legal Matters</a>	<a href="#">189</a>
<a href="#">Experts</a>	<a href="#">189</a>
<a href="#">Where You Can Find More Information</a>	<a href="#">189</a>
<a href="#">Index to Financial Statements</a>	<a href="#">F-1</a>

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Neither we, the selling stockholders nor the underwriters have authorized anyone to provide you with information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We, the selling stockholders and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give to you. We and the selling stockholders are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our common stock or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

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## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the "Risk Factors" section and our financial statements and the related notes appearing at the end of this prospectus, before making an investment decision.*

### **Our Company Overview**

Ophthotech is a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the back of the eye, with a focus on developing therapeutics for age-related macular degeneration, or AMD. AMD is a disorder of the central portion of the retina, known as the macula, which is responsible for central vision and color perception. There are two forms of AMD, wet AMD and dry AMD. Our most advanced product candidate is Fovista, which is in Phase 3 clinical development for use in combination with anti-VEGF drugs that represent the current standard of care for the treatment of wet AMD. If our Phase 3 clinical development program progresses as planned and the results are favorable, we plan to submit applications for marketing approval for Fovista in 2016. Wet AMD is the leading cause of blindness in people over the age of 55 in the United States and the European Union. We are also developing our product candidate Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD, and expect to initiate a Phase 2/3 clinical trial of Zimura for this indication in late 2014 or early 2015. There are currently no therapies approved by regulatory authorities for geographic atrophy, which, according to a study published in the peer reviewed journal *Ophthalmology*, affects approximately 8 million people worldwide.

### ***Development of Fovista for the Treatment of Wet AMD***

We are developing our product candidate Fovista to be administered in combination with anti-VEGF drugs for the treatment of wet AMD. In 2012, we completed a large Phase 2b clinical trial in newly diagnosed wet AMD patients in which 1.5 mg of Fovista administered in combination with one of the standard of care drugs, Lucentis, demonstrated statistically significant superiority compared to Lucentis monotherapy based on the primary endpoint of mean change in visual acuity from baseline at 24 weeks. Patients receiving the combination of 1.5 mg of Fovista and Lucentis gained a mean of 10.6 letters from baseline on a standardized chart of vision testing compared to a mean gain of 6.5 letters from baseline for patients receiving Lucentis monotherapy, representing a 62% comparative benefit from baseline. Based on retrospective analyses of commonly evaluated parameters used in wet AMD trials, Fovista combination therapy resulted in improved visual outcome, with more patients experiencing vision gain and fewer patients experiencing vision loss, in a broad range of patient groups in this trial compared to Lucentis monotherapy. Fovista was generally well tolerated in this clinical trial.

We have initiated a pivotal Phase 3 clinical program to evaluate the safety and efficacy of Fovista combination therapy for the treatment of newly diagnosed wet AMD patients compared to current standard of care anti-VEGF monotherapy. Our Phase 3 clinical program consists of three separate Phase 3 clinical trials, two of which will evaluate Fovista in combination with Lucentis and the other of which will evaluate Fovista in combination with each of Avastin or Eylea, the other two standard of care drugs. All three of these Phase 3 clinical trials will incorporate significant aspects from the design of our completed Phase 2b clinical trial. We plan to enroll a total of 1,866 patients at more than 225 centers internationally across the three trials. We have initiated enrollment in the two trials evaluating Fovista administered in combination with Lucentis. We expect to activate initial trial sites in the third trial in this Phase 3 clinical program in the United States by the end of the first quarter of 2014. We expect to have initial, top-line data from this Phase 3 clinical program available in 2016. If the results of this Phase 3 clinical program are favorable, we plan to submit applications for marketing approval for Fovista in both the United States and the European Union before the end of 2016.

Wet AMD is characterized by abnormal new blood vessel formation, referred to as neovascularization, which results in blood vessel leakage and retinal distortion. If untreated, neovascularization in wet AMD patients typically results in formation of a scar, or fibrosis, under the macular region of the retina, which is referred to as subretinal fibrosis. A study on the burden of AMD published in 2006 in the peer reviewed journal *Current Opinion in Ophthalmology* estimated that 1,250,000 people in the United States suffer from wet AMD. In addition, AMD Alliance International reports that approximately 200,000 new cases of wet AMD arise each year in the United States. The percentage of individuals with wet AMD increases substantially with age, and we expect that the number of cases of wet AMD will increase with growth of the elderly population in the United States.

The current standard of care for wet AMD is monotherapy administration of drugs that target vascular endothelial growth factor, or VEGF, one of several proteins involved in neovascularization. The anti-VEGF market for the treatment of wet AMD consists predominantly of two drugs that are approved for marketing and primarily prescribed for the treatment of wet AMD, Lucentis and Eylea, and off-label use of the cancer therapy Avastin. In 2012, annual worldwide sales of Lucentis and Eylea for all indications totaled approximately \$4.8 billion. Avastin was used off-label to treat approximately 60% of Medicare beneficiaries in 2008 who receive anti-VEGF therapy for wet AMD. Retinal specialists in the largest markets in the European Union use off-label Avastin to treat approximately 27% of patients with wet AMD.

The use of anti-VEGF therapy has significantly improved visual outcomes for wet AMD patients compared to untreated patients newly diagnosed with wet AMD. However, we believe that persistence or growth of neovascularization and the development of fibrosis under the retina are involved in limiting the visual benefit from anti-VEGF monotherapy, and a significant unmet medical need remains. For example, based on results of third-party clinical trials, after one year of treatment with an anti-VEGF drug, approximately 18% to 22% of newly diagnosed wet AMD patients lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, and approximately 62% to 75% of newly diagnosed wet AMD patients did not achieve an ability to read an additional 15 or more letters on the standardized chart of vision testing. In addition, in 2013, the peer reviewed journal *Ophthalmology* published the results of an uncontrolled study of patients who had received two years of treatment with Lucentis in clinical trials and then received additional treatment with Lucentis at a physician's discretion for two more years. When assessed at their last evaluation in this study, approximately 46% of such patients had lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing. Moreover, in 2013, *Ophthalmology* published the results of a separate follow-up study of a cohort of these same patients. When assessed approximately three years after completing their participation in the prior study, approximately one-third had poor outcomes, defined as the loss of the ability to read 15 or more letters on a standardized chart of vision testing, according to the study conclusions. In addition, approximately 57% of such patients had lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, compared to baseline prior to receiving therapy in the original clinical trials, and approximately 37% had visual acuity at the level of legal blindness, defined as visual acuity of 20/200 or worse. The study authors noted that wet AMD patients remain at risk for substantial visual decline.

Based on our initial assessment of retinal images of patients who experienced loss of vision following treatment with either 1.5 mg of Fovista in combination with 0.5 mg of Lucentis or Lucentis monotherapy in our completed Phase 2b clinical trial, results from preclinical studies and our review of recent scientific literature, we believe that wet AMD patients who receive anti-VEGF monotherapy may remain at increased risk for the development of subretinal fibrosis. We believe that the development of subretinal fibrosis in these patients may, in part, be responsible for the deterioration of vision that many wet AMD patients experience over time, notwithstanding treatment with an anti-VEGF drug.

In a study published in 2013 in *American Journal of Ophthalmology*, 40% of wet AMD patients exhibited subretinal fibrosis and retinal scarring after two years of treatment with Lucentis. According to a retrospective analysis of the Comparisons of AMD Treatment Trials published in 2013 in the peer reviewed *Journal of Ophthalmology*, 32% of newly diagnosed wet AMD patients developed retinal scarring after one year of treatment with either Lucentis or Avastin, while 45% of newly diagnosed wet AMD patients developed retinal scarring after two years of treatment with either Lucentis or Avastin.

We believe that Fovista's mechanism of action, when administered in combination with an anti-VEGF drug, may result in two relevant biological responses: neovascular regression and inhibition of subretinal fibrosis. Fovista binds to and inhibits a protein known as platelet derived growth factor, or PDGF, causing the stripping of pericytes, which are cells that cover the outside of newly formed blood vessels. After the pericytes are stripped from the new blood vessels, endothelial cells lining the inside of the newly formed blood vessels are left unprotected and are highly vulnerable to the effects of anti-VEGF therapy. Fovista also inhibits migration of other retinal cells attracted by PDGF, such as retinal pigment epithelium, or RPE, cells and glial cells, which play a role in the formation of subretinal fibrosis. We further believe that the administration of Fovista in combination with anti-VEGF drugs in patients with wet AMD may cause regression of neovascularization and may inhibit subretinal fibrosis more effectively than anti-VEGF monotherapy. We believe that Fovista may provide meaningful added benefit in the treatment of wet AMD regardless of which anti-VEGF drug is administered in combination with Fovista.

#### ***Development of Zimura with Initial Focus on Dry AMD***

We are developing our product candidate Zimura, which we previously referred to as ARC1905, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. Zimura is an inhibitor of complement factor C5, which we refer to as C5, a protein that is associated with complement mediated inflammation and cell damage, which we believe may be involved in the development of dry AMD.

Dry AMD is a significant cause of moderate and severe loss of central vision, affecting vision in both eyes in most patients. Dry AMD results in progressive and chronic degeneration of the macula characterized by variable thinning and dysfunction of retinal tissue. Dry AMD is typically associated with yellow-white dots or deposits under the retina, known as drusen. Unlike in wet AMD, there is a complete absence of pathological neovascularization in dry AMD.

Deterioration of vision in dry AMD is usually gradual over a period of months and years and is considered irreversible. Significant vision loss results if dry AMD evolves into a more severe form of the disease known as geographic atrophy. Geographic atrophy appears as severe, abrupt and deep levels of macular tissue loss. In addition, dry AMD can also progress to wet AMD. Although dry AMD is the most common form of AMD, there are no therapies approved by the U.S. Food and Drug Administration, or FDA, or European Medicines Agency, or EMA, to treat this condition. According to a 2011 publication from AMD Alliance International, approximately 30 million people worldwide have some form of AMD, with dry AMD accounting for 85% to 90% of these cases. A study published in *Ophthalmology* in 2012 analyzing age and gender variations in AMD prevalence estimates that approximately 8 million dry AMD patients worldwide are affected by geographic atrophy.

Multiple published studies have implicated local inflammation in the pathogenesis of dry AMD. Specifically, these studies suggest that the complement pathway which consists of a series of proteins involved in the defense against infection and modulates a variety of immune and inflammatory responses, has a central role in dry AMD. The complement system is generally tightly regulated and requires the proper balance of activation and inhibition of proteins to function properly. Poorly regulated or aberrant activation of proteins in the complement pathway without a balanced or proportional inhibition of other proteins may result in the production of immune mediated inflammation, or inflammation that is triggered by activation of the immune response, and damage to

normal tissue. We believe that excessive activation of C5, which is one of the complement proteins, and the resulting formation of downstream complement molecule results in tissue damage that plays an important role in the development of both dry AMD and certain forms of wet AMD. Our product candidate Zimura is designed to inhibit C5 activation.

We have completed a small, multicenter, uncontrolled, open label Phase 1/2a clinical trial evaluating the safety and tolerability of Zimura administered as a monotherapy to patients with geographic atrophy. We did not observe any evidence of drug related adverse events in this clinical trial. We observed a trend in this clinical trial, in favor of the higher of two dose groups, of a relative reduction in the mean growth of the geographic atrophy lesion area, as measured by an independent reading center, at 24 weeks. When the injections were administered in a reduced dosing schedule during the subsequent 24 weeks, this relative trend in reduced growth in geographic atrophy lesion area was no longer present. We believe this apparent trend in reduction of growth in geographic atrophy lesion area when Zimura was dosed more frequently, together with the relative loss of the benefit when Zimura was dosed less frequently, may suggest a possible drug effect. In addition, recently released clinical data from a third party targeting the complement pathway also exhibited a trend in reduction of geographic atrophy growth with a pronounced effect in patients with specific biomarkers.

Based on the results of our Phase 1/2a clinical trial and the recent results from the third-party clinical trial, we plan to initiate a Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with geographic atrophy in late 2014 or early 2015. We also plan to evaluate Zimura and Fovista to be administered in combination with anti-VEGF drugs for the treatment of a subpopulation of wet AMD patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy fails, who we refer to as anti-VEGF resistant, and who are believed to have complement mediated inflammation. We plan to initiate a Phase 2 clinical trial of Zimura and Fovista administered in combination with an anti-VEGF drug in this second indication in 2015.

### **Our Strategy**

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing novel therapeutics to treat diseases of the back of the eye, with a particular focus on AMD. The key elements of our strategy to achieve this goal are:

- *Complete Phase 3 clinical program evaluating Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD and, if successful, seek marketing approval for Fovista in this indication.* We have initiated a pivotal Phase 3 clinical program evaluating Fovista administered in combination with anti-VEGF drugs for the treatment of newly diagnosed wet AMD patients. Based on our estimates regarding patient enrollment, we expect to have initial, top-line data from this Phase 3 clinical program available in 2016. Our Phase 3 clinical trials will continue after such submissions in accordance with the protocols for these trials.
- *Further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions.* We are planning to initiate a Phase 2 clinical trial to assess whether the use of Fovista in combination with anti-VEGF drugs can reduce the number and frequency of intravitreal injections required to effectively treat wet AMD. In addition, we are planning to initiate a Phase 2 clinical trial of Fovista in combination with anti-VEGF drugs for the treatment of anti-VEGF resistant wet AMD patients. We plan to initiate these two clinical trials in 2014 and expect to receive initial results from these two clinical trials in 2015. We are also planning to initiate a Phase 2 clinical trial to assess whether the use of Fovista in combination with anti-VEGF drugs can inhibit the development of subretinal fibrosis in wet AMD patients. We plan to initiate this clinical trial in 2014 and expect to receive initial results from this clinical trial in late 2015 or early 2016. We are also evaluating other ophthalmic conditions for which we believe Fovista treatment may be beneficial. We are

planning to supply Fovista for a clinical trial to be conducted by the National Eye Institute, part of the U.S. National Institutes of Health, to evaluate Fovista's potential to inhibit the visual loss resulting from retinal complications associated with von Hippel-Lindau disease, an inherited disease characterized by multiple benign and malignant tumors and cysts in the eye and other organs. We expect this clinical trial will commence in late 2014. We are also planning to initiate, potentially in 2015, a clinical trial to assess the potential therapeutic benefit of Fovista, and in particular its potential to inhibit the development of retinal scarring, in proliferative vitreoretinopathy, a complication associated with retinal detachment.

- *Advance the development of Zimura for the treatment of AMD.* We are developing our product candidate Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. We plan to initiate a Phase 2/3 clinical trial in patients with geographic atrophy in late 2014 or early 2015 and expect to receive interim results from this clinical trial in 2016. We also plan to initiate in 2015 a Phase 2 clinical trial evaluating the safety and efficacy of Zimura and Fovista administered in combination with an anti-VEGF drug in anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation.
- *Maximize commercial potential of Fovista and Zimura.* We have retained worldwide commercialization rights to Fovista and Zimura. If either of Fovista or Zimura receives marketing approval, we plan to commercialize such product candidate in the United States with our own 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 Fovista and Zimura in markets outside the United States.
- *Opportunistically in-license or acquire products, product candidates and technologies.* We believe that our focus on diseases of the back of the eye and our experienced management team will make us an attractive collaborator or acquirer for companies seeking to out-license or sell rights to complementary products, product candidates or technologies in our area of focus. We generally expect that we will not engage in early stage research and drug discovery and will thus avoid the related costs and risks of these activities.

#### **Potential for Fovista in Wet AMD**

We intend to seek a broad label for Fovista for the treatment of patients with wet AMD in combination with anti-VEGF drugs. We believe that Fovista may provide meaningful added benefit in the treatment of wet AMD regardless of which anti-VEGF drug is administered in combination with Fovista. We also believe that Fovista may have the potential to inhibit the development of subretinal fibrosis, thereby improving longer-term visual outcomes for wet AMD patients.

- *Visual Acuity Benefit.* In our Phase 2b clinical trial, we observed a visual benefit in patients treated with the combination of 1.5 mg of Fovista and Lucentis that was evident early in and sustained over the course of treatment. The relative magnitude of visual benefit increased over the study period. We believe that these results suggest that Fovista may provide benefit to patients when used in combination with Lucentis. We also believe that these results may be supported by Fovista's proposed mechanism of action, which we believe, when administered in combination with an anti-VEGF drug, may result in two relevant responses: neovascular regression and inhibition of subretinal fibrosis.
- *Phase 3 Clinical Trials Build Upon and Incorporate Phase 2b Clinical Trial Design.* Two of the three Phase 3 clinical trials included in our Phase 3 clinical program are evaluating the safety and efficacy of Fovista administered in combination with Lucentis. We believe that the following

aspects of our two Phase 3 clinical trials of Fovista administered in combination with Lucentis may reduce the risk that we will have unexpected outcomes in these two clinical trials:

- We have made no meaningful changes to the inclusion and exclusion criteria in these Phase 3 clinical trials from those we used in our Phase 2b clinical trial.
- We have not changed the primary endpoint, mean change in visual acuity from baseline, that we used in our Phase 2b clinical trial. However, we will assess mean change in visual acuity from baseline in these Phase 3 clinical trials at 12 months, instead of at 24 weeks as in our Phase 2b clinical trial.
- We are further improving our ability to detect any statistically significant differences in outcomes between the treatment and control arms of our Phase 3 clinical trials by substantially increasing both the number of patients who will receive 1.5 mg of Fovista administered in combination with Lucentis and the number of patients who will receive Lucentis monotherapy as compared to our Phase 2b clinical trial.
- We are using a dose of Fovista that exhibited a favorable safety profile in our Phase 2b clinical trial.

To support our efforts to seek a broad label for Fovista, we plan to include a third Phase 3 clinical trial to evaluate the safety and efficacy of Fovista administered in combination with each of Avastin or Eylea compared to Avastin or Eylea monotherapy.

- *Potential to Enhance Efficacy of Current Standard of Care.* Based on results of third-party clinical trials, after one year of treatment with an anti-VEGF drug, approximately 18% to 22% of newly diagnosed wet AMD patients lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, and approximately 62% to 75% of such patients did not achieve an ability to read an additional 1 or more letters on the standardized chart of vision testing. Data from two large, recently published third-party clinical studies show that 40% to 45% of wet AMD patients develop subretinal fibrosis after two years of treatment with an anti-VEGF drug. We believe that Fovista may enhance the regression of neovascularization and may also inhibit the development of subretinal fibrosis in the eye when administered in combination with an anti-VEGF drug, and therefore may potentially provide meaningful added benefit in the treatment of wet AMD as compared to anti-VEGF monotherapy.

#### **Risks Associated with Our Business**

Our business is subject to a number of risks of which you should be aware of before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus immediately following this prospectus summary. These risks include the following:

- Our Phase 3 clinical program for Fovista may not be successful. The results of our Phase 2b clinical trial of Fovista may not be predictive of the result of our Phase 3 clinical program for Fovista due, in part, to the fact that we have no clinical data on Fovista combination therapy in any clinical trial longer than 24 weeks, that we have modified the methodology used to determine a patient's eligibility under certain of the inclusion and exclusion criteria for our Phase 3 clinical trials as compared to our Phase 2b clinical trial, that we have no clinical data on the effects of Fovista when administered in combination with Avastin or Eylea and that we plan to conduct our Phase 3 clinical trials at many clinical centers that were not included in our Phase 2b clinical trial.
- Although we have initiated two of the three clinical trials in our Phase 3 clinical program for Fovista in the United States and certain other countries outside of the United States, the U.S. Food and Drug Administration or regulatory authorities in European countries or elsewhere may



require us to conduct additional nonclinical studies or require us to modify our proposed Phase 3 clinical program to receive clearance to initiate our third clinical trial or to continue any of the three clinical trials once initiated, which may result in our incurring increased expense or delay in the completion of such program. In connection with our seeking scientific advice with respect to our potential application for marketing approval for Fovista in the European Union, the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, has advised us that we should justify particular aspects of the protocols for one of our Phase 3 clinical trials, that we should consider conducting toxicity studies with Fovista in combination with Avastin or Eylea, that, given that Avastin is not approved for intravitreal use in Europe, the final label for Fovista in the European Union may not be as broad as the label we intend to pursue and that there will be a requirement for additional data to bridge the results from our Phase 3 trials evaluating Fovista administered in combination with Lucentis as compared to Lucentis monotherapy to the less frequent dosing regimens of Lucentis and Eylea approved in the European Union. Discussions with the CHMP are ongoing.

- Adverse results from other clinical trials involving Fovista would be disclosed in and could negatively impact our applications for marketing approval for Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD. We are currently planning additional clinical trials outside of our Phase 3 clinical program to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions. In addition, we are planning to supply Fovista for other third-party sponsored clinical trials. Adverse safety events or negative or inconclusive efficacy results in any of these trials may impact the progress of our Phase 3 clinical program or our ability to obtain marketing approval for Fovista, notwithstanding successful completion of our Phase 3 clinical program.
- Our clinical trials for Zimura and our other product candidates may not be successful. We have very limited data regarding the safety and efficacy of Zimura for the treatment of geographic atrophy. In addition, we have no clinical data on the effects of Zimura when administered in combination with both Fovista and an anti-VEGF drug. Our prior clinical trials involving Zimura were small, were primarily directed towards evaluating safety and tolerability rather than efficacy and did not include control arms. Furthermore, we have had only preliminary discussions with regulatory authorities regarding the design of our planned Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy. Our eventual trial design could differ greatly from our current planned trial design. We expect that we will be required by regulatory authorities to conduct additional clinical studies of Zimura prior to seeking marketing approval in this indication.
- We currently depend heavily on the success of Fovista and Zimura. Our ability to generate product revenues from Fovista, which may not occur for several years, if ever, will depend substantially on the successful development and commercialization of Fovista in combination with anti-VEGF drugs for the treatment of wet AMD and on our receipt of marketing approval with labeling that does not include significant patient population, administration or use restrictions. Similarly, our ability to generate product revenues from Zimura, which also may not occur for several years, if ever, will depend on several factors in relation to the indication in which we pursue commercialization. We are party to agreements, specifically an acquisition agreement with OSI (Eyeteck), Inc., which agreement is now held by OSI Pharmaceuticals, LLC, a subsidiary of Astellas US, LLC, and license agreements with Archemix Corp. and Nektar Therapeutics, that impose significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to our product candidates.

- If we are unable to obtain required marketing approvals for, commercialize, obtain and maintain patent protection for or gain market acceptance by physicians, patients and third-party payors of Fovista, Zimura or any of our other product candidates, or experience significant delays in doing so, our business will be materially harmed and our ability to generate revenue will be materially impaired.
- The degree of market acceptance of Fovista, Zimura or any other product candidate that we develop, if approved for commercial sale, will depend on availability of third-party coverage and adequate reimbursement, particularly by Medicare, given our target market for persons over age 55.
- We hold patents covering the composition of matter of Fovista and patents and pending patent applications covering methods of Fovista's use in combination with certain anti-VEGF drugs for the treatment of wet AMD in the United States and certain other jurisdictions. Our pending patent applications covering methods of Fovista's use in combination with certain anti-VEGF drugs may not result in patents being issued that protect our technology or products, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Once our patents covering the composition of matter of Fovista in a particular jurisdiction expire, which is expected to occur in 2017 in the United States and 2018 in Europe and Japan, competitors will be able to offer and sell products containing the same active pharmaceutical ingredient in that jurisdiction so long as these competitors do not infringe any of our other patents covering Fovista or its method of use, do not violate the terms of any marketing or data exclusivity that may be granted to us by regulatory authorities and obtain any necessary marketing approvals from regulatory authorities. Our U.S. composition of matter patents covering Zimura are expected to expire in 2025.
- We have a limited operating history. We currently have no commercial products and we have not received marketing approval for any product candidate.
- We have incurred significant operating losses since inception. As of September 30, 2013, we had a deficit accumulated during the development stage of \$162.7 million. We expect to incur significant expenses and increasing operating losses over the next several years and will need substantial additional funding. Our future capital requirements will depend on many factors, including the progress and costs of our Phase 3 clinical program for Fovista and our other planned clinical programs.
- The expected future funding under our royalty agreement with Novo A/S of approximately \$41.7 million is subject to enrollment of specified numbers of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations. We have sold Novo A/S two royalty interests, each represented by low single-digit percentages of worldwide sales of Fovista. The aggregate royalty percentage we ultimately owe Novo A/S will be determined by the amount of funding provided by Novo A/S. If we fail to satisfy our diligence obligations or breach any other of our obligations under the royalty agreement with Novo A/S and fail to cure the breach within the applicable grace period, Novo A/S could seek to foreclose on the collateral, including Fovista intellectual property, securing our obligations. If Novo A/S successfully does so, we would lose our rights to develop and commercialize Fovista.

#### **Our Corporate Information**

We were incorporated under the laws of the State of Delaware on January 5, 2007 under the name Ophthotech Corporation. Our executive offices are located at One Penn Plaza, 19<sup>th</sup> Floor, New York, New York 10119, and our telephone number is (212) 845-8200. Our website address is [www.ophthotech.com](http://www.ophthotech.com). The information contained on, or that can be accessed through, our website is

not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

In this prospectus, unless otherwise stated or the context otherwise requires, references to "Ophthotech," "we," "us," "our" and similar references refer to Ophthotech Corporation. Fovista™ and Zimura™ are trademarks of Ophthotech Corporation. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

**Implications of Being an Emerging Growth Company**

As a company with less than \$1 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we may remain an emerging growth company until the end of the 2018 fiscal year. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

## THE OFFERING

Common Stock  
Offered by Us 1,900,000 shares

Common Stock  
Offered by the  
Selling  
Stockholders 385,714 shares

Common Stock  
to be  
Outstanding  
After This  
Offering 33,318,575 shares

Option to  
Purchase  
Additional  
Shares  
Granted by the  
Selling  
Stockholders The selling stockholders have granted the underwriters an option for a period of 30 days to purchase up to 342,857 additional shares of our common stock.

Use of Proceeds We intend to use the net proceeds we receive from this offering to fund additional clinical trials to further evaluate the potential of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need; to fund a Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy, a severe form of dry AMD, and a Phase 2 clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of certain wet AMD patients; and for working capital and other general corporate purposes.

We will not receive any proceeds from any sale of our shares of common stock in this offering by the selling stockholders.

See "Use of Proceeds" for more information.

Risk Factors You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

NASDAQ  
Global Select  
Market  
Symbol "OPHT"

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The number of shares of our common stock to be outstanding after this offering is based on 31,418,575 shares of our common stock outstanding as of January 31, 2014.

The number of shares of our common stock to be outstanding after this offering excludes:

- 3,669,651 shares of our common stock issuable upon the exercise of stock options outstanding as of January 31, 2014, at a weighted-average exercise price of \$15.19 per share;
- 794,970 additional shares of our common stock that are available for future issuance as of January 31, 2014, under our 2013 stock incentive plan; and
- 87,656 shares of our common stock issuable upon the exercise of warrants outstanding as of January 31, 2014, at a weighted-average exercise price of \$6.32 per share.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise of the outstanding options or warrants described above; and
- no exercise by the underwriters of their option to purchase up to 342,857 additional shares of our common stock from the selling stockholders.

## SUMMARY FINANCIAL INFORMATION

You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statements of operations data for the years ended December 31, 2012 and 2011 from our audited financial statements included in this prospectus. We have derived the statements of operations data for the nine months ended September 30, 2013, and 2012 and the balance sheet data as of September 30, 2013 from our unaudited financial statements included in this prospectus. The unaudited financial data include, in the opinion of our management, all adjustments, consisting of normal recurring adjustments, that are necessary for a fair statement of our financial position and results of operations for these periods. Our historical results for a prior period are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results to be expected for a full fiscal year.

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2011	2013	2012
	(unaudited)			
	(In thousands, except per share data)			
<b>Statement of Operations Data:</b>				
Revenue	\$ —	\$ —	\$ —	\$ —
Operating expenses:				
Research and development	6,792	13,896	17,836	4,794
General and administrative	6,889	5,738	9,145	5,341
Total operating expenses	13,681	19,634	26,981	10,135
Loss from operations	(13,681)	(19,634)	(26,981)	(10,135)
Interest (expense) income	(507)	2	(1,454)	(256)
Loss on extinguishment of debt	—	—	(1,091)	—
Other loss	(374)	(30)	(1,231)	(340)
Net loss before income taxes benefit	(14,562)	(19,662)	(30,757)	(10,731)
Income tax benefit	—	1,029	—	—
Net loss	(14,562)	(18,633)	(30,757)	(10,731)
Accretion of preferred stock dividends	(7,063)	(6,838)	(5,891)	(5,288)
Net loss attributable to common stockholders	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>	<u>\$ (36,648)</u>	<u>\$ (16,019)</u>
Per share information:				
Net loss attributable to common stockholders per share, basic and diluted	<u>\$ (14.89)</u>	<u>\$ (18.27)</u>	<u>\$ (23.21)</u>	<u>\$ (11.07)</u>
Weighted-average shares outstanding—basic and diluted	<u>1,452</u>	<u>1,394</u>	<u>1,579</u>	<u>1,447</u>
Unaudited pro forma basic and diluted net loss attributable to common stockholders per share	<u>\$ (0.65)</u>			
Unaudited pro forma basic and diluted weighted-average shares outstanding	<u>22,491</u>			

Pro forma basic and diluted net loss per common share is computed using a weighted-average number of common shares outstanding and gives effect to the automatic conversion of all outstanding shares of our preferred stock, including shares of our series C preferred stock that we issued and sold in May 2013 and August 2013 and additional shares of preferred stock that were issued as accrued stock dividends, into an aggregate of 21,038,477 shares of our common stock upon the closing of our initial public offering, which occurred on September 30, 2013.

	As of September 30, 2013	
	(unaudited)	
	Actual	As Adjusted(1)(2)
	(in thousands)	
<b>Balance Sheet Data:</b>		
Cash and cash equivalents	\$ 236,079	\$ 291,538
Total assets	\$ 238,376	\$ 293,835
Royalty purchase liability	\$ 41,667	\$ 41,667
Common stock	\$ 31	\$ 33
Additional paid in capital	\$ 351,431	\$ 406,888
Deficit accumulated during the development stage	\$ (162,661)	\$ (162,661)
Total stockholders' equity	\$ 188,801	\$ 244,260

- (1) The as adjusted balance sheet data give effect to our issuance and sale of 1,900,000 shares of common stock in this offering at the public offering price of \$31.50 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We will not receive any proceeds from any sale of shares of our common stock in this offering by the selling stockholders.
- (2) The unaudited as adjusted balance sheet data do not give effect to our receipt on January 23, 2014 of the second tranche of \$41.7 million in royalty financing under our royalty purchase agreement with Novo A/S.

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. If any of the following risks occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the market price of our common stock could decline, and you might lose all or part of your investment.*

### **Risks Related to Our Financial Position and Need for Additional Capital**

***We have incurred significant operating losses since our inception. We expect to incur losses for at least the next several years and may never achieve or maintain profitability.***

Since inception, we have incurred significant operating losses. Our net loss was \$30.8 million for the nine months ended September 30, 2013, \$14.6 million for the year ended December 31, 2012 and \$18.6 million for the year ended December 31, 2011. As of September 30, 2013, we had a deficit accumulated during the development stage of \$162.7 million. To date, we have not generated any revenues and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, our royalty purchase and sale agreement with Novo A/S and our initial public offering, which we closed in September 2013. We received net proceeds from the initial public offering of \$175.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We have devoted substantially all of our financial resources and efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year.

Our most advanced product candidates, Fovista and Zimura, are still in clinical development. We expect our expenses to increase substantially as compared to prior periods, particularly as we continue the development of Fovista in our Phase 3 clinical program for the treatment of wet AMD, initiate additional Phase 2 clinical trials further evaluating the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions and continue the development of Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. We are party to agreements, specifically an asset acquisition agreement with OSI (Eyetechnology), Inc., or Eyetechnology, which agreement is now held by OSI Pharmaceuticals, LLC, or OSI Pharmaceuticals, a subsidiary of Astellas US, LLC, and license agreements with Archemix Corp., or Archemix, and Nektar Therapeutics, or Nektar, that impose significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to Fovista. See "Business—Acquisition and License Agreements" for more information. Furthermore, we expect to incur additional costs associated with being a public company, including legal, compliance, accounting and investor and public relations expenses, as well as increased insurance premiums.

Our expenses also will increase if and as we:

- undertake additional clinical development of Fovista, if it is approved, in support of our efforts to broaden the label for Fovista;
- conduct additional clinical trials of Zimura that may be required by regulatory authorities for us to seek marketing approval of Zimura for the treatment of geographic atrophy;
- in-license or acquire the rights to other complementary products, product candidates or technologies for the treatment of ophthalmic diseases;
- seek marketing approval for any product candidates that successfully complete clinical trials;

- expand our outsourced manufacturing activities and establish sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our clinical, manufacturing and planned future commercialization efforts.

If we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or regulatory authorities in other jurisdictions to perform clinical trials or studies in addition to those we currently expect to conduct, or if there are any delays in completing the clinical trials of Fovista or Zimura, or the development of any of our other product candidates, our expenses could increase.

Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, our product candidates, and in particular, Fovista, 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:

- initiating and obtaining favorable results from our Phase 3 clinical program for Fovista;
- if initiated, obtaining favorable results, especially with respect to safety, in our other planned clinical trials involving Fovista;
- subject to obtaining favorable results from our Phase 3 clinical program, applying for and obtaining marketing approval for Fovista;
- establishing sales, marketing and distribution capabilities to effectively market and sell Fovista in the United States with our own specialty sales force targeting retinal specialists;
- establishing collaboration, distribution or other marketing arrangements with third parties to commercialize Fovista in markets outside the United States;
- protecting our rights to our intellectual property portfolio related to Fovista; and
- ensuring the manufacture of commercial quantities of Fovista.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease 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 continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

***Our short operating history may make it difficult for you 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 2007. Our operations to date have been limited to organizing and staffing our company, acquiring rights to product candidates, business planning, raising capital and developing Fovista, Zimura and our other product candidates. We have not yet demonstrated our ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, 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 you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.



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

***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 our expenses to increase substantially as compared to prior periods in connection with our ongoing activities, particularly as we continue the clinical development of and seek marketing approval for Fovista. Additionally, we expect our expenses to increase in connection with our initiation of additional Phase 2 clinical trials evaluating Fovista's potential to provide benefit in wet AMD, our initiation of additional clinical trials evaluating Fovista's potential to treat other ophthalmic conditions and our continued development of Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. Our expenses will increase if we suffer any delays in our Phase 3 clinical program for Fovista, including delays in receipt of regulatory clearance to begin our Phase 3 clinical trials in jurisdictions where clearance is required and we have not yet obtained clearance or delays in enrollment of patients. If we obtain marketing approval for Fovista, Zimura or any other product candidate that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Furthermore, we expect to incur additional costs associated with being a public company, hiring additional personnel and expanding our facilities. 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.

We expect to obtain initial, top-line data from our Fovista Phase 3 clinical program in 2016. We expect that the net proceeds we receive from this offering, together with our existing cash and cash equivalents of \$236.1 million as of September 30, 2013, the \$41.7 million received under our royalty agreement with Novo A/S in January 2014 and potential future funding of \$41.7 million under such royalty agreement, will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2016. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. This estimate assumes, among other things, that we receive the full financing amount available under our royalty agreement with Novo A/S on a timely basis. The royalty agreement provides that we will use the remaining proceeds we received and future proceeds, if any, under such royalty agreement primarily to support clinical development and regulatory activities for Fovista and for certain other permitted purposes. We are planning to spend significant additional funds on our Phase 3 clinical program for Fovista, on our other planned clinical programs, including additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need, an additional planned clinical trial evaluating Zimura for the treatment of geographic atrophy and an additional planned clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation, and for general corporate purposes and working capital. Costs related to our clinical programs could exceed our expectations if we experience delays in our clinical trials, including because of the timing of our patient enrollment, the availability of drug supply for our clinical trials or for other reasons. Our costs will also increase if we increase investigator fees for our clinical trials or decide to expand the scope of our clinical trials and programs, including, for example, by expanding the geographic mix of sites at which patients are enrolled, or to increase other corporate or licensing activities or staffing. These costs will also increase if we decide to expand the scope of our clinical programs.

Our current Phase 3 clinical program for Fovista is expected to continue through at least 2017, and substantial expenditures to complete the Phase 3 clinical program will be required after the receipt of initial, top-line data. Moreover, we are at the early stages of formulating our clinical development plan for Zimura. We expect the clinical development of Zimura will continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete the clinical development of either Fovista or Zimura, complete process development and manufacturing scale-up activities associated with Fovista and Zimura and potentially seek marketing approval for Fovista or Zimura, or the nature, timing or costs of the efforts necessary to complete the development of any other product candidate we may develop.

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

- the scope, progress, costs and results of our Phase 3 clinical program for Fovista;
- the progress, costs and results of our planned additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need;
- the scope, progress, results and costs of our planned Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy and whether and to what extent additional clinical trials may be required by regulatory authorities for us to seek marketing approval in this indication and our Phase 2 clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation;
- the costs and timing of process development and manufacturing scale-up activities associated with Fovista and Zimura;
- the costs, timing and outcome of regulatory review of Fovista and Zimura;
- the costs of commercialization activities for Fovista or Zimura if we receive, or expect to receive, marketing approval for either product candidate, including the costs and timing of expanding our outsourced manufacturing activities and establishing product sales, marketing and distribution capabilities;
- subject to receipt of marketing approval, revenue received from commercial sales of Fovista or Zimura, after milestone payments and royalties;
- the scope, progress, results and costs of our clinical trials for any other product candidates that we may develop;
- our ability to establish collaborations on favorable terms, if at all;
- the extent to which we in-license or acquire rights to complementary products, product candidates or technologies; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property-related claims.

Our commercial revenues, if any, will be derived from sales of Fovista, Zimura 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, Fovista, Zimura 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 that we have sufficient funds for our current or future operating plans.

***If we fail to enroll patients in our Phase 3 clinical trials of Fovista as planned or fail to comply with our obligations in our royalty agreement with Novo A/S, we could lose access to funds that are important to our business, which may force us to delay or terminate the development of Fovista. In addition, a default under the royalty agreement with Novo A/S would permit Novo A/S to foreclose on the Fovista intellectual property.***

In May 2013, we entered into a royalty purchase and sale agreement, or royalty agreement, with Novo A/S for a financing of up to \$125.0 million in return for the sale to Novo A/S of royalty interests in worldwide sales of Fovista. We received approximately \$83.3 million of this royalty financing in two separate tranches in May 2013 and January 2014. We are obligated to pay Novo A/S royalties in the low to mid single-digit percentages of worldwide sales of Fovista, with the royalty percentage determined by the amount of funding provided by Novo A/S.

We are subject to diligence and other obligations under our royalty agreement with Novo A/S. If we fail to enroll the specified numbers of patients in our Phase 3 clinical trials of Fovista and satisfy additional closing conditions under the royalty agreement or fail to satisfy our other obligations, Novo A/S will have no further obligation to pay additional funds to us under the royalty agreement. We would then need to raise substantial additional funding through public or private equity offerings, debt financings, corporate collaboration and licensing arrangements or other financing alternatives. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay or terminate our research and development programs, including for Fovista, or any future commercialization efforts.

In addition, our obligations under our royalty agreement with Novo A/S are secured by collateral, which includes certain intellectual property rights, including all of our intellectual property rights relating to Fovista and regulatory approvals, if any, of Fovista. If we fail to satisfy our diligence obligations or breach any other of our obligations under the royalty agreement with Novo A/S and fail to cure the breach within any applicable grace period, Novo A/S could declare an event of default. In such event, Novo A/S could seek to foreclose on the collateral securing our obligations. If Novo A/S successfully does so, we would lose our rights to develop and commercialize Fovista.

Our obligations under our royalty agreement with Novo A/S and the pledge of our intellectual property rights in and regulatory approvals, if any, of Fovista as collateral under such agreement may limit our ability to obtain debt financing.

***Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, 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, collaborations, strategic alliances and marketing, distribution or licensing arrangements. The potential funding pursuant to our royalty agreement with Novo A/S is subject to enrollment of specified numbers of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations. We do not have any other committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder 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 assets, including intellectual property rights, as collateral to secure our obligations under our royalty agreement with Novo A/S may limit our ability to obtain debt financing.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products 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.

### **Risks Related to Product Development and Commercialization**

***We depend heavily on the success of our lead product candidate, Fovista, which we are developing to be administered in combination with anti-VEGF drugs for the treatment of patients with wet AMD. In addition, we also depend on the success of Zimura, which we are developing with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. If we are unable to complete the clinical development of either of these product candidates, if we are unable to obtain marketing approvals for either of these product candidates, or if either of these product candidates is approved and we fail to successfully commercialize the product candidate or experience significant delays in doing so, our business will be materially harmed.***

We have invested a significant portion of our efforts and financial resources in the development of Fovista to be administered in combination with anti-VEGF drugs for the treatment of patients with wet AMD. There remains a significant risk that we will fail to successfully develop Fovista. The results of our Phase 2b clinical trial may not be predictive of the results of our Phase 3 clinical program due, in part, to the fact that we have no clinical data on Fovista combination therapy in any clinical trial longer than 24 weeks, that we have modified the methodology used to determine a patient's eligibility under certain of the inclusion and exclusion criteria for our Phase 3 clinical trials as compared to our Phase 2b clinical trial, that we have no clinical data on the effects of Fovista when administered in combination with Avastin or Eylea and that we plan to conduct our Phase 3 clinical trials at many clinical centers that were not included in our Phase 2b clinical trial.

We do not expect to have initial, top-line data from our Phase 3 clinical program for Fovista available until 2016. The timing of the availability of such top-line data and the completion of our Phase 3 clinical program is dependent, in part, on our ability to locate and enroll a sufficient number of eligible patients in our Phase 3 clinical program on a timely basis. The timing of the availability of initial, top-line data from our Phase 3 clinical trial evaluating the safety and efficacy of Fovista administered in combination with each of Avastin or Eylea may be subject to particular variability because we have no clinical experience testing Fovista administered in combination with Avastin or Eylea. Avastin is not approved for intravitreal use in treating wet AMD, and regulatory authorities may not allow, or physicians and patients may choose not to participate in, a clinical trial in which Avastin is administered in combination with Fovista for the treatment of wet AMD. Even if we ultimately obtain statistically significant, positive results from our Phase 3 clinical program, we do not expect to submit applications for marketing approval for Fovista until the end of 2016.

If we are not able to obtain data from our Phase 3 clinical trial evaluating Fovista administered in combination with each of Avastin or Eylea when data from our other two Phase 3 clinical trials evaluating Fovista administered in combination with Lucentis are available, we may nonetheless decide to proceed with submitting applications for marketing approval for Fovista administered only in combination with Lucentis. If we submit applications for marketing approval for Fovista only in combination with Lucentis, we may determine either to delay seeking approval of Fovista in combination with Avastin or Eylea until after regulatory authorities have considered and acted on our applications for Fovista in combination with Lucentis, or to amend our applications once data from our third Phase 3 clinical trial become available. If we were to delay seeking approval of Fovista in combination with Avastin or Eylea pending regulatory action on our applications for Fovista in combination with Lucentis, the FDA or other regulatory authorities could defer taking action on our applications while data remain outstanding from our third Phase 3 clinical trial. Moreover, if we subsequently amend our applications for marketing approval when data from our third Phase 3 clinical trial become available, we may experience further delays in our application process. Additionally, we expect that our Phase 3 clinical trials will continue in accordance with their protocols after we submit applications for marketing approval, and the conclusions of those trials may yield data that are

inconsistent with the initial data used to support our applications. Furthermore, we expect to commence additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need during the course of our ongoing Phase 3 clinical development program. We are also planning to supply Fovista for other third-party sponsored clinical trials. Adverse safety events or negative or inconclusive efficacy results in any of these trials may impact the progress of our Phase 3 clinical program. In addition, adverse results from any of these additional planned clinical trials would be disclosed in and could negatively impact our applications for marketing approval for Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD. As a result of these and other factors, we cannot accurately predict when or if Fovista will prove effective or safe in humans or will receive marketing approval.

In addition, we have invested substantial financial resources in the development of Zimura for the treatment of patients with both dry and wet AMD. There remains a significant risk that we will fail to successfully develop Zimura. We have very limited data from our completed Phase 1/2a clinical trial evaluating the safety and effectiveness of Zimura for the treatment of dry AMD and our completed Phase 1/2a clinical trial evaluating the safety and effectiveness of Zimura administered in combination with Lucentis for the treatment of wet AMD. These trials enrolled 47 patients and 60 patients, and neither trial included a control arm. Furthermore, we have no clinical data on the effects of Zimura when administered in combination with both Fovista and an anti-VEGF drug.

We do not expect to receive interim results from our planned Phase 2/3 clinical trial of Zimura for the treatment of dry AMD until 2016. Furthermore, we do not expect to receive initial results from our planned Phase 2 clinical trial of Zimura and Fovista administered in combination with an anti-VEGF drug until 2016. The timing of the completion of and the availability of initial results from these planned clinical trials is dependent, in part, on our ability to complete manufacturing scale-up activities for Zimura and to locate and enroll a sufficient number of eligible patients in our planned trials on a timely basis. The timing of the receipt of initial results from our Phase 2 clinical trial evaluating the safety and efficacy of Zimura and Fovista administered in combination with an anti-VEGF drug may be subject to particular variability because we have no clinical experience testing Zimura administered in combination with Fovista and an anti-VEGF drug.

Although our current development plan for Zimura calls for us to initiate a Phase 2/3 clinical trial evaluating the safety and efficacy of Zimura in treating patients with geographic atrophy, we may not initiate or complete this clinical trial for Zimura or any other clinical trial for Fovista, Zimura or any of our other product candidates in accordance with our plans.

Other than with respect to our Phase 3 clinical program for Fovista, we are still in the early planning stages of our clinical trials. Although our plans reflect our current expectations regarding the endpoints, duration and number of patients to be included in our planned Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy, we have only had preliminary discussions with regulatory authorities regarding our trial design. As we continue these discussions, our plans may change significantly based on feedback from such regulatory authorities.

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 our product candidates, and in particular, Fovista and Zimura. The success of these product candidates will depend on several factors, including the following:

- obtaining favorable results from clinical trials;
- making arrangements with third-party manufacturers and receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities;

- for Fovista, receipt of marketing approvals from applicable regulatory authorities for the use of Fovista in combination with anti-VEGF drugs for the treatment of wet AMD and in particular, which anti-VEGF drugs are included in any such approval given that Avastin, one of the current standard of care anti-VEGF drugs, is not approved for intravitreal use;
- for Zimura, receipt of marketing approvals from applicable regulatory authorities for the use of Zimura for the treatment of dry AMD or the use of Zimura administered in combination with Fovista and anti-VEGF drugs for the treatment of wet AMD;
- the scope of the label that may be approved by applicable regulatory authorities, including the specific indication for which the product may be approved;
- launching commercial sales of the product candidate, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidate, if and when approved, by patients, the medical community and third-party payors;
- for Fovista, continued, widespread use of anti-VEGF therapies in the treatment of wet AMD in combination with which Fovista will be used;
- effectively competing with other therapies, including the existing standard of care, and other forms of drug delivery;
- maintaining a continued acceptable safety profile of the product candidate following approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity; and
- protecting our rights in our intellectual property portfolio.

Successful development of Fovista for the further treatment of wet AMD, the treatment of additional ophthalmic conditions, if any, or for use in other patient populations and our ability, if it is approved, to broaden the label for Fovista 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 Fovista, Zimura or any of our other product candidates, which would materially harm our business.

***If clinical trials of Fovista, Zimura 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 positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of Fovista, Zimura or any other product candidate.***

Before obtaining approval from regulatory authorities for the sale of any product candidate, 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.

Our Phase 2b clinical trial evaluated a combination of Fovista and Lucentis. In this trial, patients treated with a combination of 0.3 mg of Fovista and Lucentis did not achieve statistically significant superiority compared to Lucentis monotherapy based on the pre-specified primary endpoint of mean change in visual acuity from baseline at the 24 week timepoint. Although a combination of 1.5 mg of

Fovista and Lucentis demonstrated statistically significant superiority in this trial compared to Lucentis monotherapy based on the pre-specified primary endpoint of mean change in visual acuity from baseline at the 24 week timepoint, we may nonetheless fail to achieve success in our Phase 3 clinical trials involving a combination of 1.5 mg of Fovista and Lucentis for a variety of potential reasons.

- The primary endpoint of mean change in visual acuity in our Phase 2b clinical trial was measured 24 weeks after the first dose of Fovista. The primary endpoint of mean change in visual acuity in our Phase 3 clinical program will be measured 12 months after the first dose of Fovista. We have no clinical data on Fovista combination therapy in any clinical trial longer than 24 weeks. We have modified the methodology used to determine a patient's eligibility under certain of the inclusion and exclusion criteria for our Phase 3 clinical trials as compared to our Phase 2b clinical trial. If the positive results we observed at 24 weeks in our Phase 2b clinical trial are not observed at 12 months, we likely will not receive marketing approval for Fovista.
- Retrospective subgroup analyses that we performed on the results of our Phase 2b clinical trial may not be predictive of the results of our Phase 3 clinical program. Furthermore, our retrospective analysis of retinal images of subretinal fibrosis from our Phase 2b clinical trial, to date, is based only on our initial assessment of a group of patients who experienced poor visual outcome following treatment with either 1.5 mg of Fovista in combination with 0.5 mg of Lucentis or Lucentis monotherapy in the trial. We have not conducted any statistical analysis with respect to these retinal images, and we may reconsider our belief regarding the anti-fibrotic effects of Fovista in light of further analysis that we plan to undertake. In addition, we intend to have an independent third-party reading center review these retinal images. It is possible that our initial findings will not be confirmed by the reading center. Although we believe that our retrospective analyses further support the results from our primary endpoint and our proposed mechanism of action, retrospective analyses performed after unblinding trial results can result in the introduction of bias and are given less weight by regulatory authorities than pre-specified analyses. Our proposed mechanism of action, in particular, as it relates to the inhibition of subretinal fibrosis, although scientifically rational, may not be supported by our confirmatory analysis of our Phase 2b retinal images or by future clinical trials. Our belief regarding Fovista's potential, when administered in combination with an anti-VEGF drug, to inhibit subretinal fibrosis and retinal scarring, may change based on such confirmatory analysis, subsequent clinical trials or other factors.
- We plan to conduct our Phase 3 clinical trials at many clinical centers that were not included in our Phase 2b clinical 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 1.5 mg of Fovista administered in combination with an anti-VEGF drug and anti-VEGF drug monotherapy.

Furthermore, our Phase 3 clinical program involves two Phase 3 clinical trials testing a combination of 1.5 mg of Fovista and Lucentis for the treatment of wet AMD and one trial testing a combination of 1.5 mg of Fovista with each of Avastin or Eylea for the treatment of wet AMD. We have no clinical efficacy data on the effects of Fovista when administered in combination with Avastin or Eylea for the treatment of patients with wet AMD. Avastin is not approved for such use.

Fovista administered in combination with Lucentis was generally well tolerated in our Phase 1 and Phase 2b clinical trials. However, the results of these clinical trials may not be predictive of the results of our Phase 3 clinical program for Fovista due, in part, to the fact that we have no clinical safety data on patient exposure to Fovista administered in combination with any anti-VEGF drug for longer than 24 weeks and that we have no clinical safety data on the effects of Fovista when administered in combination with Avastin or Eylea.

In general, the FDA and similar regulatory authorities outside the United States require two adequate and well controlled clinical trials demonstrating safety and effectiveness for marketing approval. If a combination of 1.5 mg of Fovista and Lucentis fails to achieve superiority over Lucentis monotherapy with statistical significance on the primary endpoint of mean change in visual acuity from baseline at 12 months in both of our Phase 3 clinical trials evaluating the safety and efficacy of this combination, we likely will not receive marketing approval for Fovista even if the combination of 1.5 mg of Fovista with Avastin or Eylea achieves superiority over Avastin or Eylea monotherapy with statistical significance on the primary endpoint in one of our Phase 3 clinical trials. There are a variety of other possible outcomes of our Phase 3 clinical trials. As described below, positive outcomes in one or more of our Phase 3 clinical trials may not be sufficient for the FDA or similar regulatory authorities outside the United States to grant marketing approval for Fovista.

- If a combination of 1.5 mg of Fovista and Lucentis achieves superiority over Lucentis monotherapy with statistical significance on the primary endpoint in only one of our Phase 3 clinical trials and the combination of 1.5 mg of Fovista with Avastin or Eylea does not achieve superiority over Avastin or Eylea monotherapy with statistical significance on the primary endpoint in our other Phase 3 clinical trials, we likely will not receive marketing approval for Fovista.
- If a combination of 1.5 mg of Fovista and Lucentis achieves superiority over Lucentis monotherapy with statistical significance on the primary endpoint in only one of our Phase 3 clinical trials and the combination of 1.5 mg of Fovista with Avastin or Eylea achieves superiority over Avastin or Eylea monotherapy with statistical significance on the primary endpoint in our other Phase 3 clinical trial, the FDA or similar regulatory authorities outside the United States may nonetheless not grant marketing approval for Fovista.
- Even if a combination of 1.5 mg of Fovista and an anti-VEGF drug achieves superiority over an anti-VEGF drug monotherapy with statistical significance on the primary endpoint in two or all three of our Phase 3 clinical trials, the FDA or similar regulatory authorities outside the United States may nonetheless not grant marketing approval for Fovista if such regulatory authorities do not believe that the benefits offered by Fovista administered in combination with an anti-VEGF drug are clinically meaningful or that such benefits outweigh the observed or potential risks.

In the United States, Avastin and Eylea are two of the most widely used anti-VEGF drugs for the treatment of wet AMD. If a combination of 1.5 mg of Fovista with Avastin or Eylea does not achieve superiority over Avastin or Eylea monotherapy with statistical significance on the primary endpoint of mean change in visual acuity from baseline at 12 months in our Phase 3 clinical program, our ability to successfully commercialize Fovista in combination with any anti-VEGF drug could be harmed materially. In addition, any failure of Fovista administered in combination with Avastin or Eylea to achieve superiority over Avastin or Eylea monotherapy with statistical significance on the primary endpoint could cause the FDA or similar regulatory authorities outside the United States to require additional clinical trials or other research before granting marketing approval of Fovista for use in combination with any anti-VEGF drug, including Lucentis, for the treatment of patients with wet AMD. In addition, Avastin is not approved for use in treating wet AMD, either in the United States or outside of the United States, and regulatory authorities may not permit the product label for Fovista to include the use of Fovista in combination with Avastin if we were otherwise able to obtain marketing approval for Fovista for use in combination with other anti-VEGF drugs.

The protocols for our Phase 3 clinical trials and other supporting information are subject to review by the FDA and regulatory authorities outside the United States. The FDA is not obligated to comment on our protocols within any specified time period or at all or to affirmatively clear or approve our Phase 3 clinical program. We have submitted the protocols for our Phase 3 clinical trials to the FDA and have initiated two of the trials in our Phase 3 clinical program in the United States, both of which are evaluating the safety and efficacy of Fovista administered in combination with Lucentis,



without waiting for any such comments. We expect to activate initial trial sites in the third trial in this Phase 3 clinical program in the United States by the end of the first quarter of 2014. The FDA or other regulatory authorities may request additional information, require us to conduct additional non-clinical trials or require us to modify our proposed Phase 3 clinical program, including its endpoints, patient enrollment criteria or selection of anti-VEGF drugs, to receive clearance to initiate such program or to continue such program once initiated.

Outside the United States, we have made regulatory submissions in selected countries to initiate the two Phase 3 clinical trials of Fovista administered in combination with Lucentis and have begun to obtain approvals to proceed. We plan to submit applications seeking to initiate the third trial of Fovista administered in combination with Avastin or Eylea in the first quarter of 2014. In the European Union, as further described below, in addition to filing in selected countries with national competent authorities responsible for approving clinical trial applications, we are also continuing interactions regarding our planned application for marketing approval with the EMA's CHMP, which is the committee responsible for preparing opinions on questions concerning medicines for human use. The national competent authorities may follow the advice described below of the CHMP that we consider toxicity studies with Fovista administered in combination with Avastin or Eylea prior to initiating our corresponding Phase 3 clinical trial.

We may not receive clearance from regulatory authorities in jurisdictions outside the United States to initiate our Phase 3 clinical program in those jurisdictions on a timely basis, or at all. In addition, any modifications to our Phase 3 clinical program for Fovista may result in our incurring increased expense or in a delay in the enrollment or completion of such program.

The CHMP recently provided scientific advice on our proposed Phase 3 clinical program for Fovista and our plan to seek regulatory approval for Fovista in the European Union. As part of that scientific advice, the CHMP advised us that the planned primary endpoint for each of the Fovista Phase 3 clinical trials, mean change from baseline in best corrected visual acuity, was acceptable. In addition, the CHMP confirmed that carcinogenicity studies are not needed for our Phase 3 clinical program. The CHMP also advised us that we should justify our proposal to initiate, at the Phase 3 clinical trial stage, certain previously untested combinations of Fovista with Avastin or Eylea, and, as described above, that we should consider conducting toxicity studies with Fovista administered in combination with Avastin or Eylea prior to initiating our corresponding Phase 3 clinical trial. In addition, the CHMP informed us that the final label for Fovista, if it receives marketing approval, may be required to specify the licensed anti-VEGF drugs that were studied in combination with Fovista, given that Avastin is not approved for intravitreal use, rather than a broad label specifying Fovista for use in combination with any anti-VEGF drug. The CHMP further advised us that there will be a requirement for additional data to bridge the results from our Phase 3 clinical trials evaluating Fovista administered in combination with Lucentis as compared to Lucentis monotherapy to the less frequent dosing regimens of Lucentis and Eylea approved in the European Union.

We have responded to the CHMP on these issues and expect to receive further comments on our response from the CHMP by the end of the first quarter of 2014. We plan to adjust the dosing schedule in our Phase 3 clinical program for Fovista administered in combination with Eylea so that no bridging study would be needed for this combination. Although discussions with the CHMP regarding the need for, and possible design of, a Lucentis bridging study are ongoing, we expect that, if we determine or are required to conduct such a study, it would not have a material impact on our anticipated timing and overall expense of our Phase 3 clinical plan, including our plan to have initial, top-line data from our Phase 3 clinical program for Fovista available in 2016. We also anticipate that our existing cash and cash equivalents and potential funding under our royalty agreement with Novo A/S will be sufficient to enable us to fund our operating expenses and capital expenditure requirements, including any additional costs not previously contemplated for a possible bridging study for Fovista administered in combination with Lucentis, through at least the end of 2016.

Although our plans reflect our current expectations regarding the endpoints, duration and number of patients to be included in our planned Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy, we have only had preliminary discussions with regulatory authorities regarding our trial design. As we continue these discussions, our plans may change significantly based on feedback from such regulatory authorities. We expect that we will be required by regulatory authorities to conduct additional clinical trials of Zimura prior to seeking marketing approval in this indication.

If we are required to conduct additional clinical trials or other testing of Fovista, Zimura or any other product candidate that we develop beyond those that we 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 positive or are only modestly positive 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, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

***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 our product candidates, 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; and

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates, such as the anti-VEGF drugs we need to use in combination with Fovista, may become insufficient or inadequate.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant 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 and may harm our business and results of operations.

***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 new or continue ongoing clinical trials for Fovista, Zimura or any other product candidate that we 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 Fovista and Zimura, 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:

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

Additional financing under our royalty agreement with Novo A/S is contingent upon enrolling specified numbers of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations. Novo A/S will not be required to provide the additional royalty financing unless we enroll the specified numbers of patients. In addition, our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays in our clinical trials, 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 also 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 Fovista, Zimura or any other product candidate that we develop, we may need to abandon or limit our development of Fovista, Zimura or any other product candidate.***

If Fovista, Zimura or any other of our 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 certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Although, Fovista administered in combination with Lucentis was generally well tolerated in our Phase 1 clinical trial and our Phase 2b clinical trial, we have no clinical

safety data on patient exposure to Fovista administered in combination with Lucentis for longer than 24 weeks, and we have no clinical safety data on the effects of Fovista when administered in combination with Avastin or Eylea. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound. Our Phase 3 clinical program for Fovista involves the administration of Fovista in combination with anti-VEGF drugs, and the safety results of our trials are dependent, in part, on the safety and tolerability of the anti-VEGF drug administered in combination with Fovista. Avastin is not approved for the treatment of wet AMD, and according to third-party clinical studies, may be associated with a greater risk of serious adverse events or undesirable side effects as compared to Lucentis. Furthermore, we have very limited data regarding the safety and efficacy of Zimura for the treatment of geographic atrophy. In addition, we have no clinical data on the effects of Zimura when administered in combination with both Fovista and an anti-VEGF drug.

***Even if Fovista, Zimura 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 any of our products and product candidates may be smaller than we estimate.***

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current treatments for wet AMD, including Lucentis, Eylea and low cost, off-label use of Avastin, are well established in the medical community, and doctors may continue to rely on these treatments without Fovista. If Fovista 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 Fovista, Zimura or any other product candidate that we develop, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments, including the existing standard of care;
- any restrictions on the use of our products in combination with other medications, such as a Fovista label requiring a waiting period after the intravitreal injection of the anti-VEGF drug and prior to the intravitreal injection of Fovista;
- any restrictions on the use of our products to a subgroup of patients, such as by excluding from the Fovista label patients with pure occult subtype wet AMD;
- restrictions in the label on the use of Fovista with a particular anti-VEGF drug;
- any changes in the dosing regimen of, or the means of administering or delivering, an anti-VEGF drug with which Fovista will be used;
- our ability to offer our products at competitive prices, particularly in light of the additional cost of Fovista together with an anti-VEGF drug;
- availability of third-party coverage and adequate reimbursement, particularly by Medicare given our target market for persons over age 55;
- willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, particularly in light of the existing available standard of care;
- prevalence and severity of any side effects;
- whether competing products or other alternatives are more convenient or easier to administer, including whether co-formulated alternatives, alternatives that can be co-administered in a single

syringe or alternatives that offer a less invasive method of administration than intravitreal injection come to market; and

- strength of our marketing and distribution support.

In addition, the potential market opportunity for Fovista is difficult to estimate precisely. If Fovista receives marketing approval for the treatment of wet AMD, it will be approved solely for use in combination with an anti-VEGF drug. The market opportunity for Fovista will be dependent upon the continued use of anti-VEGF drugs in the treatment of wet AMD and the market share of such anti-VEGF drugs for which Fovista is approved as a combination therapy. In addition, because physicians, patients and third-party payors may be sensitive to the addition of the cost of Fovista to the cost of treatment with anti-VEGF drugs, we may experience downward pressure on the price we can charge for Fovista.

Our Phase 3 clinical program excludes from enrollment wet AMD patients with pure occult choroidal neovascularization. Based on enrollment of wet AMD patients in third-party clinical trials, the pure occult subtype accounts for approximately 40% of the cases of subfoveal wet AMD. If Fovista receives marketing approval for the treatment of wet AMD and the approved label excludes patients with pure occult lesions, the potential market opportunity for Fovista will be limited to the extent that physicians do not prescribe Fovista for such patients.

Our Phase 3 clinical program provides for a 30-minute delay in the injection of Fovista after the anti-VEGF drug to minimize the risk in our clinical trials of an unacceptable increase in intraocular pressure as a result of the amount of the two agents injected. If Fovista receives marketing approval for the treatment of wet AMD and the approved label requires such a waiting period, the potential market opportunity for Fovista may be limited to the extent that physicians and patients find such a waiting period unacceptable. Our ability to develop, acquire or in-license viable drug delivery technologies or methods for co-formulation may be limited, and we may not be able to respond adequately to the competitive dynamics within the wet AMD treatment market.

Our estimates of the potential market opportunity for each of Fovista and Zimura include several key assumptions based on our industry knowledge, industry publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of these assumptions proves to be inaccurate, then the actual market for Fovista or Zimura could be smaller than our estimates of our potential market opportunity. If the actual market for Fovista or Zimura is smaller than we expect, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

***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 Fovista and Zimura from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of wet AMD or other disease indications for which we may develop Fovista. Although there are currently no therapies approved by the FDA or the EMA for the treatment of dry AMD, there are also a number of pharmaceutical and biotechnology companies that are currently pursuing the development of products for this indication. 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. 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. We also will face similar

competition with respect to any other products or product candidates that we may seek to develop or commercialize in the future for the treatment of wet AMD, dry AMD or other diseases.

The current standard of care for wet AMD is monotherapy administration of anti-VEGF drugs, principally Avastin, Lucentis and Eylea. Although Avastin is not approved for such use, we are developing Fovista for administration in combination with each of these anti-VEGF drugs, including Avastin. These drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. When used for the treatment of wet AMD, Avastin is inexpensive. Physicians, patients and third-party payors may not accept the addition of Fovista to their current treatment regimens for a variety of potential reasons, including:

- if they do not wish to incur the additional cost of Fovista;
- if they perceive an additional injection to administer Fovista as undesirable;
- if they perceive the addition of Fovista to be of limited benefit to patients; or
- if they wish to treat with anti-VEGF drugs as monotherapy first and add Fovista only if and when resistance to continued anti-VEGF therapy limits further enhancement of visual outcome with anti-VEGF monotherapy.

There are also a number of products in preclinical research and clinical development by third parties to treat wet AMD, including product candidates that inhibit the function of PDGF, the molecule whose function Fovista also inhibits, product candidates that inhibit the function of both VEGF and PDGF that could obviate the separate use of an anti-PDGF agent, such as Fovista, and anti-VEGF gene therapy products that may substantially reduce the number and frequency of intravitreal injections when treating wet AMD. These companies include pharmaceutical companies, biotechnology companies, and specialty pharmaceutical and generic drug companies of various sizes, such as Regeneron Pharmaceuticals, Inc., which is working in collaboration with Bayer HealthCare, Allergan, Inc., Xcovery Vision LLC, Neurotech Pharmaceuticals, Inc., Avalanche Biotechnologies, Inc., Somalogic, Inc., and others. In addition, other companies are undertaking efforts to develop technologies to allow for a less frequent dosing schedule for anti-VEGF therapies that are currently in use. If such technologies are successfully developed and approved for use, we may need to conduct additional clinical trials of Fovista using a less frequent dosing schedule than the dosing schedule we are currently using in our ongoing Phase 3 clinical program. Any such trials may not be successful.

Moreover, there are a number of products in preclinical research and clinical development by third parties to treat dry AMD, including product candidates that are designed to suppress inflammation, such as complement system inhibitors and corticosteroids, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular enhancers. These companies include pharmaceutical companies, biotechnology companies, and specialty pharmaceutical and generic drug companies of various sizes. In particular, with respect to complement system inhibition, these companies include Genentech, Novartis's Alcon division, Alexion Pharmaceuticals, Inc. and MophoSys. Moreover, we are aware that the following companies are pursuing the clinical development of ophthalmic product candidates with other mechanisms of action for the treatment of dry AMD: Alimera Sciences, Acucela, Colby Pharmaceuticals, Allergan, Pfizer, GlaxoSmithKline and Macular.

See "Business—Competition" for more information regarding potential competitive products.

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 to use or are less expensive than Fovista, Zimura or other products that we may develop. The commercial opportunity for Fovista also could be reduced or eliminated if our competitors develop and commercialize products that reduce or eliminate the use of anti-VEGF drugs for the treatment of patients with wet AMD. 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 less expensive or more convenient products. We expect that if Fovista is approved, the cost of treatment of wet AMD with a combination of Fovista with an anti-VEGF drug will be significantly higher than the cost of treatment of wet AMD with Avastin, Lucentis or Eylea monotherapy. Insurers and other third-party payors may encourage the use of anti-VEGF drugs as monotherapy and discourage the use of Fovista in combination with these drugs. This could limit sales of Fovista.

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. 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.

***We have no experience manufacturing Fovista or Zimura at commercial scale. As a result, delays in regulatory approval of Fovista or Zimura may occur. Also, manufacturing issues may arise that could cause delays or increase costs.***

We have no experience manufacturing the chemically synthesized aptamers comprising the active pharmaceutical ingredients, or API, of Fovista or Zimura at commercial scale. We currently rely on a single third-party manufacturer to supply us with API for both Fovista and Zimura and a different, single third-party manufacturer to provide fill-finish services for both Fovista and Zimura, in all cases, on a purchase order basis. In order to obtain regulatory approval for Fovista or Zimura, these third-party manufacturers will be required to consistently produce the API used in Fovista or Zimura in commercial quantities and of specified quality or execute fill-finish services on a repeated basis and document their ability to do so. This is referred to as process validation. If the third-party manufacturers are unable to satisfy this requirement, our business will be materially and adversely affected.

Our third-party manufacturer of API for Fovista and Zimura has made only a limited number of lots of Fovista and Zimura to date and has not made any commercial lots. The manufacturing processes for Fovista and Zimura have never been tested at commercial scale, and the process validation requirement has not yet been satisfied for either product candidate. These manufacturing processes and the facilities of our third-party manufacturers, including our third-party API manufacturer and our third-party manufacturer providing fill-finish services, will be subject to inspection and approval by the FDA before we can commence the manufacture and sale of Fovista or Zimura, and thereafter on an ongoing basis. Our third-party manufacturer for API has never been inspected by the FDA and has not been through the FDA approval process for a commercial product. Our third-party manufacturer providing fill-finish services is subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. Based on the severity of the regulatory action, our clinical or commercial supply of API or our fill-finish services could be interrupted or limited, which could have a material adverse effect on our business.

The standards of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, which establishes basic guidelines and standards for drug development in the United States, the European Union, Japan and other countries, do not apply

to oligonucleotides, including aptamers. As a result, there is no established generally accepted manufacturing or quality standard for the production of Fovista or Zimura. Even though the FDA has reviewed the quality standards for Fovista to be used in our Phase 3 clinical program, the FDA has the ability to modify these standards at any time and foreign regulatory agencies may impose differing quality standards and quality control on the manufacture of Fovista. The lack of uniform manufacturing and quality standards among regulatory agencies may delay regulatory approval of Fovista or Zimura.

Also, as we or any manufacturer we engage scales up manufacturing of any approved product, we may encounter unexpected issues relating to the manufacturing process or the quality, purity and stability of the product, and we may be required to refine or alter our manufacturing processes to address these issues. Resolving these issues could result in significant delays and may result in significantly increased costs. If we experience significant delays or other obstacles in producing any approved product for commercial scale, our ability to market and sell any approved products may be adversely affected and our business could suffer.

***If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing Fovista, Zimura or any other product candidate that we develop if and when Fovista, Zimura or any other product candidate is approved.***

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales, marketing and distribution organization or outsource those functions to third parties. If Fovista receives marketing approval, we plan to commercialize it in the United States with our own focused, specialty sales force targeting retinal specialists. In addition, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize Fovista in markets outside the United States.

There are risks involved with establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution 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 our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe our products;
- the lack of complementary products to be offered by our 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.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute ourselves any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our 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 our products 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 our product candidates.

***Even if we are able to commercialize Fovista, Zimura or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.***

The regulations that govern marketing approvals, pricing 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. 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.

Our ability to commercialize Fovista, Zimura or any other product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers 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 major trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors, particularly Medicare, 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. We cannot be sure that coverage and reimbursement will be available for Fovista, Zimura or any other product that we commercialize, and, even if these are available, the level of reimbursement may not be satisfactory.

Reimbursement may 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 particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician and because, in the case of Fovista, our drug will be administered in combination with other drugs that may carry high prices. In addition, physicians, patients and third-party payors may be sensitive to the addition of the cost of Fovista to the cost of treatment with anti-VEGF drugs. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies, including in the case of Fovista, relative to monotherapy with anti-VEGF drugs. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize Fovista, Zimura or any other product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. 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 profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We may expand our product pipeline through opportunistically in-licensing or acquiring the rights to complementary products, product candidates or technologies for the treatment of ophthalmic diseases. Because we expect generally that we will not engage in early stage research and drug discovery, the future growth of our business will depend in significant 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 complementary 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 business, financial condition and prospects for growth could suffer.

***Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop or in-license.***

We face an inherent risk of product liability exposure related to the testing of Fovista, Zimura and any other product candidate that we develop in human clinical trials and will face an even greater risk if we commercially sell any products that we develop or in-license. Because our Phase 3 clinical program for Fovista involves the administration of Fovista in combination with anti-VEGF drugs, including off-label use by intravitreal injection of Avastin provided by us, we also face an inherent risk of product liability exposure related to the testing of such anti-VEGF drugs. If we cannot successfully defend ourselves against claims that our product candidates, anti-VEGF drugs administered in combination with our product candidates or our 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 may develop or in-license;
- 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 may develop or in-license.

We currently hold \$10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of \$10.0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin commercializing Fovista, Zimura 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 may enter into collaborations with third parties for the development or commercialization of Fovista, Zimura and our other product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.***

If either of Fovista or Zimura receives marketing approval, we plan to commercialize such product candidate in the United States with our own focused, specialty sales force targeting retinal specialists. In addition, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize Fovista and Zimura in markets outside the United States. We also may seek third-party collaborators for development and commercialization of our 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. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. 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.

Collaborations involving our product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, product and product candidate priorities or available funding;
- 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;
- we could grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disagreements or disputes with collaborators, including disagreements or disputes over proprietary rights, contract interpretation or the preferred course of development, might cause

delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities for us with respect to product candidates or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and be expensive;

- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights, may infringe the intellectual property rights of third parties, may misappropriate our trade secrets 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 litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, our breach of the terms of the collaboration or other reasons and, if terminated, we may need to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If a collaborator of ours were to be involved in a business combination, the foregoing risks would be heightened, and the business combination may divert attention or resources or create competing priorities. The collaborator may delay or terminate our product development or commercialization program. If one of our collaborators terminates its agreement with us, we could find it more difficult to attract new collaborators and the perception of our company in the business and financial communities could be adversely affected.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

***If we are not able to establish collaborations, we may have to alter our development and commercialization plans.***

The potential commercialization of Fovista and the development and potential commercialization of Zimura and our other product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we intend to seek to commercialize Fovista through a variety of types of collaboration arrangements outside the United States.

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 and generate product revenue.

***We rely on third parties in conducting 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-party clinical research organizations, or CROs, in conducting our completed clinical trials of Fovista and Zimura. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, in conducting our clinical trials for Fovista and Zimura, including the clinical trials in our Phase 3 clinical program for Fovista, and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. We or these third parties may terminate their engagements with us at any time 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 clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we 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, or GCPs, 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 within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

***We contract with third parties for the manufacture of both Fovista and Zimura for clinical trials and expect to continue to do so in connection with the commercialization of Fovista and for clinical trials and commercialization of any other product candidates that we 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 Fovista or Zimura and have limited personnel with manufacturing experience.

We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture clinical and commercial supplies of Fovista and Zimura, preclinical and clinical supplies of other product candidates we may develop and commercial supplies of products if and when approved for marketing by applicable regulatory authorities. Our current and anticipated future dependence upon others for the manufacture of Fovista, Zimura 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 a single third-party manufacturer to provide clinical supplies of both Fovista drug substance and Zimura drug substance. We also engage a single third-party manufacturer to provide fill-finish services for clinical supplies of both Fovista and Zimura. We obtain these supplies and services from each of these manufacturers on a purchase order basis. We do not currently have any contractual commitments for commercial supply of bulk drug substance for either Fovista or Zimura 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 Fovista or Zimura or for fill-finish services. The prices at which we are able to obtain supplies of drug substance for Fovista or Zimura and fill-finish services may vary substantially over time and adversely affect our financial results. Furthermore, we currently rely on sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill-finish of each of Fovista and Zimura.

We currently rely exclusively on Nektar to supply us with a proprietary polyethylene glycol, or PEG, reagent for Fovista under a manufacturing and supply agreement. PEG reagent is a chemical we use to modify the chemically synthesized aptamer in Fovista. The PEG reagent made by Nektar is proprietary to Nektar and, to our knowledge, is not currently available from any other third party.

We obtain a different proprietary PEG reagent used to modify the chemically synthesized aptamer in Zimura from a different supplier on a purchase order basis. We do not currently have any contractual commitments for supply of the PEG reagent we use for Zimura.

If our third-party manufacturers for Fovista drug substance, Zimura drug substance or the PEG reagent we use for Zimura fail to fulfill our purchase orders, if Nektar breaches its obligations to us under our supply agreement, or if any of these manufacturers 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 for Fovista or Zimura if our existing third-party fill-finish provider should become unavailable for any reason. We may be unable to establish any agreements with such replacement manufacturers or fill-finish providers or to do so on acceptable terms.

Under the supply agreement with Nektar, we must purchase our entire requirements for PEG reagent for Fovista exclusively from Nektar at an agreed price. In the event Nektar breaches its supply obligations as specified in the agreement, Nektar has agreed to enable a third-party manufacturer, if one is available, to supply us with PEG reagent until Nektar demonstrates that Nektar has the ability to supply all of our requirements for PEG reagent. The agreement of Nektar to enable a third-party manufacturer may be difficult to enforce in the context of a breach by Nektar of its supply obligations. We may not be able to reach an agreement with any third-party manufacturer to take on the supply of PEG reagent under such circumstances because, to our knowledge, no third party currently manufactures the PEG reagent we currently use in making the Fovista drug substance. Furthermore, the third party's right to supply us with PEG reagent would be subject to termination at any time once Nektar demonstrates that Nektar has the ability to supply all of our requirements for PEG reagent, which may limit the interest of potential third-party manufacturers in undertaking such an engagement. In addition, the process of transferring any necessary technology or process to a third-party

manufacturer would entail significant delay in or disruption to the supply of PEG reagent and, as a result, a significant delay in or disruption to the manufacture of Fovista. Furthermore, the FDA or other regulatory authorities might require additional studies to demonstrate equivalence between the Fovista drug substance made using the Nektar PEG reagent and the Fovista drug substance made using any replacement PEG reagent we propose to use or between the Nektar PEG reagent itself and any replacement PEG reagent we propose to use to make Fovista. We ultimately may be unable to demonstrate such equivalence.

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

- Fovista, Zimura and any other product that we 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 and harm our business and results of operations.

***We depend on licenses and sublicenses for development and commercialization rights to our products, product candidates and technologies. Termination of these rights or the failure to comply with obligations under these or other agreements under which we obtain such rights could materially harm our business and prevent us from developing or commercializing our products and product candidates.***

We are party to various agreements, including an acquisition agreement with OSI Pharmaceuticals and license agreements with Archemix and Nektar that we depend on for rights to Fovista, Zimura and other product candidates and technology. These agreements impose, and we may enter into additional licensing arrangements or other agreements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our acquisition agreement with OSI Pharmaceuticals and our licensing agreement with Nektar, we are obligated to pay royalties on net product sales of Fovista or other product candidates or related technologies to the extent they are covered by the agreement. Under our license agreements with Archemix and Nektar, we would not be able to avoid our payment obligations even if we believed a licensed patent right was invalid or unenforceable because the license agreements provide that our licenses to all licensed patent rights would terminate if we challenge the validity or enforceability of any licensed patent right.

We also have diligence and development obligations under our acquisition agreement with OSI Pharmaceuticals and our license agreements with Archemix and Nektar. Generally, these diligence obligations require us to use commercially reasonable efforts to develop, seek regulatory approval for and commercialize our products in the United States, the European Union and, in some cases, certain other specified countries. If we fail to comply with our obligations under current or future acquisition, license and funding agreements, or otherwise breach an acquisition, license or funding agreement, our

counterparties may have the right to terminate these agreements, in which event we might not have the rights or the financial resources to develop, manufacture or market any product that is covered by these agreements. Our counterparties also may have the right to convert an exclusive license to non-exclusive in the territory in which we fail to satisfy our diligence obligations, which could materially adversely affect 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, seek alternative sources of financing or cause us to lose our rights under these agreements, including our rights to Fovista, Zimura and other important intellectual property or technology. Any of the foregoing could prevent us from commercializing Fovista, Zimura or our other product candidates, which could have a material adverse effect on our operating results and overall financial condition.

In addition to the generally applicable diligence obligations set forth above, we have specific obligations with respect to the licensing agreements described below:

- Under the terms of the agreement with OSI Pharmaceuticals under which we acquired certain rights to develop and commercialize Fovista, if we fail to meet our diligence obligations, OSI Pharmaceuticals may terminate the agreement as to such countries with respect to which such failure has occurred, and upon such termination we will be obligated to grant, assign and transfer to OSI Pharmaceuticals specified rights and licenses related to our anti-PDGF aptamer technology and other related assets, and if we are manufacturing such anti-PDGF products at the time of such termination, may be obligated to provide transitional supply to OSI Pharmaceuticals of covered anti-PDGF products, for such countries.
- Under the terms of the amended license, manufacturing and supply agreement with Nektar, pursuant to which we obtained, among other licenses, an exclusive, worldwide license to make, develop, use, import, offer for sale and sell certain products that incorporate a specified PEG reagent linked with the active ingredient in Fovista, if we fail to use commercially reasonable efforts to achieve the first commercial sale of Fovista in the United States or one of a specified group of other countries by December 31, 2017, which date Nektar and we may agree in good faith to extend in specified circumstances, Nektar may either terminate our license or convert our license for such country to a non-exclusive license. In addition, if we fail to use commercially reasonable efforts to develop Fovista and file and seek approval of NDAs on a schedule permitting us to make first commercial sales of Fovista in specified countries by December 31, 2017, do not make such first commercial sales of Fovista by such date, or thereafter fail to use commercially reasonable efforts to continue to commercialize and market Fovista in such countries, we will be in material breach of the agreement and Nektar will have the right to terminate the agreement.

In addition to the above risks, certain of our intellectual property rights are sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. For example, the licenses from Archemix include sublicenses to us of rights to specified technology, which we refer to as the SELEX technology, licensed by University License Equity Holdings, Inc. to Gilead Sciences, Inc., or Gilead, and sublicensed by Gilead to Archemix, as well as other technology owned by Gilead and licensed to Archemix. In addition, the licenses we have obtained from Nektar include sublicenses of certain rights. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize Fovista, Zimura and other product candidates may be materially harmed. While the applicable agreements may contain contractual provisions that would in many instances protect our rights as a sublicensee in these circumstances, these provisions may not be enforceable and may not protect our rights in all instances.



Further, we do not have the right to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and their upstream licensors, which may not be forthcoming. Our business could be materially adversely affected if we are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

### **Risks Related to Our Intellectual Property**

***The patent prosecution process is expensive and time-consuming, is highly uncertain and involves complex legal and factual questions. 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.***

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing in the United States and in certain foreign jurisdictions patent applications related to our novel technologies and product candidates that are important to our business.

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. In addition, we may not pursue or obtain patent protection in all major markets. Moreover, in some circumstances, we do not have the right to control the preparation, filing or prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In some circumstances, our licensors have the right to enforce the licensed patents without our involvement or consent, or to decide not to enforce or to allow us to enforce the licensed patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights that we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign jurisdictions 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 be certain that 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. Moreover, the United States Patent and Trademark Office might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, term, enforceability and commercial value of our patent rights are highly uncertain.

Our pending and future patent applications may not result in patents being issued which protect our technology or 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 or 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 U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation and switch the U.S. patent system from a "first-to-invent" system to a "first-to-file" system. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The U.S. Patent and Trademark Office recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, 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, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, 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.

***If we are unable to obtain and maintain patent protection for our technology and products during the period of their commercialization, or if the scope of the patent protection 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 adversely affected.***

The last to expire of the U.S. patent rights covering the composition of matter of Fovista is expected to expire in 2017. Such expiration date is not long after the date by which we expect Fovista to be commercialized in the United States if we obtain marketing approval and may even be prior to such date. We own an issued U.S. patent covering methods of treating wet AMD with Fovista in combination with Avastin or Lucentis, which is expected to expire in 2024. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent restoration term of up to five years as partial compensation for patent term effectively lost during product development and the FDA regulatory review process occurring after the issuance of a patent. We may be able to obtain a patent term extension for one of these U.S. patents. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term or scope of any such extension is less than we request, any period during which we have the right to exclusively market our product will be shorter than we would otherwise expect, and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

The European patent rights covering the composition of matter of Fovista are expected to expire in 2018. Such expiration date is shortly after the date by which we expect Fovista to be commercialized in Europe, and may even be prior to such date. We own a granted European patent covering a combination of Fovista and Lucentis or Avastin for use in a method for treating wet AMD. This European patent is expected to expire in 2024.

We also have filed in the United States patent applications covering a method of treating wet AMD in patients with Fovista in combination with Eylea and in Europe and Japan a patent application covering a combination of Fovista and Eylea for use in a method for treating wet AMD. These patent applications are in the early stages of prosecution and may not result in patents being issued which protect the use of Fovista in combination with Eylea for treating wet AMD or effectively prevent others from commercializing competitive technologies and products. If a patent is granted following prosecution of any such application, that patent would be expected to expire in 2030.

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 patented method. 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. Off-label sales of other products having the same active pharmaceutical ingredient as Fovista, Zimura or any of our other product candidates would limit our ability to generate revenue from the sale of Fovista, Zimura or such other product candidates, if approved for commercial sale. In addition, European patent law generally makes the issuance and enforcement of patents that cover methods of treatment of the human body difficult. Further, once the composition-of-matter patents relating to Fovista, Zimura or any other product candidate in a particular jurisdiction, if any, expire, competitors will be able to make, offer and sell products containing the same active pharmaceutical ingredient as Fovista, Zimura or such other product candidate in that jurisdiction so long as these competitors do not infringe any other of our patents covering Fovista's or Zimura's composition of matter or method of use or manufacture, do not violate the terms of any marketing or data exclusivity that may be granted to us by regulatory authorities and obtain any necessary marketing approvals from applicable regulatory authorities. In such circumstances, we also may not be able to detect, prevent or prosecute off-label use of such competitors' products containing the same active pharmaceutical ingredient as Fovista or Zimura in combination with any anti-VEGF drug, even if such use infringes any of our method-of-treatment patents.

The Hatch-Waxman act also permits the manufacture, use, offer for sale, sale or importation of a patented invention other than a new animal drug or veterinary biological product, if the manufacture, use, offer for sale, sale or importation is solely for uses that are reasonably related to development of information that could be submitted to the FDA. For this reason, our competitors might be able under certain circumstances to perform activities within the scope of the U.S. patents that we own or under which we are licensed without infringing such patents. This might enable our competitors to develop during the lifetime of these patents drugs that compete with Fovista or Zimura, if approved.

The U.S. patent rights covering Zimura as a composition of matter are expected to expire in 2025. Such expiration date may be prior to the date by which we would be able to commercialize Zimura in the United States if we seek and obtain marketing approval. The U.S. patent rights covering methods of treating certain complement protein mediated disorders with Zimura are expected to expire in 2026. As a result, if we obtain marketing approval for Zimura, we may not be able to exclude competitors from commercializing products similar or identical to ours if such competitors do not use or promote our claimed methods of treatment or do use or promote our methods of treatment after our patents expire. Depending on potential delays in the regulatory review process for Zimura, we may be able to obtain a patent term extension for one of these patents in the United States, but we can provide no assurances that such an extension will be obtained.

Our issued patents may not be sufficient to provide us with a competitive advantage. For example, competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Even if our owned or licensed patent applications issue as patents, they may not issue with a scope broad enough to provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. We could also fail to take the required actions and pay the necessary governmental fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, term, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, if we receive marketing approval for our product candidates, other pharmaceutical companies may seek approval of generic versions of our products with the FDA or regulatory authorities in other jurisdictions. We may then be required to initiate proceedings against such companies in an attempt to prevent them from launching such generic versions. The risk of being involved in such proceedings is likely to increase if our products are commercially successful. In any such proceedings, the inventorship, ownership, scope, term, validity and enforceability of our patents may be challenged. These and other 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 prevent others from using or commercializing similar or identical technology and products or from launching generic versions of our products, or could limit the duration of the patent protection of our technology and products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for our product, which could have a material adverse effect on our business. 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 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 or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable. 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 or otherwise violating 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 products and use our proprietary technologies

without infringing or otherwise violating the intellectual property and other 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, derivation, re-examination, post-grant review, opposition, cancellation or similar proceedings before the U.S. Patent and Trademark Office or its foreign counterparts. The risks of being involved in such litigation and proceedings may also 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 or future intellectual property rights. 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 Fovista, Zimura or any other product candidate, or our intended commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

If we are found to infringe or otherwise violate 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 or to continue using a trademark. 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 and could require us to make substantial licensing and royalty payments. 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 or other intellectual property right. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could expose us to similar liabilities and have a similar negative impact on our business.

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

Many of our employees and contractors 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 and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or contractor'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 conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. Moreover, because we acquired rights to Fovista from Eyetech, Archemix and Nektar, we must rely on these parties' practices, and those of their predecessors, with regard to the assignment of intellectual property therein. 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.

***Intellectual property litigation could cause us to spend substantial resources and could 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 have a material adverse effect on 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 products, 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. We cannot guarantee that we have executed such agreements with each party that may have or have had access to our trade secrets. Moreover, because we acquired certain rights to Fovista from Eyetech, Archemix and Nektar, we must rely on these parties' practices, and those of their predecessors, with regard to the protection of Fovista-related trade secrets before we acquired them. Any party with whom we or they have executed a non-disclosure and confidentiality agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our proprietary information may also be obtained by third parties by other means, such as breaches of our physical or computer security systems.

Detecting the disclosure or misappropriation of a trade secret and 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 and Other Legal Compliance Matters**

***If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize Fovista, Zimura or any other product candidate that we develop, and our ability to generate revenue will be materially impaired.***

Our product candidates, including Fovista and Zimura, and the activities associated with their development and commercialization, including their 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 comparable authorities in other countries.

Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market Fovista, Zimura 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. 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 and efficacy. 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 Fovista, Zimura or any other product candidate that we develop is not effective, 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. The FDA or other regulatory authority may limit the approval of Fovista to use with only specified anti-VEGF drugs rather than with all anti-VEGF drugs. Such limitation could limit sales of Fovista.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. 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.

Marketing approval of novel product candidates such as Fovista and Zimura manufactured using novel manufacturing processes can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to regulatory agencies' lack of experience with them. We believe that the FDA has only granted marketing approval for one aptamer product to date. This lack of experience 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 approval or if we fail to obtain approval of Fovista, Zimura or any other product candidate that we develop, the commercial prospects for such product candidate may be harmed and our ability to generate revenues will be materially impaired.

***A fast track designation or grant of priority review status by the FDA may not actually lead to a faster development or regulatory review or approval process.***

In the United States, our lead product candidate, Fovista, received fast track designation and may be eligible for priority review status. If a drug is intended for the treatment of a serious or life-threatening disease or condition and the drug demonstrates the potential to address unmet medical needs for this disease or condition, the drug sponsor may apply for FDA fast track designation. If a drug offers major advances in treatment, the drug sponsor may apply for FDA priority review status. The FDA has broad discretion whether or not to grant fast track designation or priority review status, so even if we believe a particular product candidate is eligible for such designation or status, the FDA

could decide not to grant it. Even though Fovista has received fast track designation for the treatment of wet AMD and may be eligible for priority review status, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

***Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.***

In order to market and sell Fovista, Zimura and any other product candidate that we 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 approved for sale 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.

***Any product candidate, including Fovista and Zimura, for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.***

Any product candidate, including Fovista and Zimura, for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance, complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or may be subject to significant conditions of approval.

The FDA may also impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of risk evaluation and mitigation strategies. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations 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 and warnings in the labeling and marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can lead to significant penalties and sanctions.

***Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates, including Fovista, 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. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute 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;
- the federal False Claims Act imposes 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, 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, 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 and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Health Care Reform Law and analogous state laws require manufacturers of drugs, devices, biologics and medical supplies to report information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

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

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will 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, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.***

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

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products and could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug 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 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 potential products 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;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 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 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.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, or in-licensed products, if any, may be.

***Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.***

The pricing of prescription pharmaceuticals is also subject to governmental control outside of 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 business could be harmed, possibly materially.

***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 costs that could harm our business.***

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 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 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 our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.***

We are highly dependent on David R. Guyer, M.D., our Chief Executive Officer, Samir Patel, M.D., our President, and Bruce Peacock, our Chief Financial and Business Officer, as well as the other principal members of our management, scientific and clinical teams. 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 marketing 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, if at all, 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 are rapidly expanding our development, regulatory and sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We are currently experiencing significant and rapid growth in the number of our employees and the scope of our operations, particularly in the area of clinical development. Between January 1, 2013 and January 31, 2014, we hired more than half of our 33 employees. We also expect to continue to hire additional employees and expand the scope of our operations in the area of clinical development and, as we approach potential marketing approval for any of our product candidates, in the area of sales, marketing and distribution. To manage our 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 inherent challenges associated with managing such rapid growth, we may not be able to manage effectively 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 and this Offering**

***After this offering, our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to stockholders for approval.***

Upon the closing of this offering, assuming no exercise by the underwriters of their option to purchase additional shares, our executive officers, directors and principal stockholders and their affiliates, will, in the aggregate, beneficially own shares representing approximately 61.93% 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 could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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

Provisions in our certificate of incorporation and our by-laws 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 you might otherwise receive a premium for your 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:

- provide for 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 the board of directors;

- provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or by-laws.

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.

***If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.***

The price of our common stock in this offering will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent outstanding options or warrants are exercised, you will incur further dilution. Based on the public offering price of \$31.50 per share, you will experience immediate dilution of \$24.13 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the public offering price.

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

Our shares of common stock began trading on The NASDAQ Global Select Market on September 25, 2013. 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 your ability to sell your shares.

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.***

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology 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, you may not be able to sell the shares of common stock you acquire in this offering at or above the price you paid in this offering. 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 Fovista, Zimura and any other product candidate that we 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 personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to in-license or acquire the rights to other products, product candidates and 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 Fovista. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources, which could seriously harm our business.

***We have broad discretion in the use of our available cash and other sources of funding, including the net proceeds we receive from this offering, and may not use them effectively.***

Our management has broad discretion in the use of our available cash and other sources of funding, including the net proceeds we receive in this offering, and could spend those resources in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our available cash, including the net proceeds we receive in this offering, in a manner that does not produce income or that loses value.

***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 could occur at any time. These sales, 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 January 31, 2014, we had outstanding 31,418,575 shares of common stock. Of these shares, 20,859,451 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 initial public offering but will be able to be sold beginning on March 24, 2014. Additionally, 20,812,620 of those shares are subject to lock-up agreements entered into in connection with this offering but will be able to be sold beginning on May 12, 2014, which is the date that is 90 days after the date of this prospectus. 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 initial public offering or this offering, may be resold in the public market without restriction unless purchased by our affiliates. Moreover, assuming no exercise by the underwriters of their option to purchase additional shares, holders of an aggregate of 19,668,672 shares of our common stock, including shares issuable pursuant to outstanding warrants, have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, subject to waiver or expiration of the applicable lock-up agreements. In October 2013 and January 2014, we filed registration statements registering all shares of common stock that we may issue under our equity compensation plans. These shares 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 offerings. See "Shares Eligible for Future Sale" for more information and the "Underwriters" section of this prospectus for a description of the lock-up agreements entered into in connection with our initial public offering and this 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 shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and 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 elected to delay such adoption of new or revised accounting standards, and, as a result, we may not 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. As a result of such election, our financial statements may not be comparable to the financial statements of other public companies.

***We incur increased costs as a result of operating as a public company, and our management is now 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 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 Select 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. We currently estimate that we will incur incremental annual costs, including costs for additional personnel, of approximately \$2.0 million associated with operating as a public company, although it is possible that our actual incremental annual costs will be higher than we currently estimate.

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 2018 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 will be 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 will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to 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, 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 your 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 any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "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 prospectus include, among other things, statements about:

- the timing, costs, conduct and outcome of our clinical trials of Fovista administered in combination with anti-VEGF drugs for the treatment of wet age-related macular degeneration, or AMD, including statements regarding the timing of the initiation of, the availability of, and the costs to obtain, initial top-line results from, and the completion of such trials and the timing of regulatory filings;
- our plans to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need, including statements regarding the timing of the initiation of, and the costs to obtain and timing of receipt of initial results from, and the completion of related clinical trials;
- our plans to develop Zimura, including our plans to initiate a Phase 2/3 clinical trial evaluating the safety and efficacy of Zimura for the treatment of patients with geographic atrophy, a severe form of dry AMD, and a Phase 2 clinical trial evaluating the safety and efficacy of Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of certain forms of wet AMD, including statements regarding the timing of the initiation of, and the costs to obtain and timing of receipt of initial results from, and the completion of related clinical trials;
- our plans to develop our other product candidates, including statements regarding the timing of the initiation of, the availability of, and the costs to obtain, initial top-line results from, and the completion of clinical trials and the timing of regulatory filings;
- the timing of and our ability to obtain marketing approval of Fovista and our other product candidates, and the ability of Fovista and our other product candidates to meet existing or future regulatory standards;
- the potential advantages of Fovista and Zimura;
- the rate and degree of market acceptance and clinical utility of Fovista and Zimura;
- our estimates regarding the potential market opportunity for Fovista and Zimura;
- the potential receipt of revenues from future sales of Fovista and Zimura;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of Fovista, Zimura and our other product candidates;
- our ability to in-license or acquire complementary products, product candidates or technologies;
- our intellectual property position;
- our expectations related to our use of available cash, including the net proceeds from this offering;

- our estimates regarding expenses, future revenues, capital requirements and needs 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 you 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 prospectus, particularly in the "Risk Factors" section, that we believe 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 prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part 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 prospectus are made as of the date of this prospectus, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

## USE OF PROCEEDS

We estimate that the net proceeds to us from our issuance and sale of 1,900,000 shares of our common stock in this offering will be approximately \$55.5 million, based on the public offering price of \$31.50 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We will not receive any of the proceeds from any sale of shares in this offering by the selling stockholders.

We currently estimate that we will use the net proceeds we receive from this offering as follows:

- approximately \$25.0 million to fund additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need;
- approximately \$25.0 million to fund a Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy, a severe form of dry AMD, and a Phase 2 clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of wet AMD patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF therapy fails, who we refer to as anti-VEGF resistant, and who are believed to have complement mediated inflammation; and
- the remainder for working capital and other general corporate purposes, which may include the acquisition or licensing of other products or technologies.

This expected use of the net proceeds we receive from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds we receive from this offering and our other cash resources. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any products, businesses or technologies.

Based on our planned use of the net proceeds we receive from this offering, we estimate that such funds will be sufficient to enable us to complete our planned additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need and to complete a Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy and a Phase 2 clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation. We have based this estimate on assumptions that may prove to be wrong, and we could use these available capital resources sooner than we currently expect.

Pending our use of the net proceeds we receive from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

### PRICE RANGE OF COMMON STOCK

Our common stock has been publicly traded on The NASDAQ Global Select Market under the symbol "OPHT" since September 25, 2013. Prior to that time, there was no public market for our common stock. The following table sets forth the high and low sale prices per share for our common stock on The NASDAQ Global Select Market for the periods indicated:

	<u>High</u>	<u>Low</u>
<b>2013</b>		
Third Quarter (September 25, 2013 to September 30, 2013)	\$ 31.99	\$ 23.00
Fourth Quarter	\$ 36.60	\$ 22.61
<b>2014</b>		
First Quarter (through February 11, 2014)	\$ 33.33	\$ 28.60

On February 11, 2014, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$32.65 per share. As of January 31, 2014, we had approximately 54 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

**DIVIDEND POLICY**

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. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of September 30, 2013:

- on an actual basis;
- on an as adjusted basis to give further effect to our issuance and sale of 1,900,000 shares of our common stock in this offering at the public offering price of \$31.50 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with "Selected Financial Data," our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus.

	As of September 30, 2013	
	(unaudited)	
	Actual	As Adjusted(1)
	(in thousands)	
Cash and cash equivalents	\$ 236,079	\$ 291,538
Total liabilities	49,575	49,575
Stockholders' equity:		
Common stock—\$0.001 par value, authorized 200,000,000 shares actual and as adjusted; issued and outstanding 31,250,817 shares actual, 33,150,817 shares as adjusted	31	33
Additional paid-in capital	351,431	406,888
Deficit accumulated during the development stage	(162,661)	(162,661)
Total stockholders' equity	188,801	244,260
Total capitalization	<u>\$ 238,376</u>	<u>\$ 293,835</u>

- (1) The unaudited as adjusted capitalization data do not give effect to our receipt on January 23, 2014 of the second tranche of \$41.7 million in royalty financing under our royalty purchase agreement with Novo A/S.

The table above does not include:

- 2,620,324 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2013, at a weighted-average exercise price of \$6.51 per share;
- 739,317 additional shares of our common stock available for future issuance as of September 30, 2013 under our 2013 stock incentive plan and an additional 1,256,528 shares of common stock that became available for future issuance under our 2013 stock incentive plan on January 1, 2014; and
- 101,324 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2013, at a weighted-average exercise price of \$5.47 per share.

## DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock after this offering.

Our historical net book value as of September 30, 2013 was \$188.8 million, or \$6.04 per share of our common stock. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of September 30, 2013.

After giving effect to our issuance and sale of 1,900,000 shares of our common stock in this offering at the public offering price of \$31.50 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2013 would have been \$244.3 million, or \$7.37 per share. This represents an immediate increase in as adjusted net tangible book value per share of \$1.33 to existing stockholders and immediate dilution of \$24.13 in as adjusted net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$ 31.50
Historical net tangible book value per share as of September 30, 2013	\$ 6.04
Increase per share attributable to new investors	<u>1.33</u>
As adjusted net tangible book value per share after this offering	7.37
Dilution per share to new investors	<u>\$ 24.13</u>

The table above does not include:

- 2,620,324 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2013, at a weighted average exercise price of \$6.51 per share;
- 739,317 additional shares of our common stock available for future issuance as of September 30, 2013 under our 2013 stock incentive plan and an additional 1,256,528 shares of common stock that became available for future issuance under our 2013 stock incentive plan on January 1, 2014; and
- 101,326 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2013, at a weighted average exercise price of \$5.47 per share.

If any additional shares are issued in connection with outstanding options or warrants, you will experience further dilution.



## SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statements of operations data for the years ended December 31, 2012 and 2011 and the balance sheet data as of December 31, 2012 and 2011 from our audited financial statements included in this prospectus, which have been audited by Ernst & Young LLP, an independent registered accounting firm. We have derived the statements of operations data for the nine months ended September 30, 2013 and 2012 and the balance sheet data as of September 30, 2013 from our unaudited financial statements included in this prospectus. The unaudited financial data include, in the opinion of our management, all adjustments, consisting of normal recurring adjustments, that are necessary for a fair statement of our financial position and results of operations for these periods. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results to be expected for a full fiscal year.

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2011	2013	2012
(unaudited)				
(In thousands, except per share data)				
<b>Statement of Operations Data:</b>				
Revenue	\$ —	\$ —	\$ —	\$ —
Operating expenses:				
Research and development	6,792	13,896	17,836	4,794
General and administrative	6,889	5,738	9,145	5,341
Total operating expenses	13,681	19,634	26,981	10,135
Loss from operations	(13,681)	(19,634)	(26,981)	(10,135)
Interest (expense) income	(507)	2	(1,454)	(256)
Loss on extinguishment of debt	—	—	(1,091)	—
Other loss	(374)	(30)	(1,231)	(340)
Net loss before income taxes benefit	(14,562)	(19,662)	(30,757)	(10,731)
Income tax benefit	—	1,029	—	—
Net loss	(14,562)	(18,633)	(30,757)	(10,731)
Accretion of preferred stock dividends	(7,063)	(6,838)	(5,891)	(5,288)
Net loss attributable to common stockholders	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>	<u>\$ (36,648)</u>	<u>\$ (16,019)</u>
Per share information:				
Net loss attributable to common stockholders per share, basic and diluted	<u>\$ (14.89)</u>	<u>\$ (18.27)</u>	<u>\$ (23.21)</u>	<u>\$ (11.07)</u>
Weighted-average shares outstanding—basic and diluted	<u>1,452</u>	<u>1,394</u>	<u>1,579</u>	<u>1,447</u>
Unaudited pro forma basic and diluted net loss attributable to common stockholders per share	<u>\$ (0.65)</u>			
Unaudited pro forma basic and diluted weighted-average shares outstanding	<u>22,491</u>			

Pro forma basic and diluted net loss per common share is computed using a weighted-average number of common shares outstanding and gives effect to the automatic conversion of all outstanding

shares of our preferred stock, including shares of our series C preferred stock that we issued and sold in May 2013 and August 2013 and additional shares of preferred stock that were issued as accrued stock dividends, into an aggregate of 21,038,477 shares of our common stock upon the closing of our initial public offering, which occurred on September 30, 2013.

	As of December 31,		As of
	2012	2011	September 30, 2013 (unaudited)
	(In thousands)		
<b>Balance sheet data:</b>			
Cash and cash equivalents	\$ 4,304	\$ 6,396	\$ 236,079
Total assets	\$ 4,879	\$ 7,728	\$ 238,376
Royalty purchase liability	\$ —	\$ —	\$ 41,667
Preferred stock	\$ 113,939	\$ 106,877	\$ —
Additional paid-in capital	\$ —	\$ —	\$ 351,431
Deficit accumulated during the development stage	\$ (126,471)	\$ (105,488)	\$ (162,661)
Total stockholders' equity (deficit)	\$ (123,470)	\$ (102,487)	\$ 188,801

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, which includes forward looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described, in or implied, by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the back of the eye, with a focus on developing therapeutics for age-related macular degeneration, or AMD. Our most advanced product candidate is Fovista, which is in Phase 3 clinical development for use in combination with anti-VEGF drugs that represent the current standard of care for the treatment of wet AMD. We have completed one Phase 1 and one Phase 2b clinical trial of Fovista administered in combination with the anti-VEGF drug Lucentis. We are also developing our product candidate Zimura, with an initial focus on the treatment of patients with geographic atrophy, a severe form of dry AMD.

We have initiated a pivotal Phase 3 clinical program for Fovista, which consists of three separate Phase 3 clinical trials to evaluate the safety and efficacy of Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD compared to anti-VEGF monotherapy. Two of these trials are evaluating Fovista in combination with Lucentis and the other will evaluate Fovista in combination with each of Eylea or Avastin. We plan to enroll a total of 1,866 patients at more than 225 centers internationally across the three trials.

We have initiated enrollment in the two trials evaluating Fovista administered in combination with Lucentis. We expect to activate initial trial sites in the third trial in this Phase 3 clinical program in the United States by the end of the first quarter of 2014. Based on our estimates regarding patient enrollment, we expect to have initial, top-line data from our Phase 3 clinical program for Fovista available in 2016. If the results of this Phase 3 clinical program are favorable, we plan to submit applications for marketing approval for Fovista in both the United States and the European Union before the end of 2016. We are planning to initiate additional Phase 2 clinical trials further evaluating the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs. We are also planning additional clinical trials to assess the potential therapeutic benefit of Fovista in other ophthalmic conditions. We have retained the worldwide commercialization rights to Fovista.

We plan to initiate a Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with geographic atrophy in late 2014 or early 2015. We are also developing Zimura and Fovista to be administered in combination with anti-VEGF drugs for the treatment of a subpopulation of wet AMD patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy fails and who are believed to have complement mediated inflammation. We plan to initiate a Phase 2 clinical trial of Zimura and Fovista administered in combination with an anti-VEGF drug in this second indication in 2015.

We were incorporated and commenced active operations in early 2007. Our operations to date have been limited to organizing and staffing our company, acquiring rights to product candidates, business planning, raising capital and developing Fovista, Zimura and our other product candidates. We acquired our rights to Fovista from (OSI) Eyetech, Inc., or Eyetech, in July 2007. The acquisition included an assignment of license rights and obligations under an agreement with Archemix Corp. We

have licensed rights to our product candidate Zimura from Archemix Corp. Since inception, we have incurred significant operating losses. Our net loss was \$30.8 million for the nine months ended September 30, 2013, \$14.6 million for the year ended December 31, 2012, and \$18.6 million for the year ended December 31, 2011. As of September 30, 2013, we had a deficit accumulated during the development stage of \$162.7 million. To date, we have not generated any revenues and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, our royalty agreement with Novo A/S and our initial public offering, which we closed in September 2013. We issued and sold an aggregate of 8,740,000 shares of common stock in our initial public offering at a public offering price of \$22.00 per share, including 1,140,000 shares pursuant to the exercise by the underwriters of an over-allotment option. We received net proceeds from the initial public offering of \$175.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We have also received \$83.3 million of royalty funding to date under our royalty agreement with Novo A/S. Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. We do not expect to generate significant revenue unless, and until, we obtain marketing approval for, and commercialize, Fovista or Zimura.

We expect our expenses to increase substantially as compared to prior periods in connection with our ongoing activities, particularly as we continue the development of and seek marketing approval for Fovista, Zimura and, possibly, other product candidates. In addition, if we obtain marketing approval for Fovista, Zimura or any other product candidate that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Furthermore, we incur additional costs associated with operating as a public company, hiring additional personnel and expanding our facilities. These costs include significant legal, accounting, investor relations and other expenses that we did not incur as a private company. Moreover, additional rules and regulations applicable to public companies will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. We currently estimate that we will incur incremental annual costs, including costs for additional personnel, of approximately \$2.0 million associated with operating as a public company, although it is possible that our actual incremental costs will be higher than we currently estimate. The increased costs will increase our net loss. 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. Our ability to generate product revenues, which we do not expect will occur before 2017, at the earliest, will depend heavily on our obtaining marketing approval for and commercializing Fovista or Zimura.

### ***Research and Development Expenses***

Research and development expenses consist of costs associated with the development and clinical testing of Fovista, Zimura and our other product candidates. Our research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, and other vendors, contract manufacturing organizations and consultants; and
- employee-related expenses, including salaries, benefits, travel and share-based compensation expense.

All research and development costs are charged to operations as incurred in accordance with Accounting Standards Codification, or ASC, 730 *Research and Development*. We account for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made. From inception through September 30, 2013, we have incurred approximately \$92.7 million of total research and development expenses.

To date, the large majority of our research and development work has been related to Fovista, Zimura and a product candidate, volociximab, that we were previously developing for the treatment of wet AMD. We licensed rights to volociximab in January 2008 and then terminated the license agreement in May 2012 to focus on the development of Fovista. We anticipate that our research and development expenses will increase substantially as compared to prior periods in connection with our ongoing activities, particularly as we continue the development of and seek marketing approval for Fovista, Zimura and, possibly, other product candidates.

We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis because we record expenses by functional department. Accordingly, we do not allocate expenses to individual projects or product candidates, although we do allocate some portion of our research and development expenses by functional area and by compound, as shown below.

The following table summarizes our research and development expenses for the years ended December 31, 2012 and 2011 and for the nine months ended September 30, 2013 and 2012:

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2011	2013	2012
	(in thousands)			
Fovista	\$ 3,619	\$ 9,864	\$ 14,073	\$ 2,530
Zimura	36	547	13	31
Volociximab	23	457	7	19
Personnel related	2,749	2,813	2,971	2,068
Share-based compensation	343	120	753	124
Other	22	95	19	22
	<u>\$ 6,792</u>	<u>\$ 13,896</u>	<u>\$ 17,836</u>	<u>\$ 4,794</u>

We recorded research and development expenses from inception to September 30, 2013 of approximately \$38.4 million related to Fovista, approximately \$11.1 million related to Zimura and approximately \$5.6 million related to volociximab.

We expect to obtain initial, top-line data from our Fovista Phase 3 clinical program in 2016. We expect that the net proceeds we receive from this offering, together with our existing cash and cash equivalents of \$236.1 million as of September 30, 2013, the \$41.7 million received under our royalty agreement with Novo A/S in January 2014 and potential future funding of \$41.7 million under such royalty agreement, will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2016. We are planning to spend significant additional funds on our Phase 3 clinical program for Fovista, our other planned clinical programs, including additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need, an additional planned clinical trial evaluating Zimura for the treatment of geographic atrophy and an additional planned clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation, and for general corporate purposes and working capital. Costs related to our

clinical programs could exceed our expectations if we experience delays in our clinical trials, including because of the timing of our patient enrollment, the availability of drug supply for our clinical trials or for other reasons. Our costs will also increase if we increase investigator fees for our clinical trials or decide to expand the scope of our clinical trials and programs, including, for example, by expanding the geographic mix of sites at which patients are enrolled, or to increase other corporate or licensing activities, or staffing. These costs will also increase if we decide to expand the scope of our clinical programs or increase other corporate or licensing activities or staffing.

Our current Phase 3 clinical program for Fovista is expected to continue through at least 2017, and substantial expenditures to complete the Phase 3 clinical program will be required after the receipt of initial, top-line data. Moreover, we are at the early stages of formulating our clinical development plan for Zimura. We expect the clinical development of Zimura will continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete the clinical development of either Fovista or Zimura, complete process development and manufacturing scale-up activities associated with Fovista and Zimura and seek marketing approval for Fovista or Zimura, or the nature, timing or costs of the efforts necessary to complete the development of any other product candidate we may develop.

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

- the scope, rate of progress and expense of our research and development activities;
- the potential benefits of our product candidates over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates;
- clinical trial results;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights.

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

#### ***General and Administrative Expenses***

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

We anticipate that our general and administrative expenses will increase in future periods to support increases in our research and development and commercialization activities and as a result of increased headcount, including management personnel to support our clinical and manufacturing activities, expanded infrastructure, increased legal, compliance, accounting and investor and public relations expenses associated with being a public company and increased insurance premiums, among other factors.

### ***Change in Fair Value of Warrant Liability***

In connection with our series A preferred stock financing and our venture debt financing, we issued warrants for the purchase of shares of our series A preferred stock and series B preferred stock. We determined that these warrants were financial instruments that could have required a transfer of assets because of the redemption features of the underlying preferred stock. We classified these warrants as liabilities that were re-measured to fair value at each balance sheet date, and we recorded the changes in the fair value of the warrant liability as other loss. Upon completion of our initial public offering, or IPO, the underlying preferred stock was converted to common stock and the preferred stock warrants became exercisable for common stock. We re-measured the fair value of the warrant liability immediately prior to the completion of our IPO, and the fair value of the warrant liability at that time was reclassified to additional paid-in capital. Based on the initial public offering price of \$22.00 per share, the fair value of the warrant liability that was reclassified to additional paid-in capital was \$2.2 million. We recorded a related charge of approximately \$1.0 million and \$1.2 million as other loss in our results of operations for the three and nine months ended September 30, 2013, respectively. The warrants were reclassified to stockholders' equity upon the closing of our IPO.

### ***Interest Income***

Our cash and cash equivalents are invested primarily in money market accounts, which generate a small amount of interest income. We expect to continue that investment philosophy as we obtain more financing proceeds.

### ***Critical Accounting Policies and Significant Judgments and Estimates***

Our 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 accrued expenses and share-based compensation described in greater detail below. We base our estimates on our limited 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.

Our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this prospectus. However, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

### ***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 quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. 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 or payable 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 us 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.

#### ***Royalty Purchase Liability***

The proceeds from the first financing tranche under our royalty agreement with Novo A/S have been recorded as a liability on our balance sheet in accordance with Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 730. Because there is a significant related party relationship between us and Novo A/S, we are treating our obligation to make royalty payments under the royalty agreement as an implicit obligation to repay the funds advanced by Novo A/S, and thus have recorded the proceeds as a liability on our balance sheets. As we make royalty payments to Novo A/S in accordance with the royalty agreement, we will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, we will impute interest accordingly on a prospective basis based on such estimates, which would result in a corresponding increase in the liability balance.

#### ***Income Taxes***

As of December 31, 2012, we had approximately \$84.2 million of federal net operating loss carry-forwards. We also had federal and state research and development tax credit carry-forwards of approximately \$2.3 million available to offset 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 are fully offset by a valuation allowance at December 31, 2012 and 2011. These federal and state net operating loss and federal and state credit carry-forwards will begin to expire at various dates beginning in 2027, if not utilized. Utilization of the net operating losses 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 net operating losses and general business tax credits carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, 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 determined we have experienced an ownership change upon closing of our initial Series A tranche in August 2007. We have not completed a study to determine the impact of this ownership change on our NOL carry-forwards under Section 382 of the Code. If we experience a Section 382 ownership change in connection with this offering or 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 carry forwards may be further limited or lost.

### **Preferred Stock**

Prior to the completion of our IPO and the conversion of all outstanding shares of preferred stock into common stock, we accrued for stock and cash dividends accrued on our preferred stock on an annual basis.

### **Share-Based Compensation**

We account for all share-based compensation payments issued to employees, directors, and non-employees using an option pricing model for estimating fair value. Accordingly, share-based compensation expense is measured based on the estimated fair value of the awards on the date of grant, net of 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 single option method. In accordance with authoritative guidance, we re-measure the fair value of non-employee share-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*, which we refer to as ASC 718. Determining the amount of share-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. We recognize share-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 share-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.

We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of stock option grants to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention to pay cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life. The weighted-average assumptions used to estimate the fair value of stock options using the Black-Scholes option pricing

model were as follows for the years ended December 31, 2012 and 2011 and for the nine months ended September 30, 2013 and 2012:

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2011	2013	2012
Expected volatility	80%	79%	82%	81%
Risk-free interest rate	0.94% - 1.77%	1.72% - 2.38%	0.89% - 2.69%	1.16% - 1.51%
Expected term of options (years)	6.6	6.7	6.2	6.3
Expected annual dividend per share	\$—	\$—	\$—	\$—

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 share-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 were revised. Through September 30, 2013, actual forfeitures have not been material.

Share-based compensation expense associated with stock options granted to employees and non-employees was \$0.6 million for the year ended December 31, 2012, \$0.2 million for the year ended December 31, 2011 and \$1.6 million for the nine months ended September 30, 2013. As of September 30, 2013, we had \$11.6 million of total unrecognized share-based compensation expense, which we expect to recognize over a weighted-average remaining vesting period of approximately 3.4 years. While our share-based compensation for stock options granted to employees and non-employees to date has not been material to our financial results, in future periods, our share-based compensation expense is expected to increase as a result of recognizing our existing unrecognized share-based compensation for awards that will vest and as we issue additional share-based awards to attract and retain our employees.

For the years ended December 31, 2012 and 2011 and for the nine months ended September 30, 2013 and 2012, we allocated share-based compensation as follows:

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2011	2013	2012
	(in thousands)			
Research and development	\$ 412	\$ 159	\$ 1,052	\$ 182
General and administrative	228	89	555	101
Total	\$ 640	\$ 248	\$ 1,607	\$ 283

#### ***Pre-IPO Fair Market Value Estimates***

Prior to the completion of our initial public offering on September 30, 2013, we were required to estimate the fair market value of the common stock underlying our share-based awards when performing the fair value calculations with the Black-Scholes option-pricing model. The fair market value of the common stock underlying our share-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 market 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 market value of our common stock in order to determine an exercise price for the option grants. We determined the fair market value of our common

stock 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 market value of our common stock, including:

- external market conditions affecting the biotechnology industry;
- trends within the biotechnology industry;
- the prices at which we sold shares of preferred stock;
- the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- our results of operations and financial position;
- the status of our research and development efforts;
- our stage of development and business strategy;
- the lack of an active public market for our capital stock; and
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions.

The per share estimated fair market value of common stock in the table below represents the determination by our board of directors of the fair market 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. We computed the per share weighted average estimated fair value for stock option grants based on the Black-Scholes option pricing model. The following table sets forth information about our stock option grants since January 1, 2011 on a monthly basis for each month during which we granted stock options:

<b>Month of Grant</b>	<b>Number of shares underlying option grants</b>	<b>Exercise price per option</b>	<b>Per share estimated fair market value of common stock</b>	<b>Per share weighted average estimated fair value of options</b>
February 2011	3,812	\$ 1.65	\$ 1.65	\$ 1.36
May 2011	180,162	\$ 1.65	\$ 1.65	\$ 1.18
February 2012	16,524	\$ 1.65	\$ 1.65	\$ 1.36
April 2012	190,670	\$ 1.65	\$ 1.65	\$ 1.12
December 2012	43,218	\$ 10.03	\$ 10.03	\$ 7.61
April 2013	674,958	\$ 10.03	\$ 10.03	\$ 6.96
May 2013	132,358	\$ 13.22	\$ 13.22	\$ 9.09
July 2013	437,964	\$ 13.22	\$ 13.22	\$ 9.38
August 2013	34,064	\$ 15.99	\$ 15.99	\$ 12.69

In determining the exercise prices of the options set forth in the table above granted since January 1, 2011, our board of directors considered the most recent valuations of our common stock, which were prepared as of June 2010, December 2011, November 2012, May 2013 and August 2013, and based its determination in part on the analyses summarized below.

The intrinsic value of our approximately 1,091,000 vested options as of September 30, 2013 was \$30.8 million, based on a per share price of \$29.71, which was the last reported sale price of our common stock on The NASDAQ Global Select Market on such date, and a weighted average exercise price of \$1.36 per share. The intrinsic value of our approximately 1,529,000 unvested options as of September 30, 2013 was \$30.5 million, based on a per share price of \$29.71 and a weighted average exercise price of \$9.76 per share.

### ***Pre-IPO Valuations***

Prior to our initial public offering, our valuations utilized the probability-weighted expected return method, or PWERM, to allocate the enterprise value to the common stock. Under this method, the per share fair market value of the common stock was estimated based upon the probability-weighted present value of expected future equity values for our common stock, under various possible future liquidity event scenarios, in light of the rights and preferences of each class of stock, discounted for a lack of marketability. The future liquidity event scenarios were primarily: (1) IPO; (2) a strategic merger or sale of our company; (3) a sale of our company at a value below the cumulative liquidation preference of the preferred stockholders; or (4) a dissolution of the company. The timing of the future liquidity event scenarios was determined based primarily on input from our board of directors and management. The future values of our common stock in the IPO scenarios and the strategic merger or sale scenarios were estimated by application of the market approach based on certain key assumptions, including the following:

- for our June 2010 valuation, our expected pre-money IPO valuation to the investors on their invested capital;
- for our December 2011, November 2012, May 2013 and August 2013 valuations, recently completed IPOs of similar stage biotechnology companies;
- estimated third-party trade sale values based on a range of returns to the investors on their invested capital; and
- expected dates for a future exit or liquidity event based on key events and company timelines.

A discount for marketability was applied to reach the final valuation of the common stock because, as we were a private company, there were impediments to liquidity, including lack of publicly available information and the lack of a trading market. Our determination of the discount included factors such as our proximity to an IPO, reduced funding risk and our progress made on our clinical development program. The discount for marketability decreased as we moved closer to marketability of common shares through an event, such as an IPO, and as the risk was lowered for our company as milestones were achieved. For our September 30, 2010 valuation, we utilized a discount for marketability of 40%. We lowered this discount for marketability to 30% for our December 31, 2011 valuation, 26% for our November 30, 2012 valuation, 25% for our May 29, 2013 and 9% for our August 15, 2013 valuation. Our discount for marketability decreased over time due to the receipt of positive results from our clinical trials and to reflect an increased likelihood of a possible IPO.

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

### ***Basic and Diluted Net Loss Per Share of Common Stock***

We compute basic net loss per share of common stock by dividing net loss applicable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, excluding the dilutive effects of preferred stock and stock options. We compute diluted net loss per share of common stock by dividing the net loss applicable to common stockholders by the sum of the weighted-average number of shares of common stock outstanding during the period plus the potential dilutive effects of preferred stock and stock options outstanding during the period calculated in accordance with the treasury stock method, but such items are excluded if their effect is anti-dilutive. Because the impact of these items is anti-dilutive during periods of net loss, there was no difference between our basic and diluted net loss per share of common stock for the years ended December 31, 2012 and 2011, and for the nine months ended September 30, 2013 and 2012.

## **JOBS Act**

As an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012, we 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 are electing to delay our adoption of such new or revised accounting standards. As a result of this election, our financial statements may not be comparable to the financial statements of other public companies.

## **Results of Operations**

### ***Comparison of Nine Month Periods Ended September 30, 2013 and 2012***

#### ***Revenue***

We did not recognize any revenue for the nine months ended September 30, 2013 or for the nine months ended September 30, 2012.

#### ***Research and Development Expenses***

Our research and development expenses were \$17.8 million for the nine months ended September 30, 2013, an increase of \$13.0 million compared to \$4.8 million for the nine months ended September 30, 2012. The increase was primarily due to milestone payments, manufacturing activity and clinical trial startup costs as we continued to progress the Fovista Phase 3 clinical program.

#### ***General and Administrative Expenses***

Our general and administrative expenses for the nine months ended September 30, 2013 were \$9.1 million, an increase of \$3.8 million compared to \$5.3 million for the nine months ended September 30, 2012. The increase was primarily due to an increase in intellectual property related expenses, professional services and consulting fees and personnel costs, including additional management and corporate staffing to support our public company infrastructure.

#### ***Interest Expense***

Interest expense for the nine months ended September 30, 2013 was \$1.5 million compared to \$0.3 million for the nine months ended September 30, 2012. The amounts in both 2013 and 2012 were related to interest associated with our venture debt facility that we entered into in June 2012 and paid off in May 2013. The related interest expense for the nine months ended September 30, 2013 included a payment of \$0.8 million that was required upon the earlier of the maturity date or the date of repayment of the venture debt facility.

#### ***Loss on Extinguishment of Debt***

In May 2013, we repaid the outstanding balance on our venture debt facility. The associated \$1.1 million loss on extinguishment of debt represents the related prepayment penalties and an expense for deferred costs and unamortized debt discount, in each case, related to the venture debt facility.

#### ***Other Loss***

Other loss was \$1.2 million for the nine months ended September 30, 2013 compared to \$0.3 million for the nine months ended September 30, 2012. The \$0.9 million increase was due to the change in fair value of the preferred stock warrants.

## **Comparison of Years Ended December 31, 2012 and 2011**

### **Revenue**

We did not recognize any revenue for the year ended December 31, 2012 or for the year ended December 31, 2011.

### **Research and Development**

Our research and development expenses were \$6.8 million for the year ended December 31, 2012, a decrease of \$7.1 million compared to research and development expenses of \$13.9 million for the year ended December 31, 2011. The decrease was primarily due to a reduction in clinical expenses related to the Phase 2b clinical trial for Fovista which had activity for the full year in 2011 and concluded in the second quarter of 2012. Clinical expenses also decreased in 2012 for Zimura and volociximab as compared to 2011. Zimura completed ongoing clinical activities in 2012, and we terminated the volociximab program in May 2012 to focus on the development of Fovista. These decreases were offset in part by an increase in manufacturing activity for Fovista in 2012 as we began to develop manufacturing operations to support our Phase 3 clinical program.

### **General and Administrative Expenses**

Our general and administrative expenses were \$6.9 million for the year ended December 31, 2012, an increase of \$1.2 million compared to general and administrative expenses of \$5.7 million for the year ended December 31, 2011. The increase was primarily due to increased legal and professional fees related to corporate development and financing activities.

### **Interest Expense**

Interest expense was \$0.5 million for the year ended December 31, 2012, compared to interest expense of \$0 for the year ended December 31, 2011. The increase was due to interest associated with our venture debt facility.

### **Other Loss**

Other loss was \$0.4 million for the year ended December 31, 2012 compared to \$0 for the year ended December 31, 2011. The \$0.4 million increase was due to the change in fair value of the preferred stock warrants.

## **Liquidity and Capital Resources**

### **Sources of Liquidity**

To date, we have not generated any revenues and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, our royalty agreement with Novo A/S and our initial public offering, which we closed on September 30, 2013. We issued and sold an aggregate of 8,740,000 shares of common stock in our initial public offering at a public offering price of \$22.00 per share, including 1,140,000 shares pursuant to the exercise by the underwriters of an over-allotment option. We received net proceeds from the initial public offering of \$175.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. Our royalty agreement, which is described in more detail below, provides for financing of up to \$125.0 million in the aggregate in return for the sale to Novo A/S of royalty interests in worldwide sales of Fovista. We received \$83.3 million of this royalty financing in separate tranches in May 2013 and January 2014. Our receipt of the final amount is subject to enrollment of specified numbers of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations. In May 2013, we issued and sold an aggregate of 6,666,667 shares of our series C preferred stock at a price per share of \$2.50, for an aggregate purchase price of \$16.7 million. In August 2013, we

issued and sold an aggregate of 13,333,333 additional shares of our series C preferred stock to the same purchasers at a price per share of \$2.50, for an aggregate purchase price of \$33.3 million.

### **Cash Flows**

As of September 30, 2013, we had cash and cash equivalents totaling \$236.1 million and no debt. We primarily invest our cash and cash equivalents in U.S. Treasury securities and money market funds that invest in U.S. Treasury securities.

The following table shows a summary of our cash flows for the years ended December 31, 2012 and 2011 and the nine months ended September 30, 2013 and 2012:

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2011	2013 (unaudited)	2012 (unaudited)
	(In thousands)			
Net cash (used in) provided by:				
Operating activities	\$ (13,104)	\$ (19,123)	\$ (23,198)	\$ (9,249)
Investing activities	—	3,396	(5)	—
Financing activities	11,012	14,994	254,978	7,199
Net increase (decrease) in cash and cash equivalents	<u>\$ (2,092)</u>	<u>\$ (733)</u>	<u>\$ 231,775</u>	<u>\$ (2,050)</u>

#### **Cash Flows from Operating Activities**

Net cash used in operating activities in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. The decrease in net cash used in 2012 compared to 2011 was primarily related to decreased spending in research and development due to a reduction in clinical expenses related to our Phase 2b clinical trial for Fovista, which concluded in the second quarter of 2012. The increase in net cash used in the nine months ended September 30, 2013 compared to the nine months ended September 30, 2012 primarily related to our efforts to advance Fovista into Phase 3 clinical trials, including increased spending on Phase 3 clinical trial start up costs, manufacturing activity for Fovista and milestone payments, partially offset by the elimination of spending on our Phase 2b clinical trial for Fovista.

We expect cash used in operating activities to continue to increase substantially compared to prior periods and for the foreseeable future as we continue the development of and seek marketing approval for Fovista, Zimura and, possibly, other product candidates. In August 2013, we initiated our pivotal Phase 3 clinical program for Fovista that will consist of three separate clinical trials.

#### **Cash Flows from Investing Activities**

Net cash provided by investing activities for the year ended December 31, 2011 was \$3.4 million and consisted of proceeds from the maturity of marketable securities partially offset by purchases of fixed assets. Net cash used in investing activities for the year ended December 31, 2012, the nine months ended September 30, 2013 and for the nine months ended September 30, 2012 was de minimis in all periods.

#### **Cash Flows from Financing Activities**

Net cash provided by financing activities was \$11.0 million for the year ended December 31, 2012 and \$15.0 million for the year ended December 31, 2011. Net cash provided by financing activities for the year ended December 31, 2012 consisted primarily of borrowings under our venture debt facility. Net cash provided by financing activities for the year ended December 31, 2011 consisted primarily of proceeds from the issuance of our series B preferred stock.

Net cash provided by financing activities was \$255.0 million for the nine months ended September 30, 2013 and \$7.2 million for the nine months ended September 30, 2012. Net cash provided by financing activities for the nine months ended September 30, 2013 consisted primarily of proceeds of \$175.6 million from our initial public offering in September 2013, proceeds of \$50.0 million from our Series C financing in May 2013 and August 2013, and proceeds of \$41.7 million from our royalty agreement with Novo A/S in May 2013. These proceeds were offset by the repayment of all outstanding principal, interest and fees under our venture debt facility. Net cash provided by financing activities for the nine months ended September 30, 2012 was \$7.2 million, consisting primarily of borrowings under our venture debt facility.

## Funding Requirements

Our most advanced product candidates, Fovista and Zimura, are still in clinical development. We expect our expenses to increase substantially as compared to prior periods, particularly as we continue the development of Fovista in our Phase 3 clinical program for the treatment of wet AMD, further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need and pursue the development of Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. In addition, if we obtain marketing approval for Fovista, Zimura or any other product candidate that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Furthermore, we expect to incur additional costs associated with being a public company, including legal, compliance, accounting and investor and public relations expenses as well as increased insurance premiums. We are party to agreements, specifically an asset acquisition agreement with OSI (Eyeteck), Inc., or Eyeteck, which agreement is now held by OSI Pharmaceuticals, LLC, or OSI Pharmaceuticals, a subsidiary of Astellas US, LLC, and license agreements with Archemix Corp., or Archemix, and Nektar Therapeutics, or Nektar, that impose significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to Fovista.

Our expenses also will increase if and as we:

- undertake additional clinical development of Fovista, if it is approved, in support of our efforts to broaden the label for Fovista;
- conduct additional clinical trials of Zimura that may be required by regulatory authorities for us to seek marketing approval for Zimura for the treatment of geographic atrophy;
- in-license or acquire the rights to other complementary products, product candidates or technologies for the treatment of ophthalmic diseases;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- expand our outsourced manufacturing activities and establish sales, marketing, distribution capabilities, if we receive, or expect to receive, marketing approval for any product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

We expect to obtain initial, top-line data from our Phase 3 clinical program for Fovista in 2016. We expect that the net proceeds we receive from this offering, together with our existing cash and cash equivalents of \$236.1 million as of September 30, 2013, the \$41.7 million received under such royalty agreement with Novo A/S in January 2014 and our potential future funding of \$41.7 million under this royalty agreement, will enable us to fund our operating expenses and capital expenditure requirements



through at least the end of 2016. We estimate that such funds will be sufficient to enable us to obtain initial, top-line data from our Phase 3 clinical program for Fovista and to complete our planned additional clinical trials to further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need and to complete a Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy and a Phase 2 clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. This estimate assumes, among other things, that we satisfy the conditions of our royalty agreement with Novo A/S and that we receive the full financing amount available under such royalty agreement on a timely basis. The royalty agreement provides that we will use the remaining proceeds we received and future proceeds, if any, under the royalty agreement primarily to support clinical development and regulatory activities for Fovista and for certain other permitted purposes. Costs related to our clinical programs for Fovista could exceed these estimates if we experience delays in our clinical trials, including because of the timing of our patient enrollment, the availability of drug supply for our clinical trials or for other reasons. These costs will also increase if we decide to expand the scope of our clinical programs or increase other corporate or licensing activities or staffing.

Our current Phase 3 clinical program for Fovista is expected to continue through at least 2017, and substantial expenditures to complete the Phase 3 clinical program will be required after the receipt of initial, top-line data. Moreover, we are at the early stages of formulating our clinical development plan for Zimura, which we expect will continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete the clinical development of either Fovista or Zimura, complete process development and manufacturing scale-up activities associated with Fovista and Zimura and potentially seek marketing approval for Fovista and Zimura, or the nature, timing or costs of the efforts necessary to complete the development of Zimura and any other product candidate we may develop.

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

- the scope progress, costs and results of our Phase 3 clinical program for Fovista;
- the progress, costs and results of our planned clinical trials to further evaluate the potential benefit of Fovista in wet AMD when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need;
- the scope, progress, costs and results of our planned Phase 2/3 clinical trial evaluating Zimura for the treatment of geographic atrophy and whether and to what extent additional clinical trials may be required by regulatory authorities for us to seek marketing approval in this indication and our Phase 2 clinical trial evaluating Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation;
- the costs and timing of process development and manufacturing scale-up activities associated with Fovista and Zimura;
- the costs, timing and outcome of regulatory review of Fovista and Zimura;
- the costs of commercialization activities for Fovista or Zimura if we receive, or expect to receive, marketing approval for either product candidate, including the costs and timing of expanding our outsourced manufacturing activities and establishing product sales, marketing and distribution capabilities;
- subject to receipt of marketing approval, net revenue received from commercial sales of Fovista or Zimura, after milestone payments and royalties;

- the scope, progress, results and costs of clinical trials for any other product candidates that we may develop;
- our ability to establish collaborations on favorable terms, if at all;
- the extent to which we in-license or acquire rights to complimentary products, product candidates or technologies; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims.

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, collaborations, strategic alliances and marketing, distribution or licensing arrangements. The potential future funding pursuant to our royalty agreement with Novo A/S is subject to enrollment of specified numbers of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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 assets, including intellectual property rights, as collateral to secure our obligations under our royalty agreement with Novo A/S may limit our ability to obtain debt financing. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams 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 product candidates that we would otherwise prefer to develop and market ourselves.

### **Royalty Financing**

In May 2013, we entered into our royalty agreement with Novo A/S, pursuant to which we may obtain royalty financing in three tranches in an amount of up to \$125.0 million in return for the sale to Novo A/S of aggregate royalties at low to mid-single-digit percentages of worldwide sales of Fovista, with the royalty percentage determined by the amount of funding provided by Novo A/S. The first and second tranches of the royalty financing, in which Novo A/S purchased two low single-digit royalty interests and paid us \$83.3 million in the aggregate, closed in May 2013 and January 2014. Under the royalty agreement, Novo A/S agreed to purchase from us, and we agreed to sell to Novo A/S, an additional low single-digit royalty interest on worldwide sales of Fovista, for a purchase price of \$41.7 million. If the final royalty interest under the royalty agreement is purchased, Novo A/S will have a right to receive royalties on worldwide sales of Fovista at a mid-single-digit percentage. The closing of the final financing tranche is subject to the enrollment of a specified number of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations.

Under specified circumstances, including terminations, suspensions or delays of our Phase 3 clinical trials for Fovista, the failure of certain closing conditions to be satisfied or transactions involving a change of control of us in which the acquiring party does not meet certain specifications, Novo A/S has the option to cancel the subsequent purchase and sale of the final royalty interest. We also have the option to cancel the subsequent purchase and sale of the final royalty interest in specified circumstances, including terminations, suspensions or delays in our Phase 3 clinical trials for Fovista, any change of control of us or the completion of equity financings meeting specified thresholds.

The royalty payment period begins on the commercial launch of Fovista and ends, on a country-by-country basis, on the latest to occur of the twelfth anniversary of the commercial launch of Fovista, the expiration of certain patent rights covering Fovista, and the expiration of regulatory exclusivity for Fovista, in each applicable country. Royalty payments will be payable quarterly in arrears during the royalty period. Our obligations under our agreement with Novo A/S may also apply to certain other anti-PDGF products we may develop.

We used a portion of the proceeds that we initially received under the royalty agreement to repay in full an aggregate of \$14.4 million of outstanding principal, interest and fees under our venture debt facility. The royalty agreement provides that we will use the remaining proceeds we received, and future proceeds, if any, from the sale of royalty interests under the royalty agreement, primarily to support clinical development and regulatory activities for Fovista and, to the extent applicable, other specified products we may develop pursuant to the terms of the royalty agreement, and for general corporate expenses. We intend to use the proceeds from the second tranche of financing that we received in January 2014 to support clinical development and regulatory activities for Fovista.

The royalty agreement requires the establishment by us and Novo A/S of a joint oversight committee in relation to the development of Fovista in the event that Novo A/S does not continue to have a representative on our board of directors. The royalty agreement also contains customary representations and warranties, as well as certain covenants relating to the operation of our business, including covenants requiring us to use commercially reasonable efforts to continue our development of Fovista, to file, prosecute and maintain certain patent rights and, in our reasonable judgment, to pursue claims of infringement of our intellectual property rights. The royalty agreement also places certain restrictions on our business, including restrictions on our ability to grant security interests in our intellectual property to third parties, to sell, transfer or out-license intellectual property, or to grant others rights to receive royalties on sales of Fovista and certain other products. We are required to reimburse Novo A/S for specified legal and other expenses and to provide Novo A/S with certain continuing information rights. We have agreed to indemnify Novo A/S and its representatives with respect to certain matters, including with respect to any third-party infringement or product liability claims relating to our products. Our obligations under the royalty agreement are secured by a lien on certain of our intellectual property and other rights related to Fovista and other anti-PDGF products we may develop.

### Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of September 30, 2013:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years (in thousands)	3 - 5 years	More than 5 years
Operating Leases(1)	\$ 208	\$ 68	\$ 140	\$ —	\$ —
Total(2)	\$ 208	\$ 68	\$ 140	\$ —	\$ —

- (1) Operating lease obligations reflect our obligation to make payments in connection with leases for our office space.
- (2) This table does not include (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known with certainty, (b) any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known, (c) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above and (d) the royalty purchase liability of \$41.7 million due to the fact that the royalty payment period is not known.

Under various agreements, we may be required to pay royalties and make milestone payments. These agreements include the following:

- Under our acquisition agreement with OSI (Eyetechn), Inc., or Eyetechn, which agreement is now held by OSI Pharmaceuticals, LLC, or OSI Pharmaceuticals, a subsidiary of Astellas US, LLC, for rights to particular anti-PDGF aptamers, including Fovista, we are obligated to pay to OSI Pharmaceuticals future one-time payments of \$12.0 million in the aggregate upon marketing approval in the United States and the European Union of a covered anti-PDGF product. We also are obligated to pay to OSI Pharmaceuticals a royalty at a low single-digit percentage of net sales of any covered anti-PDGF product we successfully commercialize.
- Under a license agreement with Archemix Corp., or Archemix, with respect to pharmaceutical products comprised of or derived from any anti-PDGF aptamer, we are obligated to make future payments to Archemix of up to an aggregate of \$14.0 million if we achieve specified clinical and regulatory milestones with respect to Fovista, up to an aggregate of \$3.0 million if we achieve specified commercial milestones with respect to Fovista and, for each other anti-PDGF aptamer product that we may develop under the agreement, up to an aggregate of approximately \$18.8 million if we achieve specified clinical and regulatory milestones and up to an aggregate of \$3.0 million if we achieve specified commercial milestones. No royalties are payable to Archemix under this license agreement. From inception through September 30, 2013, we have made payments of approximately \$4.8 million resulting from this agreement, including a \$2.5 million payment to Archemix that was triggered by the initiation of our Phase 3 clinical program for Fovista in August 2013.
- Under a license agreement with Archemix with respect to pharmaceutical products comprised of or derived from anti-C5 aptamers, for each anti-C5 aptamer product that we may develop under the agreement, including Zimura, we are obligated to make future payments to Archemix of up to an aggregate of \$57.5 million if we achieve specified development, clinical and regulatory milestones and, as to all anti-C5 products under the agreement collectively, up to an aggregate of \$22.5 million if we achieve specified commercial milestones. We are also obligated to pay Archemix a double-digit percentage of specified non-royalty payments we may receive from any sublicensee of our rights under this license agreement. No royalties are payable to Archemix under this license agreement. From inception through September 30, 2013, we have made payments totaling \$2.0 million under this agreement.
- Under a license, manufacturing and supply agreement with Nektar Therapeutics, or Nektar, for specified pegylation reagents used to manufacture Fovista, we are obligated to make future payments to Nektar of up to an aggregate of \$4.5 million if we achieve specified clinical and regulatory milestones, and an additional payment of \$3.0 million if we achieve a specified commercial milestone with respect to Fovista. We are obligated to pay Nektar tiered royalties at low to mid-single-digit percentages of net sales of any licensed product we successfully commercialize, with the royalty percentage determined by our level of licensed product sales, the extent of patent coverage for the licensed product and whether we have granted a third-party commercialization rights to the licensed product. We have agreed to pay Nektar a low double-digit percentage of any upfront payment we receive in connection with granting any third-party commercialization rights to a licensed product less certain milestone payments the company has previously paid, and a higher double-digit percentage of other specified amounts, such as milestone payments, we receive in connection with any such commercialization agreement, subject to agreed minimum and maximum amounts. From inception through September 30, 2013, we have made approximately \$1.8 million in payments resulting from this agreement, including a \$1.0 million payment to Nektar that was triggered by the initiation of our Phase 3 clinical program for Fovista in August 2013.

- Under our royalty agreement with Novo A/S with respect to Fovista, we are obligated to pay Novo A/S a low to mid-single-digit percentage royalty based on worldwide sales of Fovista, with the royalty percentage determined by the amount of funding provided by Novo A/S. See "—Royalty Financing" above for further information about our royalty agreement with Novo A/S.

We also have employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

We have three leases for our offices in New York and New Jersey. We entered into our New York lease in January 2014, and the lease expires in 2020. The New York lease is subject to an early termination right, which, if exercised, would trigger a termination payment by us of approximately \$375,000. We have agreed to pay aggregate rental fees of approximately \$3.5 million over the term of the New York lease and we are also liable for taxes, operating expenses and utility and other charges related to the leased premises. We have provided the landlord with a letter of credit in an amount of approximately \$138,000 to secure our obligations under the New York lease. We entered into the lease for our main office space in New Jersey in October 2013, which expires in 2019. Under the main New Jersey lease, we have agreed to pay aggregate rental fees of approximately \$1.3 million over the term of the lease. We have also provided a cash security deposit to the landlord in the amount of \$104,968, which amount will be reduced incrementally over the term of the main New Jersey lease. We entered into the lease for our additional office space in New Jersey in September 2013, and the lease expires in September 2016. Under this lease, we have agreed to pay aggregate rental fees of approximately \$213,724 over the term of the lease. We have also provided a cash security deposit to the landlord in the amount of \$11,374.

In addition, in the course of normal business operations, we have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. Expenditures to CROs represent a significant cost in clinical development. We can elect to discontinue the work under these agreements at any time. We could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require upfront payments and even long-term commitments of cash.

### **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 under Securities and Exchange Commission rules.

### **Quantitative and Qualitative Disclosures About Market Risks**

We are exposed to market risk related to changes in interest rates. We had cash and cash equivalents of \$236.1 million as of September 30, 2013 and \$4.3 million as of December 31, 2012, consisting of cash and money market funds. 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 U.S. dollar are recorded based on exchange rates at the time such transactions arise. As of September 30, 2013 and December 31, 2012 and 2011, substantially all of our total liabilities were denominated in the U.S. dollar.

## BUSINESS

### Overview

We are a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the back of the eye, with a focus on developing therapeutics for age-related macular degeneration, or AMD. AMD is a disorder of the central portion of the retina, known as the macula, which is responsible for central vision and color perception. There are two forms of AMD, wet AMD and dry AMD. Our most advanced product candidate is Fovista, which is in Phase 3 clinical development for use in combination with anti-VEGF drugs that represent the current standard of care for the treatment of wet AMD. If our Phase 3 clinical development program progresses as planned and the results are favorable, we plan to submit applications for marketing approval for Fovista in 2016. We are also developing our product candidate Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD, and expect to initiate a Phase 2/3 clinical trial of Zimura for this indication in late 2014 or early 2015.

### *Fovista*

We are developing our product candidate Fovista to be administered in combination with anti-VEGF drugs for the treatment of wet AMD. In 2012, we completed a large Phase 2b clinical trial in newly diagnosed wet AMD patients in which 1.5 mg of Fovista administered in combination with one of the standard of care drugs, Lucentis, demonstrated statistically significant superiority compared to Lucentis monotherapy based on the primary endpoint of mean change in visual acuity from baseline at 24 weeks. Patients receiving the combination of 1.5 mg of Fovista and Lucentis gained a mean of 10.6 letters from baseline on a standardized chart of vision testing compared to a mean gain of 6.5 letters from baseline for patients receiving Lucentis monotherapy, representing a 62% comparative benefit from baseline. Based on retrospective analyses of commonly evaluated parameters used in wet AMD trials, Fovista combination therapy resulted in improved visual outcome, with more patients experiencing vision gain and fewer patients experiencing vision loss, in a broad range of patient groups in this trial compared to Lucentis monotherapy. Fovista was generally well tolerated in this clinical trial.

We have initiated a pivotal Phase 3 clinical program to evaluate the safety and efficacy of Fovista combination therapy for the treatment of newly diagnosed wet AMD patients compared to current standard of care anti-VEGF monotherapy. Our Phase 3 clinical program consists of three separate Phase 3 clinical trials, two of which will evaluate Fovista in combination with Lucentis and the other of which will evaluate Fovista in combination with each of Avastin or Eylea, the other two standard of care drugs. All three of these Phase 3 clinical trials will incorporate significant aspects from the design of our completed Phase 2b clinical trial. We plan to enroll a total of 1,866 patients at more than 225 centers internationally across the three trials. We have initiated enrollment in the two trials evaluating Fovista administered in combination with Lucentis. We expect to activate initial trial sites in the third trial in this Phase 3 clinical program in the United States by the end of the first quarter of 2014. We expect to have initial, top-line data from this Phase 3 clinical program available in 2016. If the results of this Phase 3 clinical program are favorable, we plan to submit applications for marketing approval for Fovista in both the United States and the European Union before the end of 2016. We have retained worldwide commercialization rights to Fovista.

Wet AMD is characterized by abnormal new blood vessel formation, referred to as neovascularization, which results in blood vessel leakage and retinal distortion. If untreated, neovascularization in wet AMD patients typically results in formation of a scar, or fibrosis, under the macular region of the retina. The use of anti-VEGF therapy has significantly improved visual outcomes for wet AMD patients compared to untreated patients newly diagnosed with wet AMD. However, we believe that persistence or growth of neovascularization and the development of fibrosis under the retina are involved in limiting the visual benefit from anti-VEGF monotherapy, and a significant unmet medical need remains.

Wet AMD is the leading cause of blindness in people over the age of 55 in the United States and the European Union. The current standard of care for wet AMD is monotherapy administration of drugs that target vascular endothelial growth factor, or VEGF, one of several proteins involved in neovascularization. The anti-VEGF market for the treatment of wet AMD consists predominantly of two drugs that are approved for marketing and primarily prescribed for the treatment of wet AMD, Lucentis and Eylea, and off-label use of the cancer therapy Avastin. In 2012, annual worldwide sales of Lucentis and Eylea for all indications totaled approximately \$4.8 billion. This sales number does not include Avastin, which is commonly used off-label to treat wet AMD in the United States and, to a lesser extent, in the European Union.

We believe that Fovista's mechanism of action, when administered in combination with an anti-VEGF drug, may result in two relevant biological responses: neovascular regression and inhibition of fibrosis under the retina, also known as subretinal fibrosis. Fovista binds to and inhibits a protein known as platelet derived growth factor, or PDGF, causing the stripping of pericytes, which are cells that cover the outside of newly formed blood vessels. After the pericytes are stripped from the new blood vessels, endothelial cells lining the inside of the newly formed blood vessels are left unprotected and are highly vulnerable to the effects of anti-VEGF therapy. Fovista also inhibits migration of other retinal cells attracted by PDGF, such as retinal pigment epithelium, or RPE, cells and glial cells, which play a role in the formation of subretinal fibrosis. We further believe that the administration of Fovista in combination with anti-VEGF drugs in patients with wet AMD may cause regression of neovascularization and may inhibit subretinal fibrosis more effectively than anti-VEGF monotherapy. We believe that Fovista may provide meaningful added benefit in the treatment of wet AMD regardless of which anti-VEGF drug is administered in combination with Fovista.

### **Zimura**

We are developing our product candidate Zimura, which we previously referred to as ARC1905, with an initial focus on the treatment of patients with geographic atrophy, a severe form of dry AMD. Zimura is an inhibitor of complement factor C5, which we refer to as C5, a protein that is associated with complement mediated inflammation and cell damage, which we believe may be involved in the development of dry AMD.

Dry AMD is a significant cause of moderate and severe loss of central vision, affecting vision in both eyes in most patients. Dry AMD results in progressive and chronic degeneration of the macula characterized by variable thinning and dysfunction of retinal tissue. Dry AMD is typically associated with yellow-white dots or deposits under the retina, known as drusen. Unlike in wet AMD, there is a complete absence of pathological neovascularization in dry AMD.

Deterioration of vision in dry AMD is usually gradual over a period of months and years and is considered irreversible. Significant vision loss results if dry AMD evolves into a more severe form of the disease known as geographic atrophy. Geographic atrophy appears as severe, abrupt and deep levels of macular tissue loss. In addition, dry AMD can also progress to wet AMD. Although dry AMD is the most common form of AMD, there are no therapies approved by the U.S. Food and Drug Administration, or FDA, or European Medicines Agency, or EMA, to treat this condition. According to a 2011 publication from AMD Alliance International, approximately 30 million people worldwide have some form of AMD, with dry AMD accounting for 85% to 90% of these cases. A study published in *Ophthalmology* in 2012 analyzing age and gender variations in AMD prevalence estimates that approximately 8 million people worldwide are affected by geographic atrophy.

Multiple published studies have implicated local inflammation in the pathogenesis of dry AMD. Specifically, these studies suggest that the complement pathway, which consists of a series of proteins involved in the defense against infection and modulates a variety of immune and inflammatory responses, has a central role in dry AMD. The complement system is generally tightly regulated and requires the proper balance of activation and inhibition of proteins to function properly. Poorly

regulated or aberrant activation of proteins in the complement pathway without a balanced or proportional inhibition of other proteins may result in the production of immune mediated inflammation, or inflammation that is triggered by activation of the immune response, and damage to normal tissue. We believe that excessive activation of C5, which is one of the complement proteins, and the resulting formation of downstream complement molecules, results in tissue damage that plays an important role in the development of both dry AMD and certain forms of wet AMD. Our product candidate Zimura is designed to inhibit C5 activation.

We have completed a small, multicenter, uncontrolled, open label Phase 1/2a clinical trial evaluating the safety and tolerability of Zimura administered as a monotherapy to patients with geographic atrophy, a severe form of dry AMD. We did not observe any evidence of drug related adverse events in this clinical trial. We observed a trend in this clinical trial, in favor of the higher of two dose groups, of a relative reduction in the mean growth of the geographic atrophy lesion area, as measured by an independent reading center, at 24 weeks. When the injections were administered in a reduced dosing schedule during the subsequent 24 weeks, this relative trend in reduced growth in geographic atrophy lesion area was no longer present. We believe this apparent trend in reduction of growth in geographic atrophy lesion area size when Zimura was dosed more frequently, together with the relative loss of the benefit when Zimura was dosed less frequently, may suggest a possible drug effect. In addition, recently released data from a third party targeting the complement pathway also exhibited a trend in reduction of geographic atrophy growth with a pronounced effect in patients with specific biomarkers.

Based on the results of our Phase 1/2a clinical trial and the recent results from the third-party clinical trial, we plan to initiate a Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with geographic atrophy in late 2014 or early 2015. We expect to receive interim results from this clinical trial in 2016. We also plan to evaluate Zimura and Fovista administered in combination with anti-VEGF drugs for the treatment of a subpopulation of wet AMD patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy fails, who we refer to as anti-VEGF resistant, and who are believed to have complement mediated inflammation. We plan to initiate a Phase 2 clinical trial of Zimura and Fovista administered in combination with an anti-VEGF drug in this second indication in 2015.

### ***Our Management Team***

We are led by a team of experienced pharmaceutical industry executives and recognized experts in retinal disease. Our management team includes our co-founder and Chief Executive Officer, David Guyer, M.D., and our co-founder and President, Samir Patel, M.D. Dr. Guyer and Dr. Patel were co-founders and senior executives of Eyetech Pharmaceuticals, Inc., which was acquired by OSI Pharmaceuticals, Inc. in 2005. While at Eyetech Pharmaceuticals, Dr. Guyer and Dr. Patel were responsible for the clinical development and commercialization of Macugen, the first anti-VEGF drug approved for the treatment of wet AMD. While at Eyetech Pharmaceuticals, they also were responsible for the preclinical development of Fovista, the rights to which we subsequently acquired from OSI (Eyetech), Inc. pursuant to a divestiture agreement prior to initiation of any clinical development. We believe that our senior management provides us with significant capabilities in the development and commercialization of novel therapies to treat diseases of the back of the eye.

### **Our Strategy**

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing novel therapeutics to treat diseases of the back of the eye, with a particular focus on



developing novel therapeutics for the treatment of AMD. The key elements of our strategy to achieve this goal are:

- *Complete Phase 3 clinical program evaluating Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD and, if successful, seek marketing approval for Fovista in this indication.* We are devoting a significant portion of our resources and business efforts to the clinical development of Fovista in combination with anti-VEGF drugs for wet AMD. We have initiated a pivotal Phase 3 clinical program evaluating Fovista administered in combination with anti-VEGF drugs for the treatment of newly diagnosed wet AMD patients. We have begun treating patients in two of three Phase 3 clinical trials in this program. Based on our estimates regarding patient enrollment, we expect to have initial, top-line data from this Phase 3 clinical program available in 2016. If the results of this Phase 3 clinical program are favorable, we plan to submit applications for marketing approval for Fovista in both the United States and the European Union before the end of 2016. Our Phase 3 clinical trials will continue after such submissions in accordance with the protocols for these trials.
- *Further evaluate the potential benefit of Fovista in wet AMD, when administered in combination with anti-VEGF drugs, and in other ophthalmic diseases and conditions with unmet need.* We are planning to initiate a Phase 2 clinical trial to assess whether the use of Fovista in combination with anti-VEGF drugs can reduce the number and frequency of intravitreal injections required to effectively treat wet AMD. In addition, we are planning to initiate a Phase 2 clinical trial of Fovista in combination with anti-VEGF drugs for the treatment of anti-VEGF resistant wet AMD patients. We plan to initiate these two clinical trials in 2014 and expect to receive initial results from these two clinical trials in 2015. We are also planning to initiate a Phase 2 clinical trial to assess whether the use of Fovista in combination with anti-VEGF drugs can inhibit the development of subretinal fibrosis in wet AMD patients. We plan to initiate this clinical trial in 2014 and expect to receive initial results from this clinical trial in late 2015 or early 2016. We are also evaluating other ophthalmic conditions for which we believe Fovista treatment may be beneficial. We are planning to supply Fovista for a clinical trial to be conducted by the National Eye Institute, part of the U.S. National Institutes of Health, to evaluate Fovista's potential to inhibit the visual loss resulting from retinal complications associated with von Hippel-Lindau disease, an inherited disease characterized by multiple benign and malignant tumors and cysts in the eye and other organs. We expect this clinical trial will commence in late 2014. We are also planning to initiate, potentially in 2015, a clinical trial to assess the potential therapeutic benefit of Fovista, and in particular its potential to inhibit the development of retinal scarring, in proliferative vitreoretinopathy, a complication associated with retinal detachment.
- *Advance the development of Zimura for the treatment of AMD.* We are developing our product candidate Zimura, with an initial focus on the treatment of geographic atrophy, a severe form of dry AMD. Zimura is an inhibitor of complement factor C5, a protein that is associated with complement mediated inflammation and cell damage, which we believe may be involved in the development of dry AMD. We plan to initiate a Phase 2/3 clinical trial in patients with geographic atrophy in late 2014 or early 2015 and expect to receive interim results from this clinical trial in 2016. We also plan to initiate in 2015 a Phase 2 clinical trial evaluating the safety and efficacy of Zimura and Fovista administered in combination with an anti-VEGF drug in anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation.
- *Maximize commercial potential of Fovista and Zimura.* We have retained worldwide commercialization rights to Fovista and Zimura. If either Fovista or Zimura receives marketing approval, we plan to commercialize such product candidate in the United States with our own focused, specialty sales force. We believe that retinal specialists in the United States, who perform most of the medical procedures involving diseases of the back of the eye, are sufficiently concentrated that we will be able to effectively promote Fovista and Zimura to these

specialists with a sales and marketing group of fewer than 100 persons. We expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Fovista and Zimura in markets outside the United States.

- *Opportunistically in-license or acquire products, product candidates and technologies.* We plan to expand our product pipeline through opportunistically in-licensing or acquiring the rights to complementary products, product candidates and technologies for the treatment of a range of ophthalmic diseases, principally diseases of the back of the eye. We believe that our focus on diseases of the back of the eye and our experienced management team will make us an attractive collaborator or acquirer for companies seeking to out-license or sell rights to products, product candidates or technologies in our area of focus. We generally expect that we will not engage in early stage research and drug discovery and will thus avoid the related costs and risks of these activities.

### **Potential for Fovista in Wet AMD**

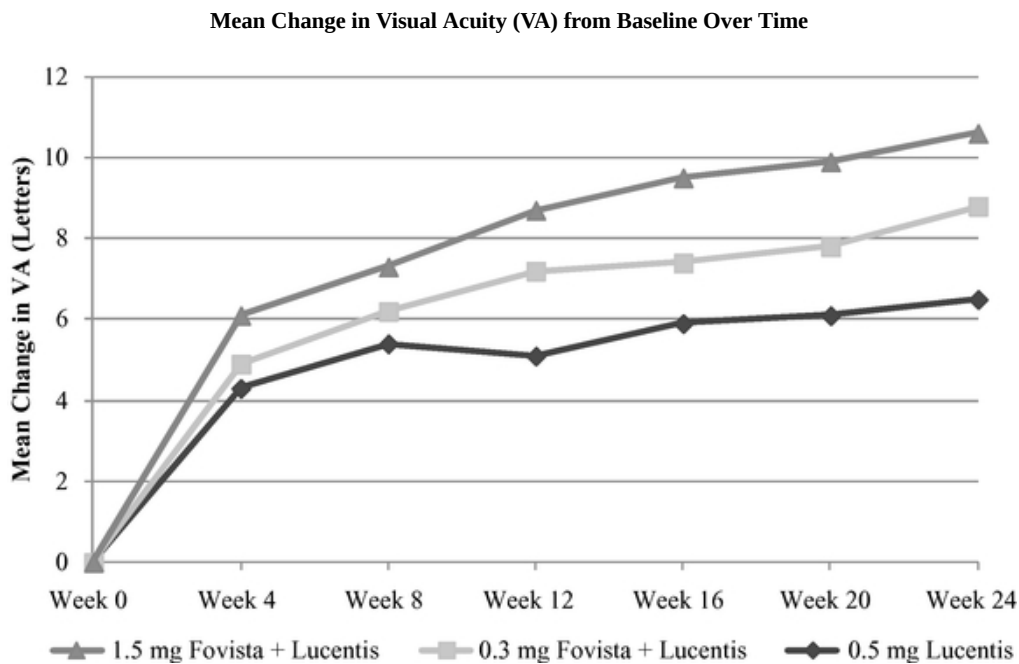
In our completed Phase 2b clinical trial, the combination of 1.5 mg of Fovista and Lucentis demonstrated statistically significant superiority compared to Lucentis monotherapy based on the primary endpoint of mean change in visual acuity from baseline at 24 weeks, providing a 62% comparative benefit from baseline. Our Phase 3 clinical program builds on and incorporates significant aspects from the design of our Phase 2b clinical trial. We intend to seek a broad label for Fovista for the treatment of patients with wet AMD in combination with anti-VEGF drugs. We believe that Fovista may provide meaningful added benefit in the treatment of wet AMD regardless of which anti-VEGF drug is administered in combination with Fovista. We also believe that Fovista has the potential to inhibit the formation of subretinal fibrosis, thereby improving longer-term visual outcomes for wet AMD patients.

#### ***Visual Acuity Benefit***

We completed a large, multicenter, randomized, double-masked, controlled Phase 2b clinical trial in 2012 in which the combination of 1.5 mg of Fovista and the anti-VEGF drug Lucentis achieved statistically significant superiority compared to Lucentis monotherapy based on the primary endpoint of mean change in visual acuity from baseline at 24 weeks. In this trial, patients treated with the combination of 0.3 mg of Fovista and Lucentis showed improvements in visual acuity compared to Lucentis monotherapy, but the combination of 0.3 mg and Lucentis did not achieve statistically significant superiority compared to Lucentis monotherapy based on the primary endpoint of mean change in visual acuity from baseline at 24 weeks.

As described in more detail below under "—Clinical Development of Fovista—Completed Phase 2b Clinical Trial of Fovista Combination Therapy for Wet AMD," the following graph sets forth

the mean change in visual acuity from baseline for each treatment group in our Phase 2b clinical trial over the course of the trial:



We observed a visual benefit in patients treated with the combination of 1.5 mg of Fovista and Lucentis early in and sustained over the course of treatment. The relative magnitude of visual benefit increased over the study period. We believe that these results suggest that Fovista may provide benefit to patients when used over time in combination with Lucentis. We also believe that these results are supported by Fovista's proposed mechanism of action, which we believe, when administered in combination with an anti-VEGF drug, may result in two relevant responses: neovascular regression and inhibition of subretinal fibrosis.

In addition, we believe that the relative visual benefit of the combination of 1.5 mg of Fovista and Lucentis compared to the relative visual benefit of the combination of 0.3 mg of Fovista and Lucentis at all timepoints exhibits a dose-response curve in which the response to treatment increases with higher drug concentrations of Fovista.

In our Phase 2b clinical trial, we observed differences on the secondary endpoint of mean change in visual acuity from baseline at 12 weeks favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy. In addition, we observed differences in other visual outcome secondary endpoints favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy. Further, we performed multiple retrospective subgroup analyses of the data from our Phase 2b clinical trial. In these retrospective analyses, we observed differences in visual outcomes from baseline favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy regardless of the baseline size of neovascularization or the baseline vision of the patient. We believe that these results suggest that the benefits of treatment with 1.5 mg of Fovista in combination with Lucentis as compared to Lucentis monotherapy may be applicable to a broad segment of patients with wet AMD.

### ***Phase 3 Clinical Trials Build Upon and Incorporate Phase 2b Clinical Trial Design***

We have initiated a pivotal Phase 3 clinical program to evaluate the safety and efficacy of Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD. We have begun treating patients in two of three Phase 3 clinical trials in this program. The primary efficacy endpoint in each of our Phase 3 clinical trials is the mean change in visual acuity from baseline, which will be assessed at 12 months after first treatment.

Two of the three Phase 3 clinical trials included in our Phase 3 clinical program are evaluating the safety and efficacy of Fovista administered in combination with Lucentis and build upon and incorporate significant aspects from the design of our Phase 2b clinical trial. We believe that the following aspects of our two Phase 3 clinical trials of Fovista administered in combination with Lucentis may reduce the risk that we will have unexpected outcomes in these two trials:

- We have made no meaningful changes to the inclusion and exclusion criteria in these Phase 3 clinical trials from those we used in our Phase 2b clinical trial. We expect that this will result in the enrollment of a patient population similar to the patient population enrolled in our Phase 2b clinical trial.
- We are not changing the pre-specified primary endpoint, mean change in visual acuity from baseline, that we used in our Phase 2b clinical trial. However, we will assess mean change in visual acuity from baseline in these Phase 3 clinical trials at 12 months, instead of at 24 weeks as in our Phase 2b clinical trial. In our Phase 2b clinical trial, the relative magnitude of visual benefit seen with the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy increased over the study period. If we observe a similar pattern of visual benefit in our Phase 3 clinical program, we believe that long-term administration of 1.5 mg of Fovista with Lucentis may be indicated.
- Our Phase 2b clinical trial was well powered to detect a statistically significant difference in mean change in visual acuity between patients treated with 1.5 mg of Fovista in combination with Lucentis and patients treated with Lucentis monotherapy. We are further improving our ability to detect any statistically significant differences in pre-specified efficacy outcomes between the treatment and control arms of our Phase 3 clinical trials by substantially increasing both the number of patients who will receive 1.5 mg of Fovista in combination with Lucentis and the number of patients who will receive Lucentis monotherapy as compared to our Phase 2b clinical trial.
- We are using a dose of Fovista that exhibited a favorable safety profile in our Phase 2b clinical trial. We are using the same standard of care anti-VEGF drug, Lucentis, in combination with Fovista and as the monotherapy control in these Phase 3 clinical trials as we used in our Phase 2b clinical trial.

***Potential to Enhance Efficacy of Current Standard of Care***

We intend to seek a broad label for Fovista in combination with anti-VEGF drugs for the treatment of patients with wet AMD. The anti-VEGF market for the treatment of wet AMD consists of Lucentis, Avastin and Eylea. The condition of many patients suffering with wet AMD improves significantly through the use of anti-VEGF drugs. However, in a substantial portion of cases the condition of the patient deteriorates over time. For example, based on results of third-party clinical trials, after one year of treatment with an anti-VEGF drug, approximately 18% to 22% of newly diagnosed wet AMD patients lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, and approximately 62% to 75% of such patients did not achieve an ability to read an additional 15 or more letters on the standardized chart of vision testing post-treatment.

In 2013, the peer reviewed journal *Ophthalmology* published a study reporting on a four-year longitudinal analysis of 555 wet AMD patients treated with an anti-VEGF drug. The study found that after four years, on average, patients lost vision compared to their visual acuity at the start of the study. Thirty-two percent of the patients in the study continued treatment for the entire four-year study period. After four years, mean visual acuity in this group of patients essentially reverted to pre-study levels. In addition, 28% of patients discontinued treatment because of poor visual outcomes. The primary reasons for discontinuation of treatment in this group were sustained low visual acuity and lack of apparent treatment response.

In addition, *Ophthalmology* also published in 2013 the results of an uncontrolled study of patients who had received two years of monthly treatment with Lucentis in clinical trials and then received additional treatment with Lucentis at a physician's discretion for two more years. When assessed at their last evaluation in this study, approximately 46% of such patients had lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing.

Moreover, in 2013, *Ophthalmology* published the results of a separate follow-up study of a cohort of these same patients. When assessed approximately three years after completing their participation in the prior study, approximately one-third had poor outcomes, defined as the loss of the ability to read 15 or more letters on a standardized chart of vision testing, according to the study conclusions. In addition, approximately 57% of such patients had lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, compared to baseline prior to receiving therapy in the original clinical trials, and approximately 37% had visual acuity at the level of legal blindness, defined as visual acuity of 20/200 or worse. The study authors noted that wet AMD patients remain at risk for substantial visual decline.

We believe that the administration of Fovista in combination with anti-VEGF drugs in patients with wet AMD may disrupt abnormal new blood vessels and cause regression more effectively than anti-VEGF monotherapy, leading to improved visual outcomes. In addition, based on our initial assessment of retinal images from patients who experienced vision loss following treatment with either 1.5 mg of Fovista in combination with 0.5 mg of Lucentis or Lucentis monotherapy in our completed Phase 2b clinical trial, results from preclinical tests and our review of recent scientific literature, we also believe that wet AMD patients who receive anti-VEGF monotherapy may remain at increased risk for the development of subretinal fibrosis. We believe that the development of subretinal fibrosis in these patients may, in part, be responsible for the deterioration of vision that many wet AMD patients experience over time, notwithstanding treatment with an anti-VEGF drug.

In a study published in 2013 in *American Journal of Ophthalmology*, 40% of wet AMD patients exhibited subretinal fibrosis and retinal scarring after two years of treatment with Lucentis. According to a retrospective analysis of the Comparisons of AMD Treatment Trials published in 2013 in the *Journal of Ophthalmology*, 32% of newly diagnosed wet AMD patients developed retinal scarring after one year of treatment with either Lucentis or Avastin, while 45% of newly diagnosed wet AMD patients developed retinal scarring after two years of treatment with either Lucentis or Avastin.

The PDGF pathway is one of the major mediators of fibrosis. In 2006, the peer reviewed *Journal of Cell Physiology* published the results of a study in which Fovista monotherapy exhibited anti-fibrotic effects in an animal model of retinal scarring. We therefore believe that Fovista's ability to inhibit the PDGF pathway may enhance regression of neovascularization and also may inhibit the development of subretinal fibrosis in the eye when administered in combination with an anti-VEGF drug. We believe continued Fovista anti-PDGF therapy may result in improved visual outcomes for patients with wet AMD as compared to anti-VEGF monotherapy.

Two of the three clinical trials included in our Phase 3 clinical program are evaluating the safety and efficacy of Fovista administered in combination with Lucentis as compared to Lucentis monotherapy. To support our efforts to seek a broad label for Fovista, we plan to conduct a third clinical trial to evaluate the safety and efficacy of Fovista administered in combination with each of Avastin or Eylea compared to Avastin or Eylea monotherapy. We believe that Fovista may provide meaningful added benefit in the treatment of wet AMD regardless of which anti-VEGF drug is administered in combination with Fovista. The Committee for Medicinal Products for Human Use, or the CHMP, of the EMA has informed us that, given that Avastin is not approved for intravitreal use in the European Union, the final label for Fovista in the European Union, if Fovista receives marketing approval, may be required to specify only the anti-VEGF drugs approved for intravitreal use that were studied in combination with Fovista, rather than a broad label specifying Fovista for use in combination with any anti-VEGF drug.

## Age-Related Macular Degeneration

Eye disease can be caused by many factors and can affect both the front and back of the eye. In its most extreme cases, eye disease can result in blindness. In the developed world, the major diseases that result in blindness are those affecting the retina, including AMD and diabetic retinopathy, and glaucoma. These diseases deny patients of their sight and, as a result, their ability to live independently and perform daily activities. Any improvement in vision, or even a slowing of the rate of vision loss, has a tremendous impact on the quality of life of patients with impaired vision.

AMD is a leading cause of vision loss in people over the age of 50 in the western world. There are two forms of AMD, dry AMD and wet AMD. According to AMD Alliance International, approximately 10 million people in the United States and 30 million people worldwide suffer from some form of AMD. AMD Alliance International estimates that dry AMD accounts for 85% to 90% of all AMD cases, while a study published in *Ophthalmology* in 2012 analyzing age and gender variations in AMD prevalence estimates that approximately 8 million people worldwide are affected by geographic atrophy. A study on the burden of AMD published in 2006 in the peer reviewed journal *Current Opinion in Ophthalmology*, estimated that 1,250,000 people in the United States, suffer from wet AMD. In addition, AMD Alliance International reports that approximately 200,000 new cases of wet AMD arise each year in the United States. Based on U.S. Census Bureau data, we estimate that over the next two decades in the United States the number of people aged 55 or older is expected to increase by approximately 36% and the number of people aged 65 and older is expected to increase by approximately 69%. We expect that this increase in the number of elderly people will result in a significant increase in the number of cases of both dry AMD, including cases of geographic atrophy, and wet AMD in the United States.

AMD is a major public health problem that has a devastating effect on patients and a significant adverse impact on the economy. AMD distorts the acute central vision necessary for daily activities such as reading, face recognition, watching television and driving and can lead to loss of central vision and blindness. According to a 2010 study sponsored by AMD Alliance International, the annual direct healthcare system costs of visual impairment worldwide due to AMD was estimated at approximately \$255 billion. According to the same study, wet AMD patients suffer a reduced quality of life and experience difficulty performing daily activities, social isolation, higher than normal rates of clinical depression, twice the risk of premature death as those who are not visually impaired, increased risk of falls and related hip fractures and premature admission to nursing homes. Wet AMD represents approximately 10% of all cases of AMD, but is responsible for 90% of the severe vision loss associated with the disease.

According to a study on the burden of AMD published in 2006 in *Current Opinion in Ophthalmology*, an average patient with AMD experiences a decrease in his or her quality of life equivalent to that of patients suffering from other diseases often perceived as more severe. For example, moderate age-related macular degeneration, defined as vision of 20/50 to 20/100 in the better-seeing eye, causes a 40% decrease in the average patient's quality of life, similar to that associated with severe cardiac angina or renal dialysis. Normal visual acuity is commonly referred to as 20/20 vision, and a person with 20/50 vision can read letters on an eye chart from 20 feet away as well as a person with normal vision can read the chart from 50 feet away.

### Wet AMD

Wet AMD is preceded by dry AMD. In a subset of patients, dry AMD converts to wet AMD when new and abnormal blood vessels invade the retina. These abnormal new blood vessels originate beneath the retina, in a layer called the choroid, and invade into the overlying retinal layers. This abnormal new blood vessel growth is generally referred to as pathological angiogenesis. In the context of wet AMD, pathological angiogenesis is associated with both the development of neovascular cells and the accumulation of other cell types and altered tissue. The pathological neovascular tissue in wet AMD is

called the choroidal neovascular complex or choroidal neovascularization. Choroidal neovascularization and adjacent and contiguous areas of blood and altered tissue are referred to as a lesion.

Abnormal new blood vessels tend to be fragile and often bleed and leak fluid into the macula, the central most portion of the retina responsible for central vision and color perception. Untreated, blood vessel growth and associated leakage typically lead to retinal distortion and eventual retinal scarring, with irreversible destruction of the macula and loss of vision resulting. This visual loss occurs rapidly with a progressive course. Approximately 90% of wet AMD cases involve subfoveal choroidal neovascularization, which is blood vessel growth directly under the central portion of the macula, known as the fovea. Our Phase 3 clinical program for Fovista will enroll patients with subfoveal wet AMD.

Wet AMD traditionally has been divided into subtypes based on the pattern of the abnormal new blood vessels using the diagnostic imaging technique fluorescein angiography or cross sectional location of the abnormal new blood vessels using the diagnostic imaging technique optical coherence tomography, or OCT. These subtypes form a continuous spectrum of pathological neovascularization based on whether the abnormal new blood vessels are well defined and delineated as determined by fluorescein angiography or whether they have invaded the RPE layer of the retina. The RPE layer of the retina lies between the choroid and the neurosensory region of the retina. Increasingly, retinal specialists, in determining the subtype classification, use OCT to assess whether the presence of abnormal new vessels is located above or below the RPE.

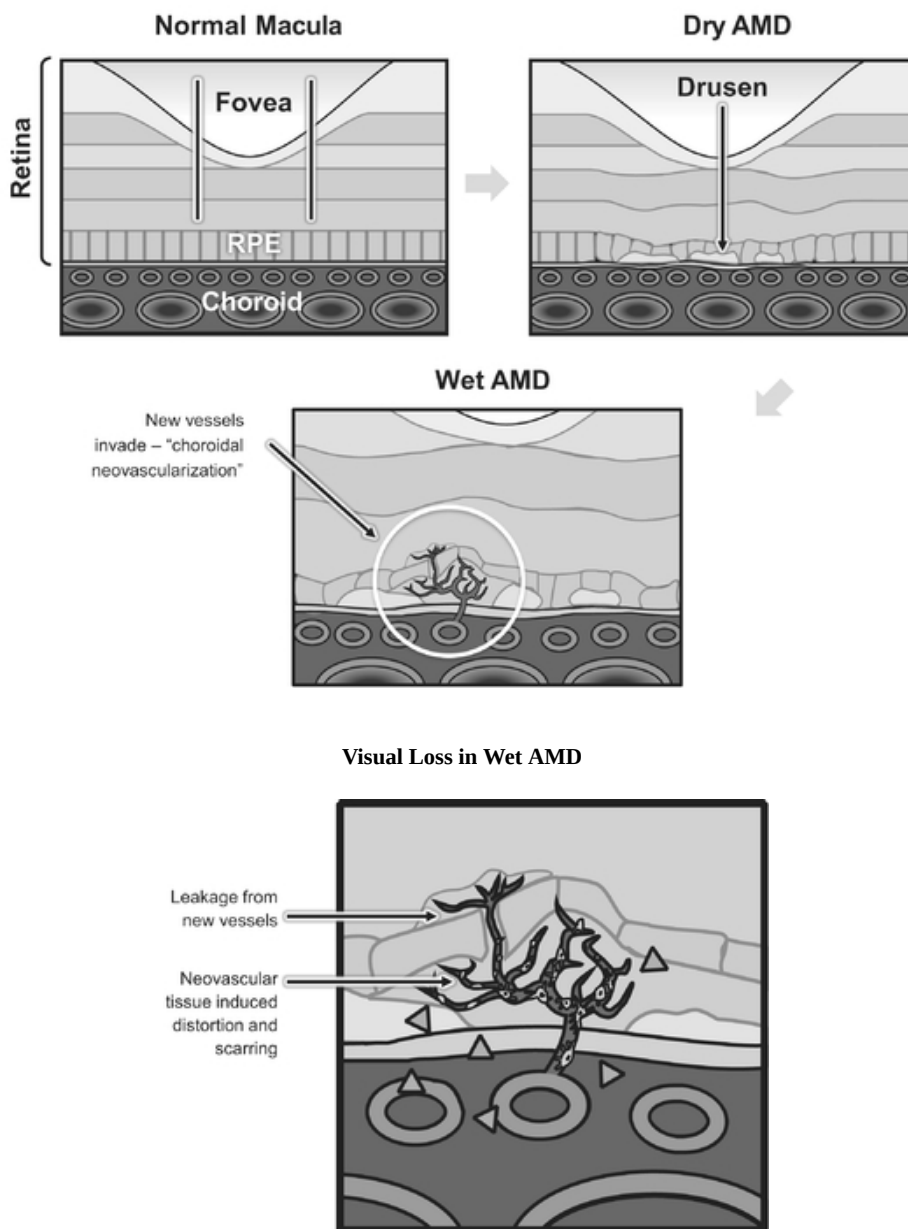
Retinal specialists historically have used fluorescein angiography in making this subtype determination of abnormal new blood cells. This technique involves injection of a fluorescent dye into the systemic circulation and capturing its image during transit through the retinal circulation using a specialized camera. Fluorescein angiography is very sensitive in detecting the presence or absence of neovascularization. However, fluorescein angiography's accuracy in subtype detection can be inconsistent. In addition, the use of fluorescein angiography is limited in detecting the location and position of the abnormal blood vessels relative to the RPE due to the variability and subjectivity inherent in the reading of the fluorescein angiogram. Currently, there is a shift toward using the latest, high resolution OCT models to image the abnormal new blood vessels and the associated leakage in wet AMD patients. OCT utilizes specialized light scattering through the biological tissues and obtains high-resolution retinal tissue images using a specialized camera. OCT images show a cross-sectional view of the retina that permits enhanced resolution of the space under the retina and at the RPE level where the neovascularization associated with wet AMD is present. OCT images allow for a more precise analysis of anatomical differences between various angiographic subtypes of CNV lesions in neovascular AMD, especially with respect to the location of the abnormal new vessels relative to the RPE.

The abnormal new blood vessels are made up of "classic" and "occult" components. The term "classic" applies to the portion or component of the patient's abnormal new blood vessels or neovascularization that is well defined by fluorescein angiography and usually represents their location above the RPE. The term "occult" applies to the portion or component of the patient's abnormal new blood vessels that are poorly defined or usually located below the RPE. The quantification of the amount of the patient's "classic" or "occult" components with respect to the neovascular lesion determines whether the lesion is "pure classic," "predominantly classic," "minimally classic" or "pure occult." The term "pure classic" applies when 100% of the lesion is composed of the classic component. The term "predominantly classic" applies when 50% or greater of the lesion is made up of the classic component. The term "minimally classic" applies when less than 50% of the lesion is made up of the classic component. The term "pure occult" or "occult lesions" applies when none of the lesion consists of the classic component and therefore the entire, or 100%, of the lesion is made up of the occult component. Based on enrollment of untreated wet AMD patients in third-party clinical trials, the pure occult subtype accounts for approximately 40% of the cases of subfoveal wet AMD in the wet AMD patient population. Some component of occult choroidal neovascularization is present in predominantly classic and minimally classic choroidal neovascularization. For example, in minimally

classic choroidal neovascularization, as observed through fluorescein angiography, up to 99% of the blood vessels may be composed of the occult component, thus only 1% different from 100% or pure occult.

Retinal specialists have historically used fluorescein angiography to determine the extent and location of abnormal new blood vessels relative to the RPE. Currently, there is a shift among retinal specialists to using OCT to image abnormal new blood vessels and associated leakage in wet AMD patients. Because of technological enhancements in OCT machines, the resolution of OCT retinal tissue imaging has increased markedly over the last few years. OCT is the current standard for retinal imaging in the United States and the European Union.

The following diagrams show cross-sections of the back of a normal eye and the progression to and mechanisms of visual loss associated with neovascularization in wet AMD:

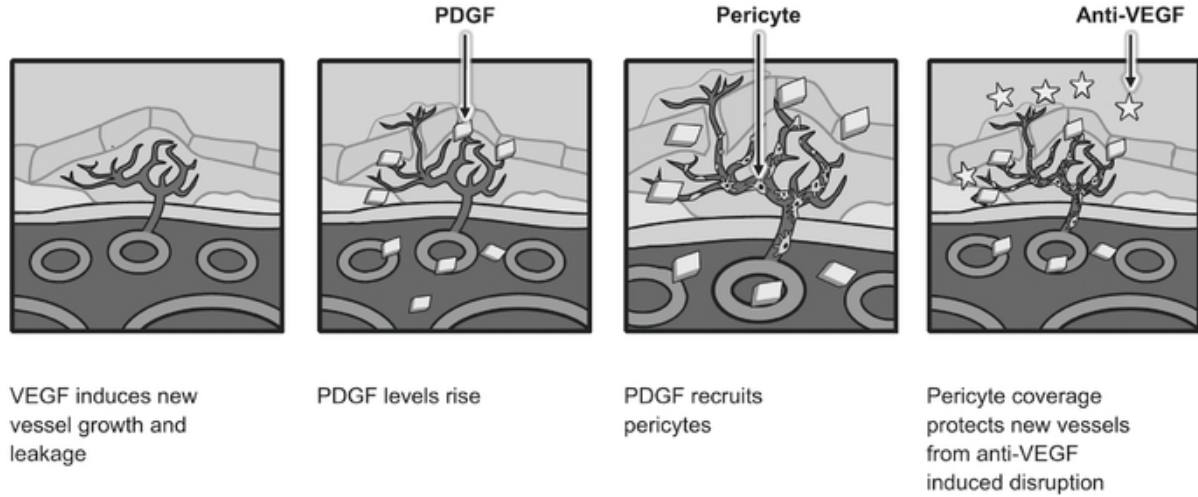




Abnormal new blood vessels are predominantly made up of two cell types, endothelial cells and pericytes. The endothelial cells line the inside of abnormal new blood vessels. Pericytes then intimately cover the outside of these blood vessels. Early in the process of abnormal new blood vessel formation, VEGF binds to a receptor on endothelial cells and causes endothelial cells to proliferate. The proliferating endothelial cells form new blood vessels. VEGF provides survival signals to endothelial cells. VEGF also is one of the most potent inducers of blood vessel permeability, which causes the new blood vessels to leak.

PDGF binds to a receptor on pericytes. The binding of PDGF provides an important cell survival signal to pericytes. PDGF also recruits pericytes to the abnormal new blood vessel, where they mature and cover the endothelial cells. Pericytes locally supply the endothelial cells with growth and survival factors, including VEGF, and play a major role in endothelial cell survival. Pericytes also physically support and stabilize the abnormal new blood vessels.

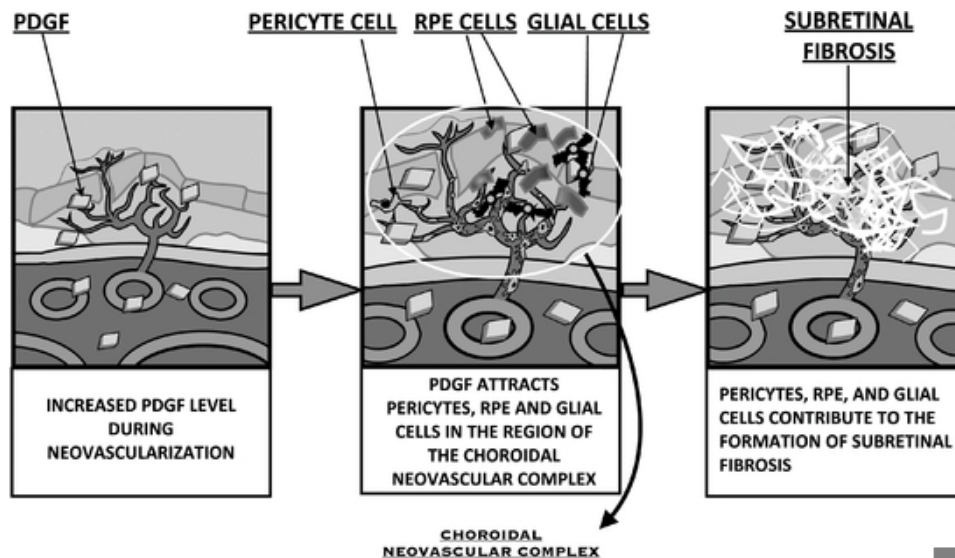
The following diagrams show cross-sections of the back of an eye and the chemical and cellular processes associated with the progression to neovascularization in wet AMD:



The neovascular tissue from patients with wet AMD has been studied extensively through microscopic examination. When examined microscopically, the choroidal neovascular complex appears similar in composition to the tissue encountered in the normal wound healing process. It contains abnormal new blood vessels consisting of endothelial cells and pericytes, and also cells from the surrounding retinal tissue, including RPE cells and glial cells. Glial cells otherwise have a number of important functions, including acting as immune defense cells within the retina.

PDGF attracts pericytes, RPE cells and glial cells, which are all involved in the formation of the choroidal neovascular complex. Third-party preclinical studies suggest that these cells also contribute to the formation of subretinal fibrosis and retinal scarring. PDGF also has been observed as a mediator of fibrosis and wound healing in other organs throughout the body.

The following diagrams show cross-sections of the back of an eye and the chemical and cellular processes associated with the progression from neovascularization to subretinal fibrosis in more advanced cases of wet AMD:



### Currently Available Therapies for Wet AMD

The current standard of care for wet AMD is administration by intravitreal injection of anti-VEGF drugs as monotherapy. The FDA has approved the anti-VEGF drugs Lucentis (ranibizumab), Eylea (aflibercept) and Macugen (pegaptanib sodium) for the treatment of wet AMD. The FDA also has approved photodynamic therapy with Visudyne (PDT) as a treatment of patients with wet AMD. In addition, although approved by the FDA as a cancer therapy, the anti-VEGF drug Avastin (bevacizumab) is used off-label to treat wet AMD. Lucentis is an antibody fragment derived from the same full length antibody from which Avastin was derived.

Lucentis and Eylea are used primarily to treat wet AMD, although they also are approved for the treatment of other diseases of eye. In 2012, annual worldwide sales of Lucentis and Eylea for all indications totaled approximately \$4.8 billion. This sales number does not include Avastin, which is commonly used off-label to treat wet AMD in the United States and, to a lesser extent, in the European Union. According to a paper published in 2011 in the peer reviewed journal *American Journal of Ophthalmology*, Avastin was used off-label to treat approximately 60% of Medicare beneficiaries in 2008 who received anti-VEGF therapy for wet AMD. In addition, according to information published in November 2012 by BioTrends Research Group, retinal specialists in the largest markets in the European Union use off-label Avastin to treat approximately 27% of patients with wet AMD.

Lucentis is marketed in the United States by F. Hoffmann-La Roche Ltd. Lucentis is marketed outside the United States by Novartis AG. Eylea is marketed in the United States by Regeneron Pharmaceuticals, Inc. and outside the United States by Bayer AG, except in Asia where it is marketed by Santen Pharmaceuticals Co. Ltd. Avastin is approved as a cancer therapy and is marketed solely for such use. Avastin is available through compounding pharmacies for off-label use to treat wet AMD at a significantly lower price per dose than either Lucentis or Eylea.

The availability of anti-VEGF drugs has significantly improved visual outcomes for patients with wet AMD who have been treated with anti-VEGF drugs as compared to untreated patients. A retrospective study published in 2012 in the peer reviewed journal *JAMA Ophthalmology* confirmed that

the prevalence of both legal blindness and moderate visual impairment in patients two years after being diagnosed with wet AMD have decreased substantially following the introduction of anti-VEGF therapy. Nonetheless, the condition of many patients with wet AMD treated with anti-VEGF drugs does not improve significantly and in a substantial portion of cases deteriorates. Moreover, on average, improvements in vision through the use of an anti-VEGF drug in the near term is followed by the loss of the initial visual gain over the longer term.

Anti-VEGF drugs prevent VEGF from binding to its natural receptor on endothelial cells in the abnormal new blood vessels, thereby inhibiting further abnormal new blood vessel growth and leakage associated with wet AMD. There is widespread agreement in the scientific community that the majority of the therapeutic benefit of anti-VEGF drugs is due to reducing or eliminating leakage. However, anti-VEGF therapy may be limited in its ability to induce disruption and regression of neovascularization. We believe that the presence of pericytes and their local production of VEGF and other factors protect endothelial cells from the effects of anti-VEGF drugs. Furthermore, a significant percentage of patients treated with an anti-VEGF drug eventually exhibit subretinal fibrosis and retinal scarring. Third-party clinical trial results suggest that altering the dose or regimen of anti-VEGF drugs administered for the treatment of wet AMD does not enhance visual outcome. Moreover, third-party clinical trials also suggest that visual outcomes for wet AMD patients receiving treatment with an anti-VEGF drug worsen over time and are often associated with the development of subretinal fibrosis and the growth of neovascular lesions over time.

Based on the results of third-party clinical trials, after one year of treatment with an anti-VEGF drug:

- approximately 18% to 22% of newly diagnosed wet AMD patients lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, in many cases further diminishing the patients' quality of life;
- approximately 62% to 75% of newly diagnosed patients did not achieve an ability to read an additional 15 or more letters on the standardized chart of vision testing and have not experienced a marked improvement in their ability to enjoy the daily activities made difficult by wet AMD; and
- a majority of patients have not achieved final visual acuity of 20/40 or better, which is necessary to obtain a driver's license in many states.

In 2013, *Ophthalmology* published a study reporting on a four-year longitudinal analysis of 555 wet AMD patients treated with Lucentis. All of the patients included in the study were treated at a single center with the same drug and retreatment criteria. The study found that after four years, on average, patients lost vision compared to their visual acuity at the start of the study. Thirty-two percent of patients continued treatment for the entire four-year study period. After four years, mean visual acuity in this group of patients essentially reverted to pre-study levels. In addition, 28% of patients discontinued treatment. The primary reasons for discontinuation of treatment were sustained low visual acuity and lack of apparent treatment response.

In addition, in 2013, *Ophthalmology* published the results of an uncontrolled study of patients who had received two years of treatment with an anti-VEGF drug in clinical trials and then received additional anti-VEGF therapy at physician's discretion for two more years. When assessed at their last evaluation in this study, approximately 46% of such patients had lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing. Moreover, in 2013, *Ophthalmology* published the results of a separate follow-up study of a cohort of these same patients. When assessed approximately three years after completing their participation in the prior study, approximately one-third had poor outcomes, defined as the loss of the ability to read 15 or more letters on a standardized chart of vision testing, according to the study conclusions. In addition,

approximately 57% of such patients had lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing, compared to baseline prior to receiving therapy in the original clinical trials, and approximately 37% had visual acuity at the level of legal blindness, defined as visual acuity of 20/200 or worse. The study authors noted that wet AMD patients remain at risk for substantial visual decline.

We believe that PDGF is one of the major mediators of the formation and stabilization of the choroidal neovascular complex and the associated development of subretinal fibrosis and retinal scarring. These two processes were associated with poor visual outcome in wet AMD patients in the CATT study. We believe the formation of subretinal fibrosis and retinal scarring leads to retinal dysfunction in the affected region, which on average, leads to poor visual outcomes in a significant portion of wet AMD patients. Two recent studies have focused on the development of subretinal fibrosis in wet AMD patients receiving treatment with an anti-VEGF drug and have implicated subretinal fibrosis as a major factor in the long-term prognosis for visual outcomes for wet AMD patients:

- An article appearing in *Ophthalmology* in 2013 focused on the development of retinal scarring in wet AMD patients receiving treatment with Lucentis or Avastin monotherapy. Findings were based on a retrospective analysis of the Comparisons of AMD Treatment Trials, or CATT, a National Eye Institute sponsored multicenter clinical trial. Approximately 1,200 newly diagnosed wet AMD patients were enrolled and treated with either Lucentis or Avastin over a period of two years. Patients with retinal scarring upon study entry or for whom one-year and two-year ocular photographs were not available were excluded from the analysis. Of the remaining 1,059 patients, 339, or 32%, developed retinal scarring after one year of treatment with either Lucentis or Avastin, while 480, or 45%, developed retinal scarring after two years of treatment with either Lucentis or Avastin. Patients with larger lesion sizes or visual acuity of less than 20/40 upon study entry were more likely to develop retinal scarring.
- In a separate paper from 2013 published in the *American Journal of Ophthalmology*, researchers in Denmark corroborated the published retrospective analysis of the CATT study described above. In the study of 197 newly diagnosed wet AMD patients treated in a single facility, 40% of eyes developed subretinal fibrosis following two years of treatment with Lucentis. Analysis of the results from this study revealed that patients that exhibited subretinal fibrosis began to develop subretinal fibrosis from and after the 3-month timepoint in the study. Moreover, the development of more severe subretinal fibrosis was associated with more severe vision loss.

## **Fovista**

We are developing our product candidate Fovista to be administered in combination with anti-VEGF drugs for the treatment of wet AMD. Fovista is designed to target PDGF. We believe that Fovista's mechanism of action, when administered in combination with an anti-VEGF drug, may result in two relevant biological responses: neovascular regression and inhibition of subretinal fibrosis. Fovista binds to and inhibits PDGF, causing the stripping of pericytes, which are cells that cover the outside of newly formed blood vessels. After the pericytes are stripped from the new blood vessels, endothelial cells lining the inside of the newly formed blood vessels are left unprotected and are highly vulnerable to the effects of anti-VEGF therapy. Fovista also inhibits migration of other retinal cells attracted by PDGF, such as RPE cells and glial cells, which play a role in the formation of subretinal fibrosis. Our belief that Fovista may inhibit subretinal fibrosis is based on both our initial assessment of retinal images from patients who experienced vision loss following treatment with either 1.5 mg of Fovista in combination with 0.5 mg of Lucentis or Lucentis monotherapy in our completed Phase 2b clinical trial, results from pre-clinical tests and the scientific literature. We further believe that the administration of Fovista in combination with anti-VEGF drugs in patients with wet AMD may cause regression of neovascularization and inhibit subretinal fibrosis more effectively than anti-VEGF monotherapy. We

believe that Fovista may provide meaningful added benefit in the treatment of wet AMD regardless of which anti-VEGF drug is administered in combination with Fovista.

VEGF and PDGF are growth factors that share some structural similarities. The VEGF family consists of multiple members, called VEGF-A, VEGF-B, VEGF-C, VEGF-D and PlGF. The PDGF family also consists of multiple members, called PDGF-AA, PDGF-AB, PDGF-BB, PDGF-CC and PDGF-DD.

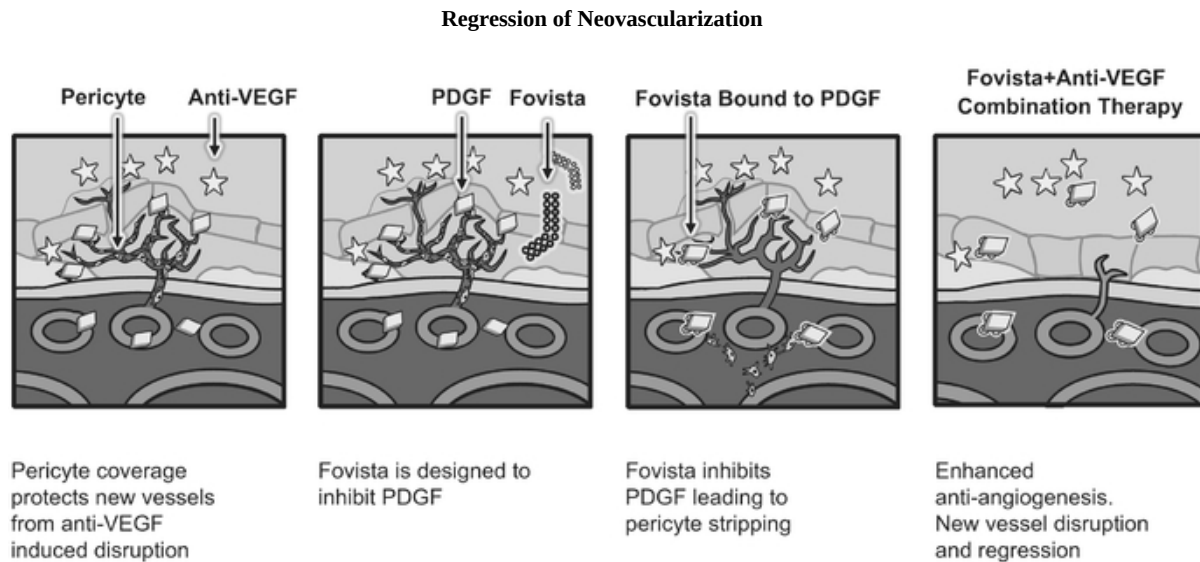
Lucentis, Avastin and Eylea all target VEGF-A, which we generally refer to as VEGF. Fovista targets PDGF-BB, which we generally refer to simply as PDGF. The biological effects of VEGF-A and PDGF-BB are mediated by binding to receptors on the cell surface. Once VEGF-A and PDGF-BB bind to their respective receptors, a variety of signals are generated inside the cell, which alters the cell's behavior. The specific receptors for VEGF-A are called VEGFR-1 and VEGFR-2. The specific receptors for PDGF-BB are called PDGFR- $\alpha$  and PDGF- $\beta$ .

The anti-VEGF drugs Lucentis, Avastin and Eylea exert their biologic effect by binding to VEGF-A, which blocks its interaction with the endothelial cell surface receptor VEGFR-2. This results in inhibition of endothelial cell proliferation, survival and vascular permeability. Fovista exerts its biologic effect by binding to PDGF-BB, which blocks its interaction to the pericyte cell surface receptor PDGF- $\beta$ . This results in stripping or death of the pericytes by interrupting the cell survival signals. PDGF-BB has been shown in multiple independent studies to be critical for pericyte survival and proliferation. Similarly, VEGF-A is critical for endothelial cell survival and proliferation. In addition, the eventual development of subretinal fibrosis and retinal scarring in wet AMD patients may limit the impact of anti-VEGF drugs in the longer term.

We have measured Fovista's inhibition of both PDGF-BB and PDGF-AB binding to both their receptors, PDGFR- $\alpha$  and PDGF- $\beta$ , by widely accepted scientific methods. In *in vitro* assays, Fovista strongly inhibits both PDGF-BB and PDGF-AB from binding to their receptors with potency equal to an antibody that directly blocks the PDGFR- $\alpha$  and PDGF- $\beta$  receptors. In preclinical models, we observed the marked stripping of pericytes from abnormally proliferating blood vessels in animals treated with Fovista. The combination of Fovista and anti-VEGF treatment in animal models of neovascularization disrupted and regressed abnormal new blood vessels to a greater degree than treatment with anti-VEGF monotherapy.

Two reported studies support our hypothesis regarding the benefit Fovista may provide in the inhibition of subretinal fibrosis. A 2005 article published in *Archives of Ophthalmology* described the presence of RPE cells and glial cells in surgically excised retinal neovascular membranes from AMD patients. The composition and appearance of these subretinal neovascular membranes was similar to the early formation of a scar. Furthermore, in 2006, the peer reviewed *Journal of Cell Physiology* published the results of a study in which Fovista monotherapy exhibited anti-fibrotic effects in an animal model of retinal scarring. Moreover, more recent scientific publications have reported on the rate of subretinal fibrosis in wet AMD patients receiving treatment with an anti-VEGF drug. Based on these preclinical and clinical results, as well as our understanding of the mechanisms of action of anti-VEGF drugs and Fovista, we believe that Fovista has the potential to provide meaningful added benefit in the treatment of wet AMD compared to anti-VEGF monotherapy. When administered in combination with anti-VEGF drugs, we believe Fovista may result in both the inhibition and regression of neovascularization, as well as inhibition of subretinal fibrosis. We believe Fovista's mechanism of action is not dependent on the specific anti-VEGF drug regimen with which Fovista is administered.

The following diagram shows what we believe is the anti-neovascularization elements of Fovista's mechanism of action:



The anti-PDGF ingredient in Fovista is a chemically synthesized aptamer. An aptamer is a single strand of nucleic acid that adopts a three-dimensional structure and binds with high specificity and affinity to a particular extracellular target, such as PDGF, in a manner similar to a monoclonal antibody. Aptamers have the following key attributes:

- aptamers are synthetically derived, making production predictable and reproducible; and
- aptamers are chemically stable and do not generate an immune response that could limit efficacy.

Fovista is a pegylated aptamer, which means that polyethylene glycol is linked to the strand of nucleic acid. This pegylation increases the half-life of Fovista, which in turn increases the time that Fovista actively targets PDGF.

Fovista is administered by intravitreal injection after a separate intravitreal injection of an anti-VEGF drug. Before a physician administers the intravitreal injections of the anti-VEGF drug and Fovista, the patient receives topical numbing drops or injection of a numbing agent. In addition, physicians typically rinse the ocular surface with an antiseptic solution. By injecting the medication into the vitreous, the physician delivers Fovista in close vicinity to the active disease site with minimal potential for exposure to non-ocular tissues. Many other therapies used to treat serious retinal disorders, including Lucentis, Avastin and Eylea, also are administered by intravitreal injection.

#### ***Clinical Development of Fovista Combination Therapy for Wet AMD***

We have completed one Phase 1 clinical trial and one Phase 2b clinical trial of Fovista administered in combination with Lucentis for the treatment of wet AMD. We have initiated a pivotal Phase 3 clinical program to evaluate the safety and efficacy of Fovista combination therapy for the treatment of newly diagnosed wet AMD patients compared to current standard of care anti-VEGF monotherapy. We expect to have initial, top-line data from this Phase 3 clinical program available in 2016. If the results of this Phase 3 clinical program are favorable, we plan to submit applications for marketing approval for Fovista in both the United States and the European Union before the end of 2016.

Our Phase 3 clinical program consists of three separate Phase 3 clinical trials, two of which will evaluate Fovista in combination with Lucentis and the other of which will evaluate Fovista in combination with each of Avastin or Eylea. All three of these Phase 3 clinical trials will incorporate significant aspects from the design of our completed Phase 2b clinical trial. We plan to enroll a total of 1,866 patients in more than 225 centers internationally across the three trials.

In July 2013, we submitted protocols for the three trials in our Phase 3 clinical program to the FDA. In August 2013, we initiated enrollment in the United States in the two trials evaluating Fovista administered in combination with Lucentis. We expect to activate initial trial sites in the third trial in this Phase 3 clinical program in the United States by the end of the first quarter of 2014. Outside the United States, we have made regulatory submissions in selected countries to initiate the two Phase 3 clinical trials of Fovista administered in combination with Lucentis and have begun to obtain approvals to proceed. We plan to submit applications seeking to initiate the third trial of Fovista administered in combination with Avastin or Eylea in certain countries outside of the United States in the first quarter of 2014. In the European Union, in addition to filing in selected countries with regulatory agencies referred to as National Competent Authorities, which are responsible for approving clinical trial applications, we are also continuing interactions regarding our planned application for marketing approval with the EMA's CHMP, which is the committee responsible for preparing opinions on questions concerning medicines for human use.

#### ***Completed Phase 1 Clinical Trial of Fovista Combination Therapy for Wet AMD***

In 2009, we completed a multicenter, uncontrolled, open label, ascending dose Phase 1 clinical trial evaluating the safety and tolerability of Fovista administered in combination with Lucentis for the treatment of subfoveal wet AMD. We conducted our Phase 1 clinical trial in 23 patients at 11 centers in the United States. Fovista was generally well tolerated in this trial.

Patients enrolled in our Phase 1 clinical trial were 50 years of age and older and newly diagnosed with subfoveal choroidal neovascularization secondary to AMD with some classic component as documented by fluorescein angiography. Although treating physicians typically do not use subtype categorization as a diagnostic tool for choosing among pharmacological agents for treating wet AMD, we used the subtype classification so as to include in our trial only wet AMD patients with at least some well-defined abnormal new blood vessels. Since we could image and measure the well-defined blood vessels, we believed that we would be able to assess the response of those blood vessels to treatment with Fovista in combination with Lucentis. If we noted regression of abnormal new blood vessels or a disruption or change in the density of abnormal new blood vessels, we believed it would support the anti-neovascularization element of our proposed mechanism of action for Fovista.

We enrolled patients with a range of baseline visual acuity. Visual acuity is measured as the number of letters, arranged in lines, that the patient can read on the Early Treatment Diabetic Retinopathy Study, or ETDRS, eye chart. Each line on the ETDRS eye chart has five letters. This is a well-established standardized chart of vision testing used in these types of trials. Normal visual acuity is commonly referred to as 20/20 vision. To qualify for enrollment in our Phase 1 clinical trial, the visual acuity in the patient's study eye had to be between 20/63 and 20/200. We enrolled patients with a wide range of lesion sizes and with a variety of other lesion characteristics.

We excluded patients from our Phase 1 clinical trial if they met any of the following key exclusion criteria:

- prior treatment for AMD in the study eye, other than oral supplements or vitamins and minerals;
- any intravitreal treatment in the study eye prior to the baseline visit, regardless of indication;

- intraocular surgery or thermal laser within three months of trial entry or any prior thermal laser in the macular region, regardless of indication;
- subfoveal scar or subfoveal atrophy; or
- diabetes mellitus.

Fovista administered in combination with Lucentis was generally well tolerated in our Phase 1 clinical trial. None of the patients experienced any dose limiting toxicities at any of the dose levels tested. We did not observe any evidence of drug related adverse events. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure. There were no adverse events related to Fovista or Lucentis, and no patients discontinued from the trial due to an adverse event. We did not observe any meaningful clinical immunologic reactions to Fovista.

Our Phase 1 clinical trial had a small sample size and a short follow up period. It was not designed to compare Fovista combination therapy to another therapy. However, we noted improvements in visual acuity and anatomical changes in the newly formed blood vessels of the eye that suggested the Fovista combination therapy was enhancing the visual outcome compared to results previously seen with anti-VEGF monotherapy.

#### ***Completed Phase 2b Clinical Trial of Fovista Combination Therapy for Wet AMD***

In 2012, we completed a multicenter, randomized, double-masked, controlled Phase 2b clinical trial evaluating the safety and efficacy of Fovista administered in combination with Lucentis for the treatment of patients newly diagnosed with subfoveal wet AMD. We conducted this trial in 449 patients at approximately 69 centers in North America, South America, Europe and Israel.

The primary objective of this trial was to evaluate the effect of two different doses of Fovista administered in combination with Lucentis compared to Lucentis monotherapy. The primary efficacy endpoint of this trial was mean change in visual acuity from baseline at 24 weeks for Fovista and Lucentis combination therapy compared to Lucentis monotherapy. Prior to enrollment in the trial, we measured each patient's visual acuity to establish a baseline. Following assessment at baseline, visual acuity was measured at each subsequent four-week timepoint. We had diagnostic imaging techniques of fluorescein angiography and OCT performed and assessed by an independent reading center at baseline and at week 24.

Secondary efficacy endpoints for this trial included the following:

- mean change in visual acuity in ETDRS letters from baseline at 12 weeks;
- proportion of patients in each treatment group gaining 15 or more ETDRS letters from baseline at 12 weeks;
- proportion of patients in each treatment group gaining 15 or more ETDRS letters from baseline at 24 weeks; and
- mean change in area of choroidal neovascularization from baseline at 24 weeks.

We randomly assigned patients in this trial to one of three treatment groups. Patients were treated and assessed once every four weeks for 24 weeks. Treatment for the three groups in the trial were as follows:

- In the first group, 149 patients received intravitreal injections of 0.3 mg of Fovista following intravitreal injections of 0.5 mg of Lucentis.
- In the second group, 152 patients received intravitreal injections of 1.5 mg of Fovista following intravitreal injections of 0.5 mg of Lucentis.
- In the third group, which served as the control arm of the trial, 148 patients received sham injections of Fovista following intravitreal injections of 0.5 mg of Lucentis.



To reduce potential bias, the protocol for our Phase 2b clinical trial provided for a double-masked design so that neither the patient nor the investigational staff involved with assessing the vision of the patient knew to which group each patient belonged. The sham injection included all steps involved in the intravitreal treatment injections with the exception that patients in the control group had an empty syringe pressed against their eye walls without a needle. This procedure mimicked an intravitreal injection and helped to maintain proper masking.

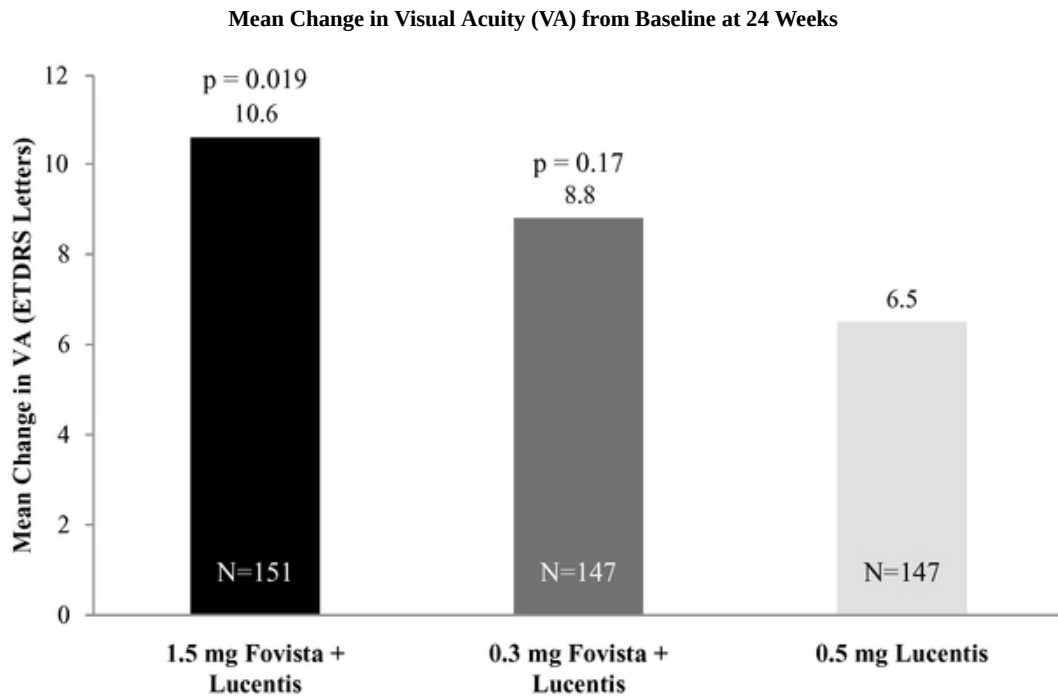
We made no meaningful changes to the inclusion and exclusion criteria in our Phase 2b clinical trial from those we used in our Phase 1 clinical trial. As in our Phase 1 clinical trial, we did not enroll patients with pure occult choroidal neovascularization because it would be difficult to adequately observe and measure the changes in the choroidal neovascular morphology using the imaging techniques that were generally available at most enrolling sites at the time we initiated our Phase 2b clinical trial. We believed that data regarding neovascular regression would be useful in assessing the effects of Fovista administered in combination with Lucentis and in supporting the anti-neovascularization element of our proposed mechanism of action for Fovista.

#### *Measures of Mean Visual Acuity—Primary Efficacy Endpoint*

*Mean Change in Visual Acuity from Baseline at 24 Weeks.* In this trial, the combination of 1.5 mg of Fovista and Lucentis demonstrated statistically significant superiority compared to Lucentis monotherapy based on the pre-specified primary endpoint of mean change in visual acuity from baseline at the 24 week timepoint. We determined 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. However, when multiple doses of a drug are tested against a single control group, a more stringent statistical method that accounts for multiple comparisons must be applied. For this purpose, we used the Hochberg multiple comparison procedure. Under the Hochberg procedure, in order to demonstrate statistical significance for any particular dose, it is necessary to establish a p-value that meets a stricter standard than the conventional standard of 0.05 or less unless each dose is statistically significant with a p-value of 0.05 or less. In the case of our Phase 2b clinical trial, in which we evaluated two doses of Fovista administered in combination with Lucentis, the Hochberg procedure required a more stringent p-value of 0.025 or less to establish statistical significance for the comparison of the combination of 1.5 mg of Fovista and Lucentis to Lucentis monotherapy.

At 24 weeks, patients receiving the combination of 1.5 mg of Fovista and Lucentis gained a mean of 10.6 ETDRS letters compared to a mean of 6.5 ETDRS letters for patients receiving Lucentis monotherapy, representing a 62% comparative benefit from baseline, with a p-value of 0.019. This result was statistically significant. At 24 weeks, patients receiving the combination of 0.3 mg of Fovista and Lucentis gained a mean of 8.8 ETDRS letters. This result was not statistically significant, having a p-value greater than 0.05, compared to Lucentis monotherapy. However, as discussed in more detail below, we believe that the relative visual benefit of the combination of 1.5 mg of Fovista and Lucentis compared to the relative visual benefit of the combination of 0.3 mg of Fovista and Lucentis at all timepoints exhibits a dose-response curve in which the response to treatment increases with higher drug concentrations of Fovista. We are not testing the combination of 0.3 mg of Fovista and Lucentis compared to Lucentis monotherapy in our Phase 3 clinical program.

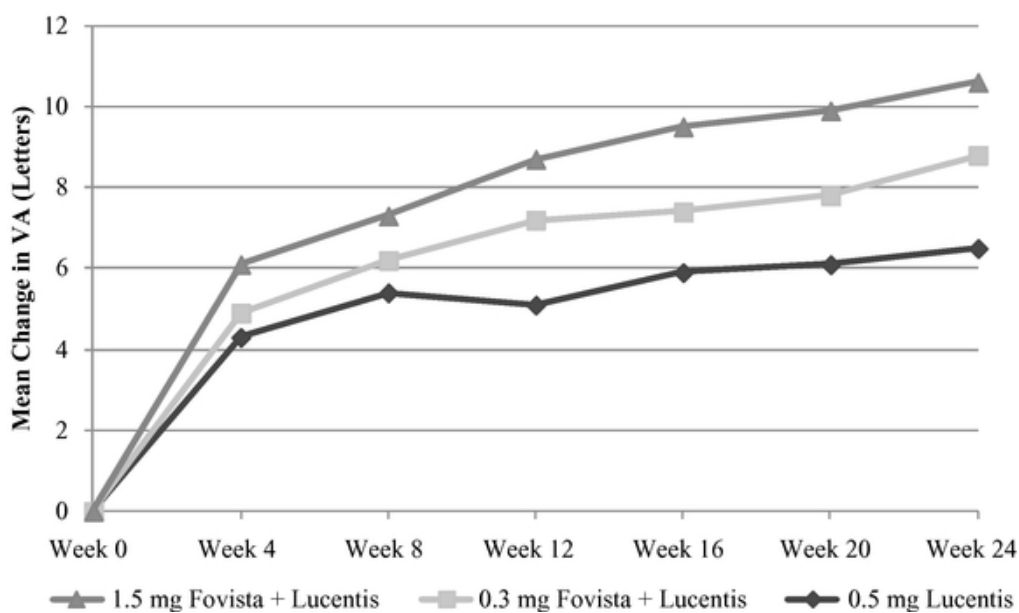
The graph below sets forth the results of the pre-specified primary endpoint in this Phase 2b clinical trial.



*Measures of Mean Visual Acuity—Mean Change in Visual Acuity From Baseline Over Time*

Patients treated with the combination of 1.5 mg of Fovista and Lucentis showed greater improvement in visual acuity from baseline compared to patients treated with Lucentis monotherapy at week four and at each subsequent four-week assessment. In addition, the relative magnitude of visual benefit favoring the combination of 1.5 mg of Fovista and Lucentis increased over the study period. The graph below sets forth the mean change in visual acuity from baseline for each treatment group over the course of the trial.

**Mean Change in Visual Acuity (VA) from Baseline Over Time**

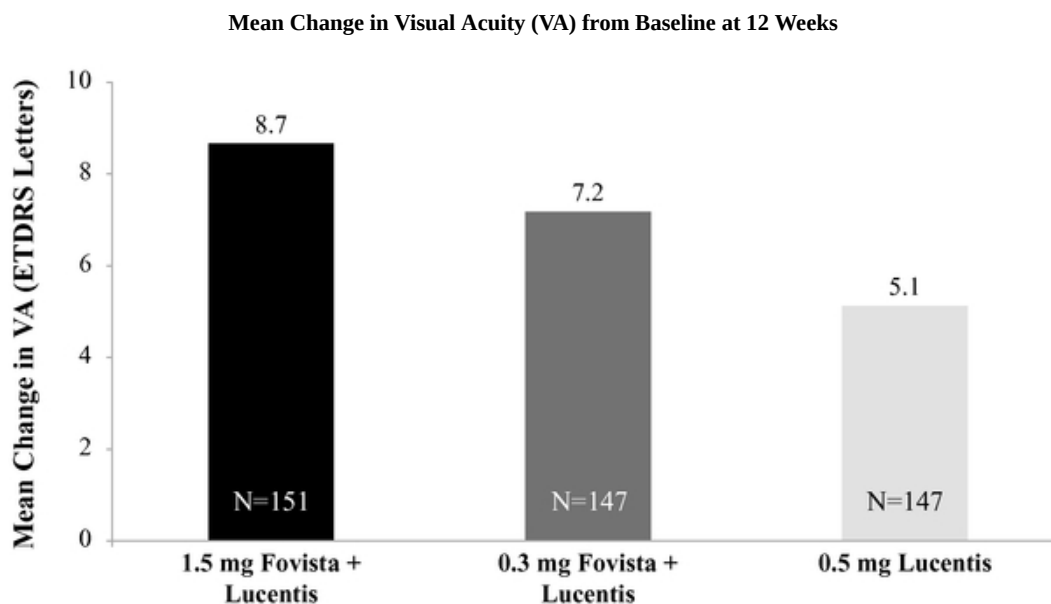


We believe that the divergence of the efficacy curves suggests an increasing relative benefit in visual outcome for the combination of 1.5 mg of Fovista and Lucentis over time compared to Lucentis monotherapy. If we observe a similar pattern of visual benefit in our Phase 3 clinical program, we believe that chronic administration of 1.5 mg of Fovista with Lucentis may be indicated. In addition, we believe that the relative visual benefit of the combination of 1.5 mg of Fovista and Lucentis compared to the relative visual benefit of the combination of 0.3 mg of Fovista and Lucentis at all timepoints exhibits a dose-response curve in which the response to treatment increases with higher drug concentrations of Fovista.

*Measures of Mean Visual Acuity—Secondary Endpoints*

We evaluated measures of visual outcomes as secondary endpoints. Results from secondary endpoints are used to help interpret the primary result of the trial and to provide information for future research and clinical development. However, the statistical analysis plan for our Phase 2b clinical trial was not designed to establish and, as a result, we could not and did not demonstrate, statistical significance with respect to these secondary endpoints. Accordingly, only descriptive analyses and trends for secondary endpoints are presented below.

*Mean Change in Visual Acuity from Baseline at 12 Weeks.* We observed differences on the secondary endpoint of mean change in visual acuity from baseline at the 12 week timepoint favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy. At 12 weeks, patients receiving the combination of 1.5 mg of Fovista and Lucentis gained a mean of 8.7 ETDRS letters compared to patients receiving Lucentis monotherapy who gained a mean of 5.1 ETDRS letters. The graph below sets forth the results of this secondary endpoint of visual acuity at 12 weeks.



*Proportion of Patients Gaining 15 or More Letters from Baseline at 12 Weeks and at 24 Weeks.* We observed differences in the proportion of patients that showed improvement of 15 ETDRS letters, or three lines, or better in visual acuity favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy both at 12 weeks and at 24 weeks of treatment.

The table below sets forth at 12 weeks and 24 weeks the number of patients in the treatment group and the percentage of patients in such treatment group who gained the specified number of lines in visual acuity and the percentage of patients whose final visual acuity improved to the specified level.

**Proportion of Patients Gaining 15 or More ETDRS Letters**

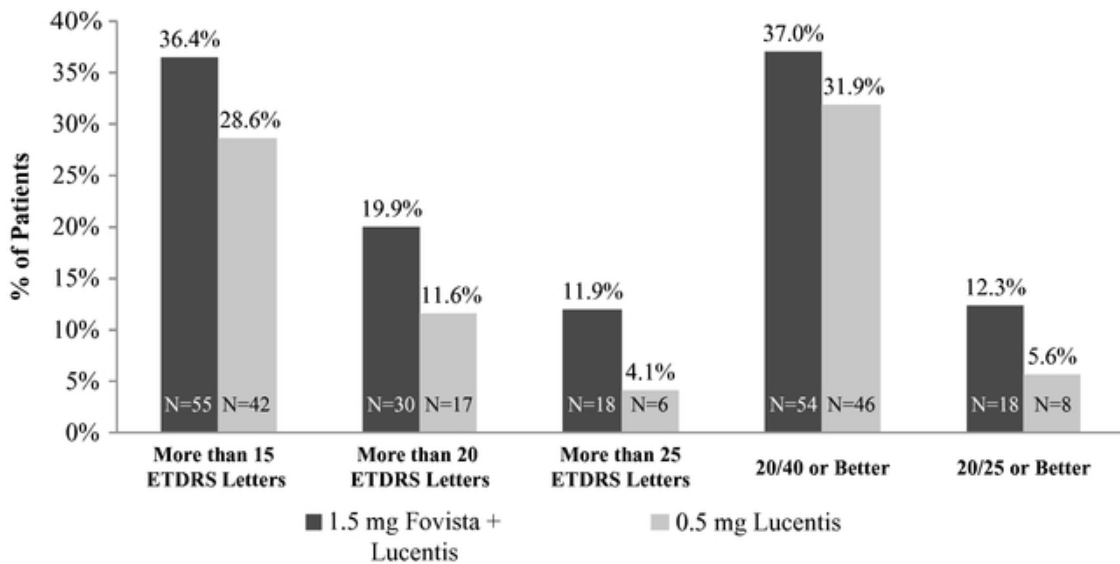
<u>Arm</u>	<u># (%) of Patients Gaining <sup>3</sup> 15 letters at Week 12</u>	<u># (%) of Patients Gaining <sup>3</sup> 15 letters at Week 24</u>
1.5 mg Fovista + Lucentis	48 (31.8)%	59 (39.1)%
0.3 mg Fovista + Lucentis	31 (21.1)%	49 (33.3)%
0.5 mg Lucentis	33 (22.4)%	50 (34.0)%

*Measures of Mean Visual Acuity—Clinically Relevant Retrospective Analyses*

We performed additional retrospective analyses of visual acuity measures that were not pre-specified primary or secondary endpoints in our Phase 2b clinical trial design. Although a retrospective analysis performed after unblinding trial results can result in the introduction of bias, we believe that these retrospective analyses may further support the results from our primary endpoint and the anti-neovascularization element of our proposed mechanism of action for Fovista.

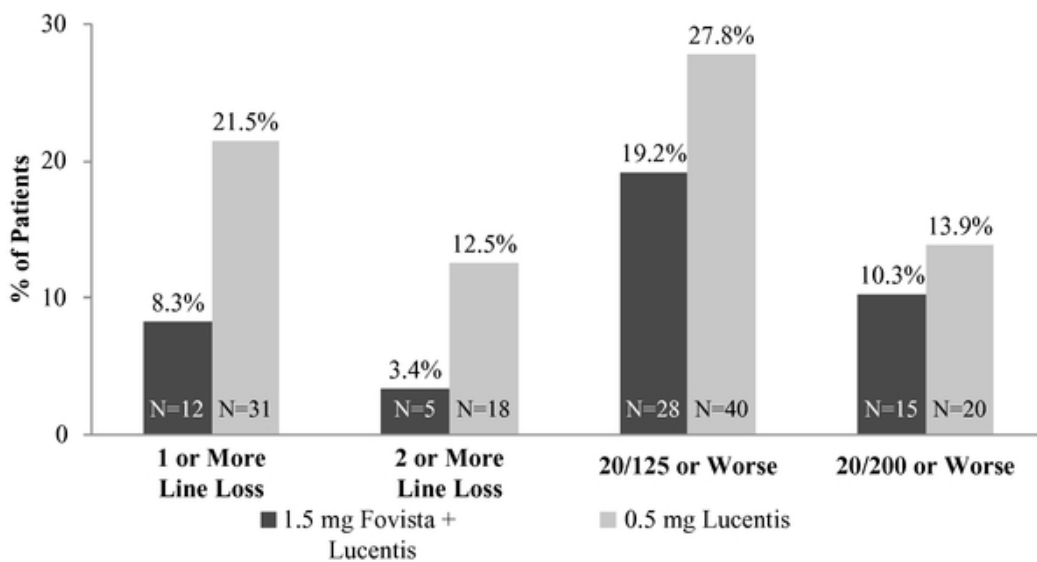
*Retrospective Analysis of Visual Gain.* We observed differences in the proportion of patients that showed improvement when measured by the number of lines of improvement in visual acuity from baseline, referred to as final visual acuity, favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy. The graphs below set forth for each of these two treatment groups at 24 weeks the percentage of patients in such treatment group who gained the specified number of lines in visual acuity and the percentage of patients whose final visual acuity improved to the specified level.

Visual Gain at 24 Weeks



*Retrospective Analysis of Visual Loss.* We observed differences in loss of visual acuity from baseline favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy. The graphs below set forth for each of these two treatment groups the percentage of patients in such treatment group who lost the specified number of lines in visual acuity and the percentage of patients whose final visual acuity declined to the specified level.

Visual Loss at 24 Weeks



*Measures of Anatomical Changes—Secondary Endpoint*

We evaluated one measure of anatomical change as a secondary endpoint. Results from secondary endpoints are used to help interpret the primary result of the trial and to provide information for future research and clinical development. However, the statistical analysis plan for our Phase 2b clinical

trial was not designed to establish and, as a result, we could not and did not demonstrate, statistical significance with respect to this secondary endpoint. Accordingly, only descriptive analyses and trends for this secondary endpoint are presented below.

*Mean Change in Area of Choroidal Neovascularization from Baseline at 24 Weeks.* In our Phase 2b clinical trial, the mean change in area of choroidal neovascularization, or CNV, from baseline at 24 weeks as determined by review of fluorescein angiograms was greater in patients treated with Lucentis monotherapy than in patients treated with the combination of 1.5 mg of Fovista and Lucentis. We believe that the inclusion of both larger and smaller CNV sizes in the single analysis of this secondary endpoint had the potential to create a distortion in the analysis of the mean change in area of CNV. This is because the average level of regression, as numerically measured, was approximately tenfold greater in the large CNV size patient group compared to the small CNV size patient group. The treatment group with the greater number of patients with larger CNV sizes will show a markedly larger amount of regression on average. That was the case in our Phase 2b trial in which the Lucentis monotherapy group had a greater proportion of patients with large CNV sizes compared to the group treated with a combination of 1.5 mg of Fovista and Lucentis. Therefore, as discussed in more detail below, we performed retrospective analyses by creating subgroups based on the size of CNV at baseline.

#### *Measures of Anatomical Changes—Retrospective Analyses*

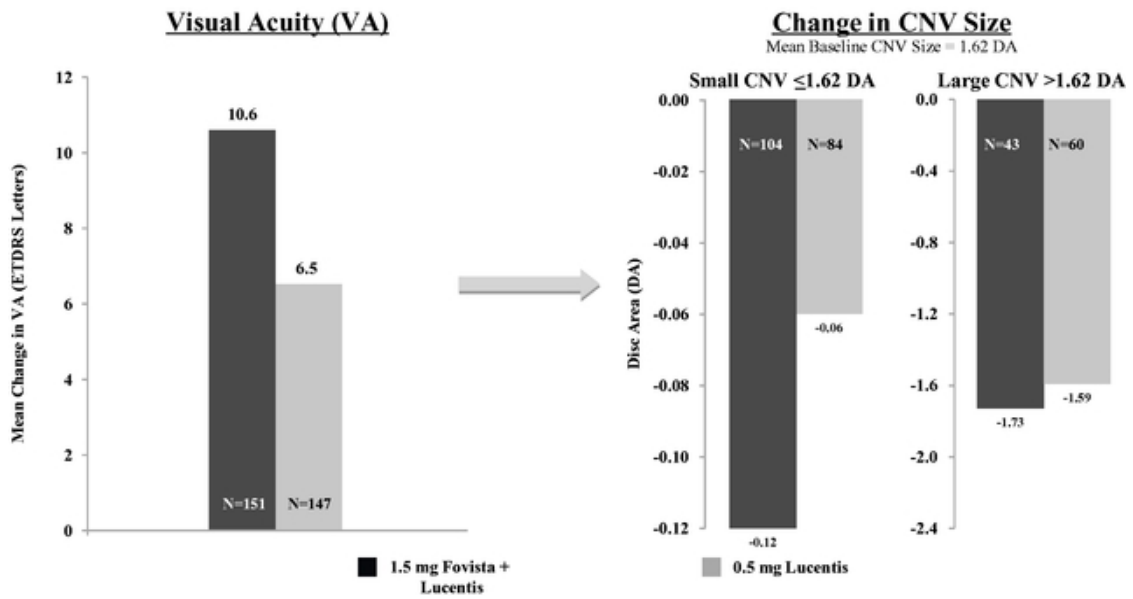
We performed retrospective analyses of anatomical changes, based on choroidal neovascularization and subretinal hyper-reflective material, that were not pre-specified primary or secondary endpoints in the trial design. Although a retrospective analysis performed after unblinding trial results can result in the introduction of bias, we believe that these retrospective analyses may further support the results from our primary endpoint and the anti-neovascularization element of our proposed mechanism of action for Fovista.

*Retrospective Analysis of Choroidal Neovascularization.* We performed several retrospective analyses of neovascular regression by creating subgroups based on CNV sizes. Size of CNV is measured in units called disc area. A disc area is the size of the area of the retina where a standard sized optic nerve emerges. We determined that the mean CNV size for all patients in the Phase 2b clinical trial at baseline was 1.62 disc areas. We created two subgroups of patients based on mean CNV size at baseline. One subgroup of patients, referred to as the large CNV size patients, had initial CNV size greater than 1.62 disc areas. The other subgroup of patients, referred to as the small CNV size patients, had initial CNV size of less than or equal to 1.62 disc areas.

We believe the results described below of our retrospective analyses of mean change in area of choroidal neovascularization from baseline at 24 weeks determined by review of fluorescein angiograms in patients treated with the combination of 1.5 mg of Fovista and Lucentis compared to patients receiving Lucentis monotherapy may support the anti-neovascularization element of our proposed mechanism of action for Fovista. We included in these retrospective analyses only those patients whose CNV size we were able to assess both at baseline and at 24 weeks.

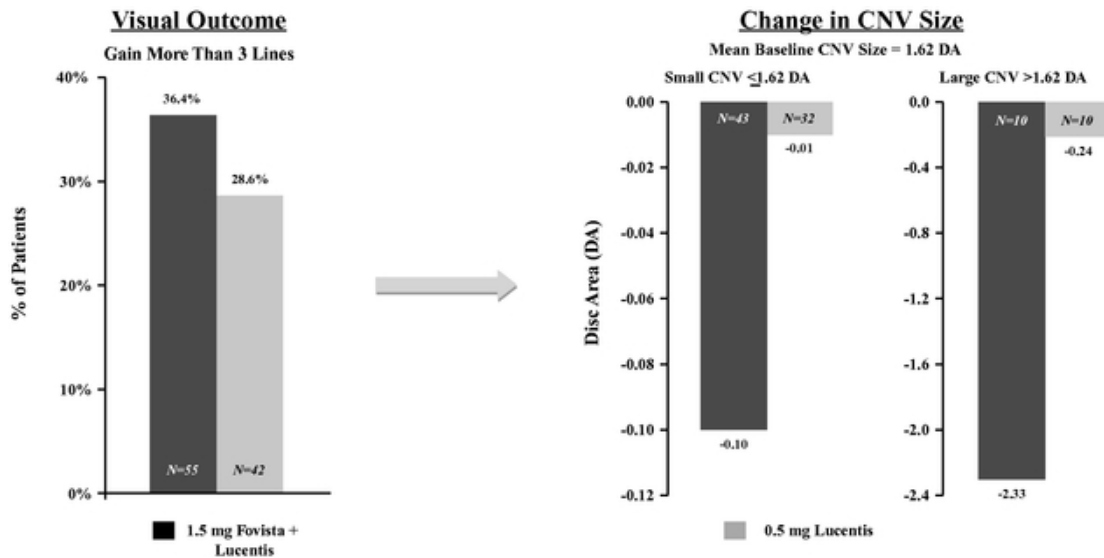
Patients in both the large CNV size patient subgroup and small CNV size patient subgroup showed greater reductions in the size of choroidal neovascularization from baseline when treated with the combination of 1.5 mg of Fovista and Lucentis as compared to patients in the applicable subgroup receiving Lucentis monotherapy. The graphs below set forth the results of this subgroup analysis.

Mean Change in Area of CNV at 24 Weeks



In addition, we performed a further retrospective subgroup analysis of patients who experienced a visual gain of more than three lines from baseline after 24 weeks of treatment. Both large CNV size patients and small CNV size patients treated with the combination of 1.5 mg of Fovista and Lucentis showed a marked reduction in the average size of choroidal neovascularization from baseline when compared to large CNV size patients and small CNV size patients treated with Lucentis monotherapy. The graphs below set forth the results of this subgroup analysis.

Mean Change in Area of CNV at 24 Weeks  
in Patients with Visual Gain of More Than 3-Lines



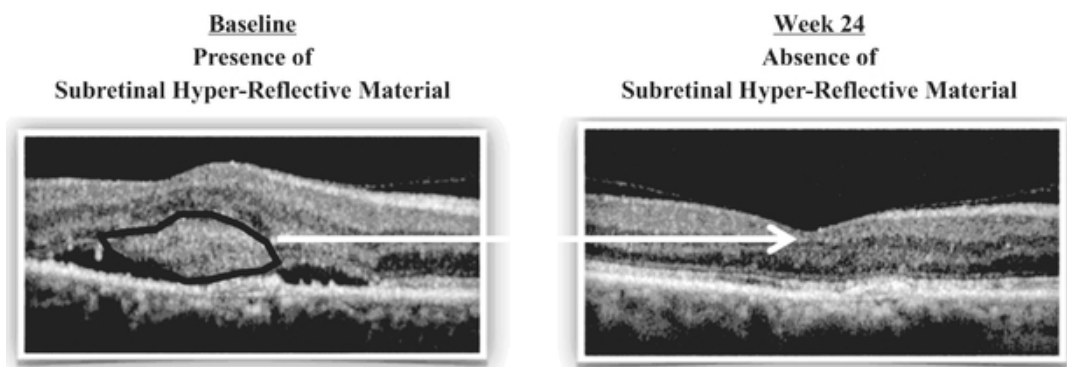
*Retrospective Analysis of Subretinal Hyper-Reflective Material.* We performed a retrospective review of OCT images of patients who participated in the trial without regard to baseline size of choroidal

neovascularization. OCT is the imaging technique most widely used today in clinical practice for the evaluation of wet AMD. Unlike fluorescein angiograms, OCT images show a cross-sectional view of the retina that permits excellent resolution of the space under the retina and at the RPE-choroid interface where the neovascularization of wet AMD is present. The presence of subretinal hyper-reflective material is thought by many experts to indicate the presence of the CNV lesion. The subsequent resolution of subretinal hyper-reflective material is thought to correlate with regression of the CNV lesion.

In our retrospective analysis, masked readers trained in the reading of the OCT retinal images assessed the retinal images of patients who participated in the trial for the presence of subretinal hyper-reflective material at baseline and at 24 weeks. We conducted this retrospective analysis based on the OCT retinal images which were read for each patient group at baseline and at week 24. The analysis at week 24 included only patients who completed the study and had OCT retinal images acceptable for analysis.

Patients treated with the combination of 1.5 mg of Fovista and Lucentis exhibited greater resolution of subretinal hyper-reflective material from baseline compared to patients treated with Lucentis monotherapy. In addition, based on our review of OCT images, patients who experienced a visual gain of more than three lines from baseline at 24 weeks and were treated with the combination of 1.5 mg of Fovista and Lucentis exhibited greater resolution of subretinal hyper-reflective material from baseline than patients who experienced a similar visual gain and were treated with Lucentis monotherapy. The graphs below set forth for each of these two treatment groups the percentage of patients in such treatment group who had subretinal hyper-reflective material at baseline and the percentage of those patients who exhibited an absence of such subretinal hyper-reflective material at 24 weeks.

**Subretinal Hyper-Reflective Material**



	<b>Presence of Subretinal Hyper-Reflective Material at Baseline</b>	<b>Absence of Subretinal Hyper-Reflective Material at Week 24</b>
<b>All Patients</b>		
1.5 mg Fovista + Lucentis	92.8% (N=141)	32.4% (N=47)
0.5 mg Lucentis	93.2% (N=138)	21.5% (N=31)
<b>Patients With Significant Visual Gain (&gt;3-Lines)</b>		
1.5 mg Fovista + Lucentis	87.3% (N=48)	53.8% (N=28)
0.5 mg Lucentis	90.5% (N=38)	38.1% (N=16)



We believe the results of our retrospective analysis of OCT retinal images at baseline and at 24 weeks in patients treated with the combination of 1.5 mg of Fovista and Lucentis compared to patients receiving Lucentis monotherapy supports the anti-neovascularization element of our proposed mechanism of action for Fovista.

*Retrospective Analysis of Subretinal Fibrosis*

Development of subretinal fibrosis is typically associated with poor visual outcomes in wet AMD patients. We are currently undertaking a retrospective analysis of retinal images from patients who experienced vision loss following treatment with either 1.5 mg of Fovista in combination with 0.5 mg of Lucentis or Lucentis monotherapy in our Phase 2b clinical trial to investigate the development of subretinal fibrosis in these patients. Our initial assessment of retinal images from these patients indicates a reduction, on average, in the development and severity of subretinal fibrosis at the 24 week timepoint in patients treated with the combination of 1.5 mg of Fovista and Lucentis compared to patients receiving Lucentis monotherapy. We plan to perform additional analyses of these retinal images focusing on the development of subretinal fibrosis employing multiple imaging comparison techniques. In addition, we have and will continue to engage independent third-party retinal experts to review these images to assess the development of subretinal fibrosis in this group of patients. It is possible that our initial findings will not be confirmed by the reading center as such analysis is subjective. However, if our initial findings are confirmed, we believe such findings will provide support for the anti-fibrotic element of our proposed mechanism of action for Fovista. Based on the internal analysis we have performed to date, we plan to further evaluate the role of Fovista, when administered in combination with an anti-VEGF drug, in inhibiting the development of subretinal fibrosis through the conduct of a Phase 2 trial, which we expect to initiate in 2014.

Safety

Fovista was generally well tolerated in this trial at both doses tested in combination with Lucentis. We did not observe any cases of infection inside the eye, or endophthalmitis. We observed one case of severe intraocular inflammation among the patients treated with 0.3 mg of Fovista in combination with Lucentis and no such cases among the patients treated with 1.5 mg of Fovista in combination with Lucentis. We did not observe any significant imbalances among treatment groups in the incidence of ocular adverse events or systemic adverse events, including cardiovascular events or stroke. The number of patients in our Phase 2b clinical trial with one or more serious systemic adverse events, the most common systemic serious adverse events in this trial organized by MedDRA system organ class, a standard method of reporting adverse events, and by antiplatelet trialists' collaboration events, a standard method of reporting cardiovascular adverse events, are set forth in the table below.

	Monotherapy Lucentis N = 148	0.3 mg Fovista + Lucentis N = 149	1.5 mg Fovista + Lucentis N = 152
<b>Patients With One or More Systemic Serious Adverse Events</b>	11 (7.4)%	13 (8.7)%	9 (5.9)%
<b>MedDRA System Organ Class(1)</b>			
Cardiac Disorders	2 (1.4)%	2 (1.3)%	2 (1.3)%
Gastrointestinal Disorders	1 (0.7)%	2 (1.3)%	3 (2.0)%
Infections	1 (0.7)%	2 (1.3)%	0 (0.0)%
Musculoskeletal Disorders	1 (0.7)%	0 (0.0)%	2 (1.3)%
Neoplasms	3 (2.0)%	3 (2.0)%	1 (0.7)%
Nervous System Disorders	3 (2.0)%	1 (0.7)%	0 (0.0)%
Respiratory Disorders	0 (0.0)%	3 (2.0)%	2 (1.3)%
<b>Any Antiplatelet Trialists' Collaboration (APTC) Event</b>			
Non-Fatal Myocardial Infarction	0 (0.0)%	0 (0.0)%	0 (0.0)%
Non-Fatal Stroke	2 (1.4)%	1 (0.7)%	0 (0.0)%
Vascular Death	1 (0.7)%	0 (0.0)%	0 (0.0)%

(1) Data are listed only for system organ classes with three or more events.

There was one serious adverse event in the study eye in each of the treatment groups. The serious adverse event was different among each of the treatment groups as shown in the table below.

	Monotherapy Lucentis N = 148	0.3 mg Fovista + Lucentis N = 149	1.5 mg Fovista + Lucentis N = 152
<b>Ocular Serious Adverse Events</b>	1 (0.7)%	1 (0.7)%	1 (0.7)%
Corneal Erosion	0 (0.0)%	0 (0.0)%	1 (0.7)%
Uveitis	0 (0.0)%	1 (0.7)%	0 (0.0)%
Visual Acuity Reduced	1 (0.7)%	0 (0.0)%	0 (0.0)%

The most common adverse events in the study eye are set forth in the table below.

#### Ocular Adverse Events Reported in Study Eye in 5% or More of Patients in Any Arm

	Monotherapy Lucentis N = 148	0.3 mg Fovista + Lucentis N = 149	1.5 mg Fovista + Lucentis N = 152
<b>Patients with One or More Adverse Events</b>	75 (50.7)%	79 (53.0)%	79 (52.0)%
Conjunctival hemorrhage	37 (25.0)%	34 (22.8)%	51 (33.6)%
Punctate keratitis	10 (6.8)%	19 (12.8)%	15 (9.9)%
Eye pain	8 (5.4)%	10 (6.7)%	13 (8.6)%
Conjunctival hyperemia	13 (8.8)%	9 (6.0)%	13 (8.6)%
Subretinal fibrosis	8 (5.4)%	6 (4.0)%	5 (3.3)%
Intraocular pressure increase	4 (2.7)%	8 (5.4)%	9 (5.9)%

Most of the common ocular adverse events in this trial were related to the intravitreal preparation and injection procedure and were not drug related. These intravitreal adverse events, as reflected in the table above, included conjunctival hemorrhage, punctate keratitis, eye pain and conjunctival hyperemia. Most adverse events of increased intraocular pressure occurred after injection, were transient, were related to the injection and were treated and resolved the same day. Mean intraocular pressure in each treatment group returned to pre-injection level at the next assessment, including at the end of the trial.

#### *Ongoing Phase 3 Clinical Program for Fovista Combination Therapy for Wet AMD*

We have initiated a pivotal Phase 3 clinical program consisting of three separate Phase 3 clinical trials to evaluate the safety and efficacy of Fovista administered in combination with anti-VEGF drugs for the treatment of newly diagnosed wet AMD patients compared to anti-VEGF monotherapy. We plan to conduct these trials with a total of 1,866 patients at more than 225 centers internationally.

The primary efficacy endpoint of our Phase 3 clinical trials is mean change in visual acuity from baseline for Fovista and anti-VEGF combination therapy compared to anti-VEGF monotherapy at 12 months. Secondary efficacy endpoints for our Phase 3 clinical trials include the following:

- proportion of patients in each treatment group gaining 20 or more ETDRS letters from baseline at month 12;
- proportion of patients in each treatment group gaining 25 or more ETDRS letters from baseline at month 12;
- proportion of patients in each treatment group losing 5 or more ETDRS letters from baseline at month 12; and
- mean change in visual acuity in ETDRS letters from baseline at month six.

Two of our three Phase 3 clinical trials are evaluating the safety and efficacy of 1.5 mg of Fovista administered in combination with Lucentis compared to Lucentis monotherapy. We have begun treating patients in these two clinical trials. The third Phase 3 clinical trial will evaluate the safety and efficacy of 1.5 mg of Fovista administered in combination with each of Avastin or Eylea compared to Avastin or Eylea monotherapy. All of these Phase 3 clinical trials incorporate significant aspects from the design of our completed Phase 2b clinical trial.

The protocols for our Phase 3 clinical trials and other supporting information are subject to review by the FDA and regulatory authorities outside the United States. The FDA is not obligated to comment on our protocols within any specified time period or at all or to affirmatively clear or approve our Phase 3 clinical program. We submitted the protocols for our Phase 3 clinical trials to the FDA in July 2013 and, in August 2013, initiated two of the trials in our Phase 3 clinical program in the United States, both of which are evaluating the safety and efficacy of Fovista administered in combination with Lucentis, without waiting for any such comments. To date, we have not received any such comments from the FDA. We expect to activate initial trial sites in the third trial in this Phase 3 clinical program in the United States by the end of the first quarter of 2014. The FDA or other regulatory authorities may request additional information, require us to conduct additional non-clinical trials or require us to modify our proposed Phase 3 clinical program, including its endpoints, patient enrollment criteria or selection of anti-VEGF drugs, to receive clearance to initiate such program or to continue such program once initiated.

Outside the United States, we have made regulatory submissions in selected countries to initiate the two Phase 3 clinical trials of Fovista administered in combination with Lucentis and have begun to obtain approvals to proceed. We plan to submit applications seeking to initiate the third trial of Fovista administered in combination with Avastin or Eylea in the first quarter of 2014. In the European Union, as further described below, in addition to filing in selected countries with national competent authorities responsible for approving clinical trial applications, we are also continuing interactions regarding our planned application for marketing approval with the EMA's CHMP, which is the committee responsible for preparing opinions on questions concerning medicines for human use. The national competent authorities may follow the advice described below of the CHMP that we consider toxicity studies with Fovista administered in combination with Avastin or Eylea prior to initiating our corresponding Phase 3 clinical trial.

The CHMP recently provided scientific advice on our proposed Phase 3 clinical program for Fovista and our plan to seek regulatory approval for Fovista. As part of that scientific advice, the CHMP advised us that the planned primary endpoint for each of the Fovista Phase 3 clinical trials, mean change from baseline in best corrected visual acuity, was acceptable. In addition, the CHMP confirmed that carcinogenicity studies are not needed for our Phase 3 clinical program. The CHMP also advised us that we should justify our proposal to initiate, at the Phase 3 clinical trial stage, certain previously untested combinations of Fovista with Avastin or Eylea, and, as described above, that we should consider conducting toxicity studies with Fovista administered in combination with Avastin or Eylea prior to initiating our corresponding Phase 3 clinical trial. In addition, the CHMP informed us that, given that Avastin is not approved for intravitreal use in the European Union, the final label for Fovista, if it receives marketing approval, may be required to specify only the anti-VEGF drugs approved for intravitreal use that were studied in combination with Fovista, rather than a broad label specifying Fovista for use in combination with any anti-VEGF drug. The CHMP further advised us that there will be a requirement for additional data to bridge the results from our Phase 3 clinical trials evaluating Fovista administered in combination with Lucentis as compared to Lucentis monotherapy to the less frequent dosing regimens of Lucentis and Eylea approved in the European Union.

We have responded to the CHMP on these issues and expect to receive further comments on our response from the CHMP by the end of the first quarter of 2014. We plan to adjust the dosing schedule in our Phase 3 clinical program for Fovista administered in combination with Eylea so that no bridging study would be needed for this combination. Although discussions with the CHMP regarding the need for, and possible design of, a Lucentis bridging study, are ongoing, we expect that, if we determine or are required to conduct such a study, it would not have a material impact on our anticipated timing and overall expense of our Phase 3 clinical plan, including our plan to have initial, top-line data from our Phase 3 clinical program for Fovista available in 2016.

For each patient enrolled in the Phase 3 clinical trials, we plan to measure the patient's visual acuity prior to treatment to establish a baseline. The protocols for each of these trials provide that patients will be treated and assessed once a month for 12 months and will continue in the trial for

another 12 months thereafter. In the second 12 months of the trials, the protocols currently provide that patients will continue to be assessed every month and treated every other month, with a final follow-up visit at 24 months. If, at any alternate month visit during the second 12 months of the trials, a patient's visual acuity has decreased by five or more ETDRS letters since the patient's previous visit, or the patient's visual acuity has decreased by any amount since the patient's previous visit and the treating physician makes certain negative findings based on fluorescein angiography or OCT, the patient also will be treated at that alternate month visit. We may, however, change aspects of the trial design, including changes to the treatment regimen to provide for longer or shorter intervals between treatments, for the second 12 months after the trials have begun but before any patients begin the second 12 months of the trials.

Based on our estimates regarding patient enrollment, we expect to have initial, top-line data from this Phase 3 clinical program available in 2016. If the results of this Phase 3 clinical program evaluating Fovista are favorable, we plan to submit applications for marketing approval seeking a broad label for Fovista in combination with anti-VEGF drugs in both the United States and the European Union before the end of 2016. In September 2013, the FDA notified us that we have obtained fast track designation for Fovista for the treatment of wet AMD.

We expect to submit applications for marketing approval of Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD in the United States and the European Union if we obtain positive outcomes in at least two of our three Phase 3 clinical trials. We believe that clinically meaningful favorable results from two of our Phase 3 clinical trials in which a combination of 1.5 mg of Fovista with an anti-VEGF drug achieves superiority over anti-VEGF drug monotherapy with statistical significance on the primary endpoint of mean change in visual acuity from baseline at 12 months, together with the results of our Phase 1 and Phase 2b clinical trials, will be sufficient to support applications for marketing approval of Fovista for the treatment of wet AMD in the United States and the European Union. However, if favorable results from two of our three Phase 3 clinical trials include results from only one of our Phase 3 clinical trials evaluating the safety and efficacy of a combination of 1.5 mg of Fovista and Lucentis, the FDA, the EMA or other regulatory authorities may not grant, or may request additional information, including the results of additional clinical trials, prior to granting, marketing approval for Fovista.

We expect to submit our applications for marketing approval based on data regarding the primary efficacy endpoint from our Phase 3 clinical trials after 12 months of treatment. We also expect that 12-month safety data will satisfy the safety database requirements for submission of our applications. Our Phase 3 clinical trials will continue after such submissions in accordance with the protocols for these trials. We may, however, change aspects of the trial design, including by making changes to the treatment regimen to provide for longer or shorter intervals between treatments, for the second 12 months after the trial has begun but before any patients begin the second 12 months of the trial. We expect that each of the FDA and the EMA will review any additional safety and efficacy data that is available from the ongoing Phase 3 clinical trials, or any other clinical trials involving Fovista, at the time of the FDA's or EMA's review of our applications for marketing approval.

In addition, we expect that we would commence a clinical trial in Japan of fewer than 100 patients in early 2017. We believe that favorable results from this small clinical trial together with the results of our Phase 1, Phase 2b and Phase 3 clinical trials will be sufficient to support an application for marketing approval of Fovista administered in combination with an anti-VEGF drug for the treatment of wet AMD in Japan.

The two Phase 3 clinical trials evaluating the safety and efficacy of 1.5 mg of Fovista administered in combination with Lucentis have the same trial design. These two trials build upon and incorporate significant aspects from the design of our Phase 2b clinical trial of Fovista administered in combination with Lucentis while evaluating the administration of Fovista combination therapy over a longer overall treatment period in a greater number of patients. In these first two trials, we are randomly assigning

patients to one of two treatment groups with approximately 311 patients in each group. Treatment for the two groups in each of these two trials is as follows:

- Patients in the first group receive intravitreal injections of 1.5 mg of Fovista following intravitreal injections of 0.5 mg of Lucentis.
- Patients in the second group, which serves as the control arm of the trial, receive sham injections of Fovista following intravitreal injections of 0.5 mg of Lucentis.

We expect that the third of these three Phase 3 clinical trials will follow a similar trial design. In this third trial, we plan to randomly assign patients to one of two treatment groups with approximately 311 patients in each group. Treatment for the two groups in this trial is as follows:

- Patients in the first group will be further randomized in a 1:1 ratio to receive intravitreal injections of one of the following treatments:
  - 1.5 mg of Fovista following intravitreal injections of 1.25 mg of Avastin; or
  - 1.5 mg of Fovista following intravitreal injections of 2.0 mg of Eylea.
- Patients in the second group, which will serve as the control arm of the trial, will be further randomized in a 1:1 ratio to receive one of the following treatments:
  - sham injections of Fovista following intravitreal injections of 1.25 mg of Avastin; or
  - sham injections of Fovista following intravitreal injections of 2.0 mg of Eylea.

We have made no meaningful changes to the inclusion and exclusion criteria in these Phase 3 clinical trials from those we used in our Phase 2b clinical trial. As was the case in both our Phase 1 clinical trial and our Phase 2b clinical trial, we are not enrolling patients with characteristics associated with pure occult choroidal neovascularization even though measurements of changes in choroidal neovascularization are not an endpoint in the Phase 3 clinical trials. To ensure that uniform criteria are applied in characterizing patients' lesions, we have engaged a centralized reading center to review the fluorescein angiogram and OCT of each patient's affected eye. The reading center will use OCT, together with fluorescein angiography, to assess the abnormal new blood vessels for characteristics associated with occult neovascularization at the time of enrollment. Currently there is a shift toward using the latest, high-resolution OCT models to image the abnormal new blood vessels and the associated leakage in wet AMD patients. The use of fluorescein angiography for imaging has been replaced by OCT in the United States and the European Union as the standard for retinal imaging for wet AMD. OCT utilizes specialized light scattering through the biological tissues and obtains high-resolution retinal tissue images using a specialized camera. OCT images show a cross-sectional view of the retina that permits enhanced resolution of the space under the retina and at the RPE level where the neovascularization associated with wet AMD is present. Considerable technological advances in the latest generation of OCT machines have markedly improved the resolution of retinal imaging. OCT images now allow for a more precise analysis of anatomical differences between various angiographic subtypes of CNV lesions in neovascular AMD. The assessment of the location of the abnormal blood vessels relative to the RPE is more precise employing OCT compared to the inherent variability and inconsistency in subtype determinations made by certified readers using fluorescein angiography. Fluorescein angiography will continue to be used because of its high sensitivity in detecting the presence of an active neovascular lesion. To assess choroidal neovascularization at the time of enrollment for characteristics associated with occult and other subtypes of neovascularization, the centralized reading center will use OCT, which has replaced fluorescein angiography as the standard for retinal imaging. We believe that use of a centralized reading center enables us to confirm patient eligibility and properly classify neovascular characteristics and the associated leakage in an accurate and standardized manner before enrolling them in the trial.

Furthermore, as was the case in both our Phase 1 clinical trial and our Phase 2b clinical trial, there is to be a 30-minute delay in the injection of Fovista after the anti-VEGF drug.

**Potential Additional Studies of Fovista for Wet AMD Patients as Part of Our Phase 3 Clinical Program**

Each element of our Phase 3 clinical trial design has the potential to affect the label for Fovista if we receive marketing approval from the FDA, the EMA or another regulatory authority. In each of the cases described below, if we determine that a related change to the approved label has the potential to increase the use or market acceptance of Fovista, we likely would conduct an appropriate clinical trial in cohorts of patients as part of our Phase 3 clinical program, in a separate pre-marketing approval clinical trial or in a post-marketing approval clinical trial.

*Exclusion of Occult Lesions.* Treating physicians typically do not use subtype categorization as a diagnostic tool for choosing among pharmacological agents for treating wet AMD. The process for determining whether or not a wet AMD patient has pure occult choroidal neovascularization has evolved considerably in the United States and European Union over the last five years, with OCT replacing fluorescein angiography as the diagnostic standard. There is significant variability and inconsistency among physicians and reading centers with respect to the determination of the presence and amount of the occult component of lesions using fluorescein angiography. Different reading centers may categorize a patient differently on the basis of the same image if fluorescein angiography is used to assess the occult component of choroidal neovascularization. We believe the use of OCT to assess choroidal neovascularization at the time of enrollment in our Phase 3 clinical trials will alleviate some of the variability and inconsistency inherent in using fluorescein angiography. OCT will be used to assess the characteristics of abnormal new vessels, which historically, using fluorescein angiography, have been associated with the subtype occult neovascularization. OCT is the current standard of imaging of wet AMD patients and we believe that the use of OCT will provide a more precise analysis of the anatomical differences between the various angiographic subtypes of CNV lesions in neovascular AMD. Microscopic examination of retinas taken from deceased patients who suffered from choroidal neovascularization shows that abnormal new blood vessels characterized as occult choroidal neovascularization using fluorescein angiography have similar morphology to those characterized as classic choroidal neovascularization, including pericyte coverage.

The FDA, EMA or other regulatory authority will determine, based on the data we present and the FDA's, EMA's or other regulatory authority's assessment of risks and benefits to patients, whether the label for Fovista, if approved, will exclude its use for the treatment of patients who were not primarily enrolled on the basis of OCT assessment. If we determine that the potential Fovista label may exclude its use for the treatment of patients with certain OCT criteria, we likely would conduct an appropriate clinical trial to evaluate the safety and efficacy of 1.5 mg of Fovista administered in combination with an anti-VEGF drug for the treatment of patients who were excluded on the basis of OCT imaging.

*Waiting Period Prior to Injection of Fovista.* An intravitreal injection results in an elevation of intraocular pressure, or IOP, which usually is transient. Labels for the currently approved anti-VEGF drugs include descriptions related to monitoring IOP after intravitreal injection of these drugs. We have provided for a delay in the intravitreal injection of Fovista to minimize the risk in our clinical trials of an unacceptable increase in IOP as a result of the amount of the two agents injected. We have not seen any meaningful or sustained increase in IOP in our clinical trials of Fovista to date, and we believe that Fovista likely could be delivered by intravitreal injection immediately after the anti-VEGF drug without an unacceptable increase in IOP. However, if we apply for marketing approval for Fovista, the FDA, the EMA or other regulatory authorities will determine, based on the data we present and the regulatory authority's assessment of risk to patients, whether the label for Fovista will provide for the administration of Fovista immediately after the anti-VEGF drug, 30 minutes after the anti-VEGF drug or after some other waiting period. If we determine that the potential Fovista label may provide for a waiting period between the administration of the anti-VEGF drug and Fovista, we likely would conduct an appropriate clinical trial to evaluate the safety of administration of Fovista immediately after the administration of the anti-VEGF. Additionally, our preclinical research shows that Fovista

could be co-formulated with an anti-VEGF drug, and we may conduct a clinical trial to evaluate the safety of such a co-formulation.

## Potentially Expanding the Use of Fovista

### *Additional Planned Phase 2 Clinical Trials Further Evaluating Potential to Provide Benefit in Wet AMD*

In addition to conducting our Phase 3 clinical program for Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD, we plan to further test Fovista in clinical trials to evaluate its potential to provide benefit to patients with wet AMD:

- *Reduction of Treatment Burden Trial in Wet AMD.* In our Phase 3 clinical program, both Fovista in combination with anti-VEGF drugs, as well as anti-VEGF monotherapy, are administered monthly during the first year of dosing. We believe that Fovista combination therapy may allow for less frequent dosing and patient visits compared to anti-VEGF monotherapy, thus reducing patient treatment burden. In retrospective analyses of our completed Phase 2b clinical trial of Fovista, we observed that treatment with Fovista combination therapy, on average, results in a larger reduction in the size of the choroidal neovascular complex in wet AMD patients, compared to treatment with anti-VEGF monotherapy. We believe that the reduction in the size of the choroidal neovascular complex implies a reduction in the number of cellular elements releasing angiogenic mediators, including VEGF and PDGF, which may translate into a reduced need for intravitreal injections to achieve similar levels of inhibition of these mediators. We plan to initiate in 2014 an initial Phase 2 clinical trial involving up to approximately 30 wet AMD patients to assess, through the observation throughout the trial period of visual and anatomical markers that we believe correspond to choroidal neovascularization, whether the use of Fovista in combination with anti-VEGF drugs can reduce the number and frequency of intravitreal injections required to effectively treat wet AMD. We expect to receive initial results from this initial Phase 2 clinical trial during 2015. Data from this initial trial would inform the design of a subsequent clinical trial involving approximately 100 wet AMD patients. If the results of the initial clinical trial are instructive, we would expect to initiate this subsequent clinical trial during 2015 and to receive interim results from this trial in 2016.
- *Treatment Failure Trial in Wet AMD.* A subpopulation of wet AMD patients treated with anti-VEGF monotherapy either do not achieve significant visual gain or experience visual decline. This response is often categorized as anti-VEGF resistance. In some third-party clinical trials, after one year of treatment with an anti-VEGF drug monotherapy approximately 18% to 22% of newly diagnosed wet AMD patients have lost additional vision, defined as the loss of the ability to read one or more letters on a standardized chart of vision testing. Third-party preclinical studies suggest that pericyte coverage of abnormally proliferating new blood vessels may be a potential cause of anti-VEGF resistance. We therefore believe that Fovista administered in combination with an anti-VEGF drug may result in improved visual outcomes in these anti-VEGF resistant patients. We plan to initiate in 2014 an initial Phase 2 clinical trial that would involve up to approximately 30 wet AMD patients who are anti-VEGF resistant to investigate whether Fovista administered in combination with an anti-VEGF drug may prove beneficial. We expect to receive initial results from this initial Phase 2 clinical trial in early 2015. The results of this initial trial would inform the design of a subsequent clinical trial involving approximately 100 anti-VEGF resistant wet AMD patients. If the results of the initial clinical trial are instructive, we would expect to initiate this subsequent clinical trial in 2015 and to receive initial results from this trial in 2016. Additionally, following the initial clinical trial, we also intend to initiate a further clinical trial with Fovista and Zimura administered in combination with an anti-VEGF drug. See "Clinical Development of Zimura—Planned Phase 2 Clinical Trial in Wet AMD" for our clinical development plans for this trial.
- *Anti-Fibrosis Trial in Wet AMD.* Data from two large, recently published third-party clinical studies show that 40% to 45% of wet AMD patients develop subretinal fibrosis after two years of treatment with an anti-VEGF drug. Wet AMD patients who develop subretinal fibrosis have



worse visual outcomes, on average, compared to patients who do not develop subretinal fibrosis. In preclinical animal models of subretinal fibrosis, Fovista mediated inhibition of PDGF reduced the amount of scar tissue formation. We believe that our initial assessment of retinal images from patients who experienced vision loss following treatment with either 1.5 mg of Fovista in combination with Lucentis or Lucentis monotherapy in our completed Phase 2b Fovista trial is consistent with our hypothesis that Fovista mediated PDGF inhibition may be associated with inhibition of retinal scar formation. We plan to initiate in 2014 a Phase 2 clinical trial involving approximately 100 patients with wet AMD patients in approximately 25 trial sites to investigate the effect of the administration of Fovista in potentially reducing the formation of subretinal fibrosis, independent of the specific anti-VEGF regimen administered to patients. We expect to receive initial results from this Phase 2 clinical trial by late 2015 or early 2016.

In addition, we expect to supply Fovista for use in small, investigator sponsored, pilot clinical trials designed to assess the safety and efficacy of differing treatment regimens of Fovista administered in combination with each anti-VEGF drug. These trials will include the previously untested combinations of Fovista with Avastin or Eylea. We anticipate that the trials will seek to evaluate differing treatment regimens, including variations to the order in which Fovista and the anti-VEGF drug are administered and to the time between intravitreal injections.

#### ***Planned Clinical Trials of Fovista in Additional Indications***

We are also exploring clinical development of Fovista for the treatment of a number of ophthalmic conditions with unmet medical need in which PDGF inhibition with Fovista administration may be beneficial. We are considering the potential therapeutic benefit of Fovista administered in combination with an anti-VEGF drug for the treatment of the following indications:

- ***Von Hippel-Lindau Disease.*** Von Hippel-Lindau disease, or VHL, is an inherited disease characterized by multiple benign and malignant tumors and cysts in the eye and other organs. Deficiency of the protein "pVHL" in multiple cell types is thought to cause VHL. In the eye, tumors consisting of blood cells called retinal capillary hemangiomas, or RCH, are the most common and earliest manifestation of VHL. These tumors cause significant retinal leakage and may lead to significant vision loss. Smaller lesions, located a significant distance from the central regions of the retina can be treated by laser or freezing via cryotherapy. However, larger and poorly situated lesions are usually untreatable or have poor visual prognoses. PDGF levels have been shown to be elevated in cells with deficiency of pVHL. Therefore, we believe that a combination of Fovista with an anti-VEGF drug may prove beneficial in RCH patients. We plan to supply Fovista for a clinical trial conducted by the National Eye Institute, which we expect the National Eye Institute may initiate in 2014 and may involve approximately 20 VHL patients with RCH. VHL is rare, and we estimate that there are approximately 5,000 people with the disease in the United States.
- ***Proliferative Vitreoretinopathy.*** Proliferative vitreoretinopathy, or PVR, is a complication that occurs in approximately 5% to 10% of cases of retinal detachment. It is characterized by various degrees of scarring in the retina. In its moderate to severe form, it may become recurrent with a subsequent poor visual outcome. It is usually treated by surgical intervention. However, the recurrent form is often untreatable. Local concentrations of PDGF have been shown to be elevated in patients suffering from PVR. In addition, results from animal studies indicate that PDGF may play a significant role in mediating PVR related retinal scarring by attracting other retinal cells, such as RPE cells and glial cells, which play a role in scar formation. In an animal model of PVR, Fovista strongly inhibited retinal scarring. Therefore, we believe that a combination of Fovista with surgical intervention may prove beneficial in these PVR patients. We are considering initiation in 2015 of a clinical trial involving approximately 20 patients with PVR to investigate the potential benefit of Fovista administered in combination with surgical intervention. We estimate that there are approximately 5,000 to 10,000 new cases of PVR in the United States each year.

## Dry AMD

Dry AMD is a significant cause of moderate and severe loss of central vision, affecting vision in both eyes in most patients. Although dry AMD is the most common form of AMD, there are no therapies approved by the FDA or EMA to treat this condition. According to a 2011 publication from AMD Alliance International, approximately 30 million people worldwide have some form of AMD, with dry AMD accounting for 85% to 90% of these cases. A study published in *Ophthalmology* in 2012 analyzing age and gender variations in AMD prevalence estimates that approximately 8 million people worldwide are affected by a severe form of dry AMD known as geographic atrophy.

Dry AMD results in progressive and chronic degeneration of the macula characterized by variable thinning and dysfunction of retinal tissue. Dry AMD is typically associated with yellow-white dots or deposits under the retina, known as drusen. Unlike in wet AMD, there is complete absence of pathological neovascularization in dry AMD. The presence of drusen, in the absence of pathological neovascularization, is critical for making the diagnosis of dry AMD in patients over 50 years of age.

The progression of visual outcomes for patients with dry AMD is variable. Most patients experience mild to moderate loss of visual function, manifesting in blurring of central vision in the affected eye, as a result of progressive degeneration of the light-sensitive photoreceptor elements in the macula. Deterioration of vision in dry AMD is usually gradual over a period of months and years and is considered irreversible. There are two settings in which visual loss from dry AMD may lead to severe vision loss:

- *Geographic Atrophy.* With severe and progressive macular degeneration, a readily identifiable pattern of severe degeneration called geographic atrophy forms, which consequently leads to profound and irreversible vision loss. Geographic atrophy is readily diagnosed by macular visualization using standard diagnostic instruments utilized by ophthalmologists. Geographic atrophy appears as severe, abrupt and deep levels of macular tissue loss. It has sharp margins of characteristic degeneration compared to surrounding macular tissue.
- *Conversion to Wet AMD.* Dry AMD progresses to the wet form of the disease in approximately 10% of patients, leading to more rapid and further visual loss.

### ***The Complement Cascade***

The complement cascade consists of a series of proteins involved in the defense of a host body against infectious agents, or pathogens, and other foreign proteins. The complement cascade modulates a variety of immune and inflammatory responses to these pathogens and foreign proteins. Under normal circumstances, complement proteins, together with antibodies and white blood cells, act beneficially to protect the host body by removing the pathogens and foreign proteins, together with other cellular debris. The complement system is generally tightly regulated, achieving the proper balance of activation and inhibition depending on the host body's requirements. Poorly regulated or aberrant activation of the complement cascade, without a balanced or proportional inhibition of complement proteins, may result in the formation of inflammation-inducing proteins and molecules. These inflammation-inducing byproducts of the complement cascade have the potential to inflict damage to normal tissue known as immune or complement mediated damage.

Though the complement cascade can be activated through different pathways, these pathways eventually converge with the generation of an enzyme known as C3 convertase. C3 convertase cleaves, or separates, to form a protein called C3, which itself cleaves to form a molecule known as C3b. C3b is an important element of the body's immune response, as it binds to pathogens and makes them susceptible to destruction by white blood cells. Subsequent downstream reactions continue after the formation of C3b, with the eventual cleavage of another complement pathway protein known as C5. The cleavage of C5 results in the formation of other molecules known as terminal fragments, which are

part of the terminal events of the complement pathway. One terminal fragment, known as C5a, is a potent mediator of inflammation and induces the release of VEGF from affected cells. The other terminal event is the generation of the membrane-attack complex, or MAC. The cellular response to the formation of MAC on affected cells can result in cell damage, cell death and the release of various angiogenic mediators, such as PDGF.

### ***Complement-Mediated Pathology of AMD***

Multiple published studies have implicated local inflammation resulting from poorly regulated or aberrant activation of the complement cascade in the development of both the dry and wet forms of AMD. For example, in third-party preclinical studies, analysis of both human and primate retinal drusen deposits, which are the hallmark of dry AMD, have been found to contain components of complement proteins. In addition, young patients, between the ages of 25 and 35, diagnosed with a kidney disease known as membranoproliferative glomerulonephritis have been observed to have developed retinal drusen deposits. The retinal drusen deposits are structurally and compositionally similar to those found in dry AMD patients. Complement activation is associated with membranoproliferative glomerulonephritis and may explain drusen formation in these patients, which would be otherwise unexpected in healthy subjects of a similar young age.

Inflammation is mediated by the presence of white blood cells. In third-party preclinical studies, choroidal neovascularization in animal subjects has been inhibited by the depletion of a specific white blood cell blood type known as monocytes. Similar effects on choroidal neovascularization have also been observed through the inhibition of other factors involved in inflammation. Furthermore, in the same preclinical retinal model, pharmacologic and genetic inhibition of C5a and MAC have inhibited neovascularization, suggesting that the inflammation responsible for choroidal neovascularization is complement mediated. In 2005, multiple studies published in the journal *Science* linked variations in the genetic sequence coding for specific complement regulatory proteins with a higher risk of developing both the dry and wet forms of AMD.

We believe one or more unidentified triggering events may lead to aberrant activation of the complement system in the macular region of AMD patients. Complement mediated inflammation in the macular tissue may result in the accumulation of drusen, damage to retina cells and the release of angiogenic mediators, potentially resulting in the development of the dry and wet forms of AMD.

### **Zimura**

We are developing our product candidate Zimura for the treatment of dry AMD and certain forms of wet AMD. Zimura is designed to target and inhibit the complement protein C5. We believe Zimura binds to and inhibits C5 from cleaving into later stage proteins, or terminal fragments. By inhibiting the formation of complement system terminal fragments, Zimura may decrease complement mediated inflammation and the release of VEGF and PDGF, thereby result in therapeutic benefit in patients with dry AMD and certain forms of wet AMD. Zimura is a chemically synthesized, pegylated aptamer. Zimura is administered by intravitreal injection.

### ***Clinical Development of Zimura***

We have completed one Phase 1/2a clinical trial of Zimura for the treatment of dry AMD. We are planning a Phase 2/3 clinical trial designed to evaluate the safety and efficacy of Zimura administered for the treatment of dry AMD. We expect to initiate our planned Phase 2/3 clinical trial for dry AMD in late 2014 or early 2015 and to receive initial interim results from this trial in 2016.

We are also evaluating Zimura's potential to improve visual outcomes in anti-VEGF resistant wet AMD patients. We believe that, in a subgroup of these patients, Zimura may assist in inhibiting complement mediated inflammation and improve visual outcomes, when administered in combination

with Fovista and an anti-VEGF drug. We have completed one Phase 1/2a clinical trial of Zimura administered in combination with Lucentis for the treatment of wet AMD. Our wet AMD clinical development plan for Zimura is to initiate a Phase 2 clinical trial to evaluate the safety and efficacy of Zimura administered in combination with Fovista and an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients who are believed to have complement mediated inflammation. We plan to initiate this Phase 2 clinical trial in 2015 and expect to receive initial results from this trial in 2016.

#### ***Completed Phase 1/2a Clinical Trial of Zimura for Dry AMD***

In 2011, we completed a multicenter, uncontrolled, open label Phase 1/2a clinical trial evaluating the safety and tolerability of Zimura administered as a monotherapy in patients with geographic atrophy. We enrolled 47 patients in this trial. We randomly assigned patients in this trial to one of two dose groups. Patients received a total of five intravitreal injections of either 0.3 mg or 1.0 mg of Zimura over a 36-week treatment period. Patients received an intravitreal injection of Zimura at day 0, week 4, week 8, week 24 and week 36 of the trial, with a final follow-up visit at week 48. Zimura was generally well-tolerated in this trial. We did not observe any evidence of drug related adverse events. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure.

In addition, we performed assessments of visual acuity to detect any potential decrease in vision associated with intravitreal injections, the administered drug or natural progression of the disease if left untreated. We did not identify any drug related safety issues through measurements of visual acuity.

Our Phase 1/2a clinical trial was an uncontrolled study with a small sample size, not powered to detect a difference between Zimura dose groups with statistical significance. The primary purpose of the study was to assess safety and tolerability. However, we observed a trend, in favor of the higher of two dose groups, of a relative reduction in the mean growth of the geographic atrophy lesion area, as measured by an independent reading center, at 24 weeks. The mean growth from baseline in the geographic atrophy lesion area during the first 24 weeks of the trial, when the injections were administered more regularly, was 1.00 mm<sup>2</sup> for the 24 patients receiving the 0.3 mg dose and 0.78 mm<sup>2</sup> for the 23 patients receiving the 1.0 mg dose. When the injections were administered on a reduced dosing schedule during the subsequent 24 weeks, this relative trend in reduced growth in geographic atrophy lesion area was no longer present. We believe this apparent trend in reduction of growth in geographic atrophy lesion area when Zimura was dosed more frequently, together with the relative loss of the benefit when Zimura was dosed less frequently, may suggest a possible drug effect. In addition, recently released data from a third party targeting the complement pathway also exhibited a trend in reduction of geographic atrophy growth with a pronounced effect in patients with a specific biomarker. Given the safety profile of Zimura to date when administered by intravitreal injection, what we believe is a strong preclinical rationale, the trend in the potential benefit that we observed in our Phase 1/2a clinical trial and results observed in studies from the third party targeting the same complement pathway, we are planning to move forward with our a Phase 2/3 clinical trial evaluating Zimura in the treatment of dry AMD.

#### ***Planned Phase 2/3 Clinical Trial of Zimura in Dry AMD***

We are planning to initiate in late 2014 or early 2015 a randomized, controlled Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with geographic atrophy. We anticipate that this trial would involve approximately 300 patients at approximately 50 trial sites in both the United States and the European Union. Patients would be treated with monthly intravitreal injections of either Zimura or sham Zimura for up to 18 months. We have initiated preliminary discussions with regulatory authorities regarding the design of this clinical trial. We anticipate that the primary efficacy endpoint for the Phase 2/3 clinical trial would be the difference in the mean change in

geographic atrophy lesion area as compared to baseline. We expect to receive initial interim results from this trial in 2016.

#### ***Completed Phase 1/2a Clinical Trial of Zimura for Wet AMD***

In 2009, we completed a multicenter, ascending dose and parallel group open label Phase 1/2a clinical trial evaluating the safety and tolerability of Zimura administered in combination with Lucentis for the treatment of wet AMD. We enrolled 60 patients in this trial. Zimura was generally well tolerated in this trial when tested in combination with Lucentis. None of the patients experienced any dose limiting toxicities at any of the dose levels tested. We observed only a single adverse event assessed by the investigators to be related to Zimura, mild subcapsular cataract in one patient in the group treated with 2.0 mg of Zimura. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure. One patient withdrew from the trial as a result of a serious adverse event of bacteremia unrelated to study drug or injection procedure, which resulted in a subsequent fatality. Systemic adverse events in this trial were not frequently reported. No systemic adverse events were assessed as drug related.

In addition, we performed assessments of visual acuity primarily as safety assessments to detect any decrease in vision associated with the intravitreal drug combination or the injection procedure. We did not identify any safety issues through measurements of visual acuity. In a subgroup of 43 patients who had not previously been treated with anti-VEGF therapy and who received six injections at doses of 0.3 mg, 1.0 mg or 2.0 mg of Zimura administered in combination with Lucentis, we observed a mean increase in visual acuity from baseline at all timepoints. In a follow-up visit at week 24 of the trial, we noted improvements in mean visual acuity from baseline as follows: 13.6 letters for the 13 patients receiving the 0.3 mg dose, 11.7 letters for the 15 patients receiving the 1.0 mg dose and 15.3 letters for the 15 patients receiving the 2.0 mg dose. In this subgroup, 22 patients (51%) gained at least 15 letters, consisting of six patients (46%) in the 0.3 mg dose group, seven patients (47%) in the 1.0 mg dose group and nine patients (60%) in the 2.0 mg dose group.

#### ***Planned Phase 2 Clinical Trial of Zimura for Wet AMD***

We are planning to initiate a Phase 2 clinical trial of Zimura and Fovista administered in combination with an anti-VEGF drug for the treatment of anti-VEGF resistant wet AMD patients and who are believed to have complement mediated inflammation. We may use genetic screening for complement mediated inflammation as part of the inclusion criteria. We plan to initiate a Phase 2 clinical trial of Zimura and Fovista administered in combination with an anti-VEGF drug in approximately 100 patients in 2015 and to receive initial results from this trial in 2016. We likely would also include a group of patients with a variant of wet AMD called polypoidal choroidal vasculopathy, or PCV. There is high prevalence of PCV in Asia. We believe the therapeutic response of PCV to anti-VEGF monotherapy to date has been inconsistent and sub-optimal. We believe that complement mediated inflammation may play a role in patients with PCV.

#### **Sales and Marketing**

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 for our product candidates for which we may receive marketing approvals in territories in which we believe it is possible to access the market through a focused, specialty sales force.

If either Fovista or Zimura receives marketing approval, we plan to commercialize such product candidate in the United States with our own focused, specialty sales force. We believe that retinal specialists in the United States, who perform most of the medical procedures involving diseases of the back of the eye, are sufficiently concentrated that we will be able to effectively promote Fovista and

Zimura to these specialists with a specialty sales and marketing group of fewer than 100 persons. Intravitreal injection is a specialized procedure. In the vast majority of cases in the United States, retinal specialists perform intravitreal injections. Based on our examination of the membership lists of three prominent organizations for retinal specialists, The Macula Society, The American Society of Retina Specialists and the Retina Society, we estimate that there are approximately 2,000 retinal specialists in the United States.

In addition, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Fovista and Zimura in markets outside the United States.

### **Manufacturing**

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. Although we intend to rely on third-party contract manufacturers to produce our products, we have recruited personnel with experience to manage the third-party contract manufacturers producing Fovista, Zimura and other products that we may develop in the future.

The process for manufacturing Fovista and Zimura consists of chemical synthesis, purification, pegylation, further purification and finally freeze drying to form a powder. Each of these steps involves a relatively common chemical engineering process. The chemical synthesis is similar to small molecule manufacturing.

We currently engage a single third-party manufacturer to provide clinical supplies of both Fovista drug substance and Zimura drug substance. We also engage a different, single third-party manufacturer to provide fill-finish services for both Fovista and Zimura. We obtain these supplies and services from each of these manufacturers on a purchase order basis. Under a license, manufacturing and supply agreement with Nektar Therapeutics, or Nektar, described in more detail below under "—Acquisition and License Agreements—Nektar Therapeutics," we must purchase our entire clinical and commercial requirements for the polyethylene glycol, or PEG, reagent, which we use to make Fovista, exclusively from Nektar at an agreed price, which is subject to annual adjustment in accordance with changes in the producer price index, except under specified circumstances relating to Nektar's failure to supply, in which event Nektar has agreed to enable a third-party manufacturer to supply us. Under this agreement, Nektar has agreed to supply our entire clinical and commercial requirements for this PEG reagent, subject to certain forecasting and ordering requirements and other limitations, and has agreed to supply this PEG reagent only to us for the purpose of manufacturing a product produced by linking the active ingredient in Fovista to this PEG reagent by means of pegylation. The PEG reagent supplied by Nektar is proprietary to Nektar, and, to our knowledge, this PEG reagent is not currently available from any other third party. We obtain a different PEG reagent used to make Zimura from a different third-party manufacturer on a purchase order basis.

### **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 Fovista and Zimura, if approved, are likely to be the respective drug's efficacy, safety, method of administration, convenience, price, the level of generic competition and the availability of coverage and reimbursement from government and other third-party payors. The method of administration of Fovista and Zimura, intravitreal injection, is commonly used to administer ophthalmic drugs for the treatment of severe disease and generally accepted by patients facing the prospect of severe visual loss or blindness. However, a therapy that offers a less invasive method of administration might have a competitive advantage over one administered by intravitreal injection, depending on the relative safety of the other method of administration.

There are a variety of therapies used for the treatment of wet AMD, principally Avastin, Lucentis and Eylea. These anti-VEGF drugs are well established therapies and are widely accepted by physicians, patients and third-party payors as the standard of care for the treatment of wet AMD. Physicians, patients and third-party payors may not accept the addition of Fovista or Zimura to their current treatment regimens for a variety of potential reasons, including:

- if they do not wish to incur the additional cost of Fovista or Zimura;
- if they perceive the addition of Fovista or Zimura to be of limited benefit to patients; or
- in the case of wet AMD if they wish to treat with anti-VEGF drugs as monotherapy first and add Fovista or Zimura only if and when resistance to continued anti-VEGF therapy limits further enhancement of visual outcome with anti-VEGF monotherapy.

We are developing Fovista and Zimura for administration in combination with these anti-VEGF drugs for the treatment of wet AMD. Accordingly, we do not believe Fovista or Zimura would be directly competitive with these therapies. However, a standalone therapy for wet AMD with demonstrated improved efficacy over currently marketed therapies in this indication with a favorable safety profile and any of the following characteristics might pose a significant competitive threat to Fovista:

- a mechanism of action that does not involve VEGF;
- a duration of action that obviates the need for frequent intravitreal injection; or
- an effect on wet AMD that makes combination therapy with Fovista or Zimura unnecessary.

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. For example, a single drug, or a co-formulated injection, that combines an anti-PDGF drug and an anti-VEGF drug would be more convenient than administering an intravitreal injection of each of Fovista and an anti-VEGF drug. Such greater convenience might make such a drug or co-formulated injection more attractive to physicians and patients. An anti-VEGF gene therapy product might substantially reduce the number and frequency of intravitreal injections when treating wet AMD and make monthly intravitreal injections of Fovista unattractive to physicians and patients. Our competitors also may obtain FDA or other

regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors seek to encourage the use of generic products.

There are a number of products in preclinical research and clinical development by third parties to treat wet AMD. We expect that product candidates currently in clinical development, or that could enter clinical development in the near future, that inhibit the function of PDGF, the molecule whose function Fovista also inhibits, or inhibit the function of both VEGF and PDGF, which could obviate the separate use of an anti-PDGF agent, such as Fovista, 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 ophthalmic product candidates in clinical and preclinical development that, like Fovista, are based on PDGF inhibition:

- Regeneron Pharmaceuticals, Inc. and Bayer HealthCare have an anti-PDGF product candidate that is being co-formulated with Eylea for administration in a single intravitreal injection and that is expected to enter clinical development in early 2014.
- Allergan has an anti-PDGF, anti-VEGF DARPIn product candidate that is being co-formulated for administration in a single intravitreal injection and that is expected to enter clinical development in 2014.
- Xcovery Vision has an anti-PDGF, anti-VEGF product candidate in Phase 1 clinical development that is designed for oral administration.
- Neurotech has a PDGF antagonist that is in preclinical development that is designed as an encapsulated cell technology implant.
- Somalogic has an anti-PDGF product candidate in preclinical development.

Because there are a variety of means to block the activity and signaling of PDGF, our patents and other proprietary protections for Fovista will not prevent development or commercialization of product candidates that are different from Fovista.

There are a number of products in preclinical research and clinical development by third parties to treat dry AMD. In general, these product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include inflammation suppression, such as complement system inhibitors and corticosteroids, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular enhancers. Based upon publicly available information, we have identified, among others, the following ophthalmic product candidates in clinical development that, like Zimura, are based on complement system inhibition:

- Genentech has an intravitreally administered humanized Fab fragment targeting complement factor D, which recently completed a Phase 2 clinical trial.
- Novartis's Alcon division has an intravitreally administered product candidate that inhibits complement factor C3, which is in Phase 2 clinical development.
- Alexion Pharmaceuticals has an intravenously administered product candidate targeting complement factor C5 approved for unrelated conditions, which recently completed a Phase 2 clinical trial for dry AMD.
- Novartis and MorphoSys have a fully human antibody targeting complement factor C5, which is in Phase 2 clinical development.



Moreover, we have identified the following additional ophthalmic product candidates that are in the later stages of clinical development for the treatment of dry AMD:

- Alimera Sciences has a corticosteroid intravitreal implant, which is in a Phase 2 clinical trial that is expected to finish in late 2014.
- Acucela has an orally bioavailable selective visual cycle modulator, which is in a Phase 2b/3 clinical trial.
- Colby Pharmaceuticals has an ocular esterase cleavable prodrug of tempol hydroxylamine, which is in a Phase 2 clinical trial.
- Allergan has an  $\alpha_2$ -adrenergic receptor agonist, which has completed a Phase 2 clinical trial.
- Pfizer has a humanized monoclonal antibody that binds amyloid- $\beta$  (Ab), which is in a Phase 2 clinical trial.
- GlaxoSmithKline has an anti-amyloid B antibody, which is in a Phase 2 clinical trial.
- MacuClear has a topical systemic antihypertensive agent administered as an eye drop, which is in a Phase 2/3 clinical trial.

### **Intellectual Property**

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, 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, among other methods and where patent protection is available, by 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, and by maintaining our issued patents. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of January 31, 2014, we owned or exclusively licensed a total of 97 U.S. patents and 30 U.S. patent applications, including original filings, continuations and divisional applications, as well as numerous foreign counterparts of many of these patents and patent applications. Our patent portfolio includes the following patents and patent applications that we own or license:

- composition-of-matter patents covering Fovista, which have issued in the United States, Europe and Japan, the last to expire of which is expected to expire in the United States in 2017 and in Europe and Japan in 2018;
- patents covering the treatment of wet AMD with a combination of Fovista and an anti-VEGF-A antibody or binding fragment thereof (such as Avastin or Lucentis), or the use of Fovista in the manufacture of a medicine for the treatment of wet AMD when administered with an anti-VEGF-A antibody or binding fragment thereof, which have issued in the United States, Europe and Japan and are expected to expire in 2024, and pending patent applications covering the treatment of wet AMD with a combination of Fovista and an anti-VEGF-A antibody or binding fragment thereof or the use of Fovista in the manufacture of a medicine for the treatment of wet AMD when administered with an anti-VEGF-A antibody or binding fragment thereof, in certain other jurisdictions;
- patent applications in various jurisdictions covering the treatment of wet AMD with a combination of Fovista and Eylea, or the use of Fovista in the manufacture of a medicine for the treatment of wet AMD when administered with Eylea, which, if granted, are expected to expire in the United States in 2030;

- a U.S. patent covering methods for treating AMD with a combination of Fovista and Macugen, which is expected to expire in 2024;
- a U.S. patent covering methods for treating AMD with a combination of a particular anti-PDGFR antibody and an anti-VEGF-A antibody or binding fragment thereof, which is expected to expire in 2024;
- patent applications in various jurisdictions covering co-formulations and other proprietary technology relating to Fovista;
- composition-of-matter patents covering Zimura, which have issued in the United States, Europe and Japan, which are expected to expire in the United States and Europe in 2025 and the last of which is expected to expire in Japan in 2026;
- patents covering the treatment of certain complement mediated disorders with Zimura, Zimura for use in a method of treating certain complement mediated disorders or a composition comprising Zimura for treating certain complement mediated disorders, which have issued in the United States, Europe and Japan, and which are expected to expire in Europe in 2025 and in the United States and Japan in 2026; and
- U.S. patent applications covering co-formulations and other proprietary technology relating to Zimura.

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 U.S. 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 Fovista, 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.

## Acquisition and License Agreements

### *OSI (Eyetechn)*

In July 2007, we entered into a divestiture agreement with OSI (Eyetechn), Inc., or Eyetechn, which agreement is now held by OSI Pharmaceuticals, LLC, or OSI Pharmaceuticals, a subsidiary of Astellas US LLC, under which we acquired specified technology, rights, and other assets owned or controlled by Eyetechn relating to particular anti-PDGF aptamers, including Fovista, and assumed Eyetechn's liabilities and obligations under specified agreements between Eyetechn and Archemix Corp., or Archemix, and between Eyetechn and Nektar. These agreements with Archemix and Nektar, as subsequently amended, are described in more detail below.

We have agreed that we will not, alone or with any other party, research, develop or commercialize any compound, other than anti-PDGF products covered by the divestiture agreement, that solely and specifically binds to PDGF for its mode of action.

#### *Financial Terms*

In connection with the agreement, we paid Eyetechn a \$4.0 million upfront payment and issued Eyetechn 3,000,000 shares of our junior series A preferred stock. We are obligated to pay OSI Pharmaceuticals additional one-time payments of \$12.0 million in the aggregate upon marketing approval in the United States and the European Union, of a covered anti-PDGF product. We are obligated to pay OSI Pharmaceuticals a royalty at a low single-digit percentage of net sales of any covered anti-PDGF product we successfully commercialize. Our obligation to pay such royalties will expire on a product-by-product and country-by-country basis on the later of 10 years after the first commercial sale of each product in each country or the expiration of the last-to-expire valid claim of specified patents that cover the composition, manufacture or use of each product in each country.

#### *Diligence Obligations*

We are required to use commercially reasonable efforts to conduct the development and manufacture of a covered anti-PDGF product so as to obtain marketing approval and, thereafter, to commercialize a covered anti-PDGF product in the United States and in the European Union.

#### *Term and Termination*

The agreement, unless terminated earlier by us or by OSI Pharmaceuticals, will remain in effect until we no longer have any financial obligations to OSI Pharmaceuticals, after which the rights granted to us will become perpetual and fully paid-up. 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.

If we fail to use commercially reasonable efforts to meet our specified diligence obligations and fail to take specified steps after receiving written notice thereof from OSI Pharmaceuticals, then OSI Pharmaceuticals may terminate the agreement as to such countries with respect to which such failure has occurred, and upon such termination we will be obligated to grant, assign and transfer to OSI Pharmaceuticals specified rights and licenses related to our anti-PDGF aptamer technology and other related assets, and if we are manufacturing such anti-PDGF products at the time of such termination, may be obligated to provide transitional supply to OSI Pharmaceuticals of covered anti-PDGF products, for such countries.

## **Archemix**

In September 2011, we entered into two amended and restated exclusive license agreements with Archemix, one relating to anti-PDGF aptamers, which we refer to as the PDGF agreement, and the other relating to anti-C5 aptamers, which we refer to as the C5 agreement. The PDGF agreement superseded a 2004 agreement between Eyetech and Archemix that we assumed under the divestiture agreement described above. The C5 agreement superseded a July 2007 agreement between us and Archemix. Under these amended and restated agreements, we hold exclusive worldwide licenses (subject to certain pre-existing rights) under specified patents and technology owned or controlled by Archemix to develop, make, use, sell, offer for sale, distribute for sale, import and export pharmaceutical products comprised of or derived from any anti-PDGF aptamer or anti-C5 aptamer for the prevention, treatment, cure or control of human indications, diseases, disorders or conditions of the eye, adnexa of the eye, orbit and optic nerve, other than certain expressly excluded applications.

The licenses we received under these agreements include sublicenses to us of rights to specified technology, which we refer to as the SELEX technology, licensed by University License Equity Holdings, Inc., or ULEHI, to Gilead Sciences, Inc., or Gilead, and sublicensed by Gilead to Archemix, as well as sublicenses to us of rights to certain other technology licensed by Gilead to Archemix, including the composition-of-matter patents relating to Fovista. Our agreements with Archemix contemplate that our rights to these sublicensed technologies will survive termination of the license from ULEHI to Gilead as long as we are not in breach of the C5 agreement or PDGF agreement, as applicable, and will survive termination of the sublicense from Gilead to Archemix as long as such termination did not arise from our action or inaction, provided in each case that we agree to be bound to ULEHI or Gilead, as applicable, under the terms of our agreements with Archemix. However, if Archemix, its affiliates and all of Archemix's assignees and sublicensees, including us, cease to exercise reasonable efforts to develop commercial applications of products and services using the SELEX technology, then Archemix's rights to the SELEX technology may revert to Gilead or ULEHI, and we would lose our rights to the SELEX technology.

### ***Financial Terms***

In connection with these agreements, as amended, we paid Archemix aggregate upfront licensing fees of \$1.0 million and issued to Archemix an aggregate of 2,000,000 shares of our series A-1 preferred stock and 500,000 shares of our series B-1 preferred stock. We have also paid Archemix an aggregate of \$6.75 million in fees based on our achievement of specified clinical milestone events under these agreements.

Under the PDGF agreement, we are also obligated to make additional future payments to Archemix of up to an aggregate of \$14.0 million if we achieve specified clinical and regulatory milestones with respect to Fovista, including up to an aggregate of \$3.0 million if we achieve specified commercial milestones with respect to Fovista. Under the PDGF agreement, we also are obligated to make additional payments to Archemix of up to an aggregate of approximately \$18.8 million if we achieve specified clinical and regulatory milestones with respect to each other anti-PDGF aptamer product that we may develop under the agreement, and up to an aggregate of \$3.0 million if we achieve specified commercial milestones with respect to such other anti-PDGF aptamer product.

Under the C5 agreement, for each anti-C5 aptamer product that we may develop under the agreement, including Zimura, we are obligated to make additional payments to Archemix of up to an aggregate of \$57.5 million if we achieve specified development, clinical and regulatory milestones and, as to all anti-C5 products under the agreement collectively, up to an aggregate of \$22.5 million if we achieve specified commercial milestones. We are also obligated to pay Archemix a double-digit percentage of specified non-royalty payments we may receive from any sublicensee of our rights under the C5 agreement.

No royalties are payable to Archemix under either of the PDGF agreement or the C5 agreement.

### ***Diligence Obligations***

We are required to exercise commercially reasonable efforts in developing and commercializing at least one anti-PDGF aptamer product and at least one anti-C5 aptamer product and in undertaking investigations and actions required to obtain regulatory approvals necessary to market such products in the United States, the European Union, and Japan, and in such other markets where we determine that it is commercially reasonable to do so. We are required to complete a Phase 2 clinical trial of an anti-C5 aptamer product for age-related macular degeneration, or AMD, by December 31, 2014. If we fail to meet this timeline, but are otherwise in compliance with our diligence obligations, Archemix and we have agreed to negotiate an extension in good faith. If we breach any of these diligence obligations with respect to any given product in any given country, including failing to meet any such agreed extension date, Archemix may terminate our corresponding license to such product for such country or convert such license to a non-exclusive license.

### ***Term and Termination***

Unless earlier terminated, the PDGF agreement will expire upon the later of 10 years after the first commercial sale in any country of the last licensed product and the expiration of the last-to-expire valid claim of the licensed patents that covers a licensed product.

Unless earlier terminated, the C5 agreement will expire upon the later of 12 years after the first commercial sale in any country of the last licensed product, the expiration of the last-to-expire valid claim of the licensed patents that covers a licensed product, and the date on which no further payments of sublicensing income are to be received by us.

Either we or Archemix may terminate each of the agreements if the other party materially breaches the applicable agreement and the breach remains uncured for a specified period. Archemix may also terminate each of the agreements, or may convert our exclusive licenses under the applicable agreement to non-exclusive licenses, if we challenge or assist a third party in challenging the validity or enforceability of any of the patents licensed under the applicable agreement. We may terminate each of the agreements at any time and for any or no reason effective at the end of a specified period following our written notice to Archemix of termination.

### ***Nektar Therapeutics***

In April 2012, we amended a 2006 license, manufacturing and supply agreement between Eyetech and Nektar that we assumed under the Eyetech divestiture agreement described above. Under the agreement, as amended, Nektar has granted us the following licenses:

- an exclusive, worldwide license under specified patent rights and know-how owned or controlled by Nektar to make, have made, develop, use, import, offer for sale and sell particular products that are produced by linking the active pharmaceutical ingredient in Fovista to a specified polyethylene glycol, or PEG, reagent by means of pegylation; and
- non-exclusive sublicenses of certain other patent rights controlled by Nektar.

### ***Financial Terms***

We have paid approximately \$1.8 million and Eyetech previously paid approximately \$0.3 million, to Nektar under the agreement. We are also obligated to pay Nektar additional specified amounts in relation to certain milestone events until we grant any third-party commercialization rights to a licensed product under the agreement. Such specified milestone amounts that may be payable by us in the future include an aggregate of \$4.5 million payable upon the achievement of specified clinical and

regulatory milestones. In addition, a payment of \$3.0 million will be triggered upon the achievement of a specified commercial sale milestone with respect to Fovista.

If we grant to any third-party commercialization rights to a licensed product under the agreement, we have agreed to pay Nektar a low double-digit percentage of any upfront payment we receive from such third party, less certain milestone amounts we have paid to Nektar. In addition, in lieu of any further specified milestone amounts described in the paragraph above, we have agreed to pay Nektar, in relation to the milestone events, amounts calculated at a higher double-digit percentage of the revenues we receive from such third party in connection with any such commercialization agreement, subject to specified minimum and maximum amounts.

We are also obligated to pay Nektar tiered royalties at low to mid single-digit percentages of net sales of any licensed product we successfully commercialize, with the royalty percentage determined by our level of licensed product sales, the extent of patent coverage for the licensed product and whether we have granted a third party commercialization rights to the licensed product. Our obligation to pay such royalties will expire on a licensed product-by-licensed product and country-by-country basis on the later of 10 years after first commercial sales of such licensed product in such country, and the expiration of the last-to-expire valid claim in the licensed patents that cover such licensed product in such country.

#### ***Exclusive Supply***

Under the agreement, we must provide binding forecasts of requirements for the PEG reagent to Nektar and purchase our entire requirements for the PEG reagent, which we currently use to formulate Fovista, exclusively from Nektar at an agreed price, which is subject to annual adjustment in accordance with changes in the producer price index, except under specified circumstances relating to Nektar's failure to supply, in which event Nektar has agreed to enable a third-party manufacturer to supply us.

Under the agreement, Nektar has agreed to supply our entire clinical and commercial requirements for this PEG reagent, subject to certain forecasting and ordering requirements and certain other limitations, and has agreed to supply this PEG reagent only to us for the purpose of manufacturing a product produced by linking the active pharmaceutical ingredient in Fovista to this PEG reagent by means of pegylation.

#### ***Diligence Obligations***

Under the terms of the agreement, if we fail to use commercially reasonable efforts to achieve the first commercial sale of Fovista in the United States or one of a specified group of other countries by December 31, 2017, which date Nektar and we may agree in good faith to extend in specified circumstances, Nektar may either terminate our license or convert our license for such country to a non-exclusive license. In addition, if we fail to use commercially reasonable efforts to develop Fovista and file and seek approval of NDAs on a schedule permitting us to make first commercial sales of Fovista in specified countries by December 31, 2017, do not make such first commercial sales of Fovista by such date, or thereafter fail to use commercially reasonable efforts to continue to commercialize and market Fovista in such countries, we will be in material breach of the agreement.

#### ***Term and Termination***

The agreement, unless earlier terminated by us or Nektar, will expire upon the expiration of our obligation to pay royalties to Nektar on net sales of licensed products. We and Nektar each may terminate the agreement if the other party materially breaches the agreement and does not cure such breach within a specified cure period. We may terminate the agreement at any time, without cause, effective at the end of a specified period following our written notice to Nektar of termination, in which event we will be obligated to pay Nektar specified termination fees and reimburse Nektar for certain costs.

If we challenge the validity or enforceability of any Nektar licensed patent right, we must pay for the defense of such challenge if such challenge is not successful and our licenses under certain licensed patent rights will terminate.

## **Government Regulation**

Government authorities in the United States, at the federal, state and local level, in the European Union and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

### ***U.S. Drug Approval Process***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. 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 to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves 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 become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each 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 drug or biological product for each indication;
- submission to the FDA of a new drug application, or NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

### ***Preclinical Studies***

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess its potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some

preclinical testing may continue even 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 clinical trial on a 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.

### ***Clinical Trials***

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under 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 at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

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

- Phase 1: The drug 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.
- Phase 2: The drug 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 drug 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 safety and efficacy 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 if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

### ***Marketing Approval***

Assuming successful completion of the required clinical testing, 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 an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the new PDUFA V guidelines that



are currently in effect, the FDA has a goal of ten months from the date of the FDA's acceptance for filing of a standard non-priority NDA to review and act on the submission.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA 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 reviews an NDA to determine, among other things, whether the drug is safe and effective and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. 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.

Before approving an NDA, 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 compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

If the FDA's evaluation of the NDA and inspection of the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some 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.

### ***Special FDA Expedited Review and Approval Programs***

The FDA has various programs, including fast track designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and the drug demonstrates the potential to address unmet medical needs for this disease or condition. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. In September 2013, the FDA notified us that we have obtained fast track designation for Fovista for the treatment of wet AMD.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months from the date of the FDA's acceptance for filing of the application, rather than the standard review period of ten months under current PDUFA V guidelines. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and efficacy in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to validate and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. The FDA may withdraw our fast track designation for Fovista for the treatment of wet AMD if it believes that the designation is no longer supported by data from our clinical development program.

### ***Post-Approval Requirements***

Drugs 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.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and efficacy after commercialization.

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

Once an approval is granted, the FDA may withdraw the approval 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 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, 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 NDAs or supplements to approved NDAs, 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. Drugs 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

#### ***Hatch-Waxman Exclusivity***

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA or 505(b)(2)

NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

### ***Foreign Regulation***

In order to market any product outside of the United States, we would need to 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 our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, the approval process 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, we must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, we may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Our 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 drug under European Union regulatory systems, we may 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 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 Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a drug. The CHMP also is 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 previously received marketing approval in any European Union member state. 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.

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 (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 drug 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 drug products for which we may obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third party reimbursement may not be sufficient to

enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs 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 our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug product candidates that we are developing and could adversely affect our net revenue and results.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements for any of our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, which we collectively refer to as the Affordable Care Act or ACA, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for covered out-patient drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries, and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

#### ***New Legislation and Regulations***

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of

products regulated by the FDA. For example, the FDAAA, ACA and FDASIA provisions discussed above were enacted in 2007, 2010 and 2012, respectively. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or FDA regulations, guidance, policies or interpretations changed or what the impact of such changes, if any, may be.

### ***Healthcare Law and Regulation***

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we may 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 our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare Anti-Kickback Statute 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 either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, 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, 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 and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Health Care Reform Law will require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern

the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will 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, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

### **Employees**

As of January 31, 2014, we had 33 full-time employees, including a total of five employees with M.D. or Ph.D. degrees. Of our workforce, 19 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

### **Facilities**

Our facilities consist of office space in New York, New York and Princeton, New Jersey. We occupy approximately 6,923 square feet of office space in New York, New York under a lease that expires in 2020. We occupy approximately 8,468 square feet of office space in Princeton, New Jersey under a lease that expires in 2019. We also occupy approximately 1,800 square feet of additional office space in Princeton, New Jersey under a lease that expires in September 2016.

### **Legal Proceedings**

We are not currently subject to any material legal proceedings.



**MANAGEMENT**

The following table sets forth the name, age and position of each of our executive officers and directors as of January 31, 2014.

<b>Name</b>	<b>Age</b>	<b>Position</b>
David R. Guyer, M.D.	54	Chief Executive Officer and Chairman of our Board of Directors
Samir C. Patel, M.D.	53	President and Vice Chairman of our Board of Directors
Bruce Peacock	62	Chief Financial and Business Officer
Axel Bolte(1)(3)	42	Director
Thomas Dyrberg, M.D., D.M.Sc.(2)(3)	59	Director
Nicholas Galakatos, Ph.D.(1)(2)	56	Director
Michael Ross, Ph.D.(2)(3)	64	Director
Glenn Sblendorio(1)	58	Director

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

*David R. Guyer, M.D.* is a co-founder of our company and has served as Chairman of our board of directors since our inception in January 2007 and as our Chief Executive Officer since April 2013. Prior to serving as our Chief Executive Officer, Dr. Guyer, served as a Partner at SV Life Sciences, a venture capital firm, from 2009 to 2013, and as a Venture Partner at SV Life Sciences from 2006 to 2009. Dr. Guyer co-founded Eyetech Pharmaceuticals Inc. and served as Chief Executive Officer and as a member of its board of directors from 2000 to 2006. Prior to co-founding Eyetech Pharmaceuticals, Dr. Guyer was a Professor and served as Chairman of the Department of Ophthalmology at New York University School of Medicine. Dr. Guyer received a B.S. from Yale College and an M.D. from Johns Hopkins Medical School. Dr. Guyer completed his ophthalmology residency at Wilmer Ophthalmological Institute, Johns Hopkins Hospital and a retinal fellowship at the Massachusetts Eye and Ear Infirmary at Harvard Medical School. We believe that Dr. Guyer is qualified to serve on our board of directors because of his extensive executive leadership experience, his extensive experience in the life sciences industry as an entrepreneur and venture capital investor, and his service on our board of directors and the board of directors of other life sciences companies.

*Samir C. Patel, M.D.* is a co-founder of our company and has served as our President and a member of our board of directors since our inception in January 2007. Dr. Patel served as our Chief Executive Officer from our inception until April 2013. Dr. Patel co-founded Eyetech Pharmaceuticals and served as its Chief Medical Officer and as a member of its board of directors from 2000 to 2006. Prior to co-founding Eyetech Pharmaceuticals, Dr. Patel was an Associate Professor and served as director of the Retina Service in the residency program in the Department of Ophthalmology and Visual Science at the University of Chicago. Dr. Patel received a B.A. from Boston University and an M.D. from the University of Massachusetts Medical School. Dr. Patel completed his ophthalmology training at the University of Chicago and his training in retinal surgery from the Massachusetts Eye and Ear Infirmary at the Harvard Medical School. We believe that Dr. Patel is qualified to serve on our board of directors because of his extensive experience in the life sciences industry and as an entrepreneur and his many years of service as our Chief Executive Officer.

*Bruce A. Peacock* has served as our Chief Financial Officer since August 2013 and our Chief Business Officer since September 2010 and is also our treasurer. Since May 2006, Mr. Peacock also has served as a Venture Partner at SV Life Sciences, a venture capital firm. Mr. Peacock served as President and Chief Executive Officer of Alba Therapeutics, a biopharmaceutical company, from April

2008 to February 2011, and has served as Co-Chairman of the board of directors of Alba Therapeutics since April 2008. Prior to joining SV Life Sciences, Mr. Peacock served as Chief Executive Officer and a Director of The Little Clinic, a medical care services company. Previously, Mr. Peacock served as President and Chief Executive Officer and a director of Adolor Corporation, a publicly-held biotechnology company; as President, Chief Executive Officer and a member of the board of directors of Orthovita, Inc., a publicly-held orthopedic biomaterials company; as Executive Vice President, Chief Operating Officer and a member of the board of directors of Cephalon, Inc.; as Chief Financial Officer of Cephalon, Inc.; and as Chief Financial Officer of Centocor, Inc. Mr. Peacock serves as a member of the boards of directors of Discovery Laboratories, Inc., Invisible Sentinel Inc. and Ocean Power Technologies, Inc. and has served as a member of the boards of directors of Pharmacopeia, Inc., Ligand Pharmaceuticals Incorporated, and NeurogesX, Inc. Mr. Peacock earned a bachelor's degree in Business Administration from Villanova University and is a certified public accountant.

*Axel Bolte* has served as a member of our board of directors since August 2007. Since March 2003, Mr. Bolte has served as investment advisor to HBM Partners AG, a provider of investment advisory services in the life sciences industry. From March 2001 to February 2003, Mr. Bolte was an investment manager of NMT New Medical Technologies AG, a Swiss venture capital company focused on life sciences. Prior to joining NMT New Medical Technologies AG, Mr. Bolte served as a scientist at Serono SA, a biotechnology company. He currently serves or has served on the board of directors of several biotechnology companies, including Newron Pharmaceuticals SpA, Nabriva Therapeutics AG, PTC Therapeutics, Inc., MPex Pharmaceuticals, Inc., Lux Biosciences, Inc. and Kolltan Pharmaceuticals, Inc. Mr. Bolte received a degree in Biochemistry from the Swiss Federal Institute of Technology, Zurich, Switzerland and an M.B.A. from the University of St. Gallen, Switzerland. We believe that Mr. Bolte is qualified to serve on our board of directors because of his many years of service as one of our directors, his extensive experience as a venture capital investor in the life sciences industry and his service on the board of directors of other life sciences companies.

*Thomas Dyrberg, M.D., D.M.Sc.* has served as a member of our board of directors since August 2007. In December 2000, Dr. Dyrberg joined Novo A/S, a limited liability company wholly-owned by the Novo Nordisk Foundation that is responsible for managing the Foundation's assets, where he serves as a Senior Partner. Dr. Dyrberg serves or has served on the board of directors of Veloxis A/S, Lux Biosciences, Inc., Allocure Inc., Delenex AG, Sapphire Inc., Gloucester Inc. and Hemofocus A/S. In 1990, he joined Novo Nordisk A/S, initially working in Health Care Discovery. From 1996 to 2000, Dr. Dyrberg served as an International Clinical Project Manager at Novo Nordisk A/S. Dr. Dyrberg received a D.M.Sc and an M.D. from the University of Copenhagen. Dr. Dyrberg has held research positions at the Hagedorn Research Institute in Denmark, and at the Scripps Research Institute in California. We believe that Dr. Dyrberg is qualified to serve on our board of directors because of his many years of industry experience, his extensive experience as a venture capital investor in the life sciences industry and his service on the board of directors of other life sciences companies.

*Nicholas Galakatos, Ph.D.* has served as a member of our board of directors since December 2009. Dr. Galakatos co-founded and has served as a Managing Director of Clarus Ventures, a global venture capital firm focused on life science investments, since its inception in 2005. Dr. Galakatos has been a venture capital investor since 1992, initially at Venrock Associates and then at MPM Capital where he served as a General Partner of the BioVentures II and BioVentures III funds. From 1997 to 2000, Dr. Galakatos served as Vice President, New Business and a member of the Management Team at Millennium Pharmaceuticals, Inc. (presently Takeda). Dr. Galakatos currently serves or has served on the board of directors of several other biotechnology companies, including Affymax, Inc., Aveo Pharmaceuticals, Inc., NanoString Technologies, Inc., Catabasis Pharmaceuticals, Inc. and Portola Pharmaceuticals, Inc. Dr. Galakatos received a B.A. in Chemistry from Reed College and a Ph.D. in organic chemistry from the Massachusetts Institute of Technology. Dr. Galakatos performed postdoctoral studies in Molecular Biology at Harvard Medical School. We believe that Dr. Galakatos is qualified to serve on our board of directors because of his many years of service as one of our

directors, his extensive experience in the life sciences industry and his service on the board of directors of other life sciences companies.

*Michael Ross, Ph.D.* has served as a member of our board of directors since May 2013. Dr. Ross has served as a Managing Partner at SV Life Sciences, a venture capital firm, since January 2001. Dr. Ross served as a Managing Partner at Didyma, LLC, a biotechnology management consulting firm, from 1999 to 2002. Previously, Dr. Ross served as the Chief Executive Officer of CyThera, Inc., Carta Proteomics Inc., MetaXen LLC and Arris Pharmaceutical Corporation. Earlier in his career, Dr. Ross was employed at Genentech, serving in several roles, including Vice President of Development and later Vice President of Medicinal and Biomolecular Chemistry. Dr. Ross serves or has served on the boards of directors of Arris Pharmaceutical Corporation and Archemix Corp., and the board of directors of the Thayer School of Engineering at Dartmouth College. Dr. Ross received an A.B. from Dartmouth College, a Ph.D. in chemistry from the California Institute of Technology and completed post doctorate training in molecular biology at Harvard University. We believe that Dr. Ross is qualified to serve on our board of directors because of his extensive executive leadership experience and knowledge of the life sciences industry and his service on the board of directors of other life sciences companies.

*Glenn Sblendorio* has served as a member of our board of directors since July 2013. Mr. Sblendorio currently serves as the President and Chief Financial Officer of The Medicines Company, a medical solutions company, which he joined in March 2006. Mr. Sblendorio has served as a member of the board of directors of The Medicines Company since July 2011 and of Amicus Therapeutics Inc. since June 2007. Prior to joining The Medicines Company, Mr. Sblendorio served as Executive Vice President and Chief Financial Officer of Eyetech Pharmaceuticals, Inc. from February 2002 until it was acquired by OSI Pharmaceuticals, Inc. in November 2005. From July 2000 to February 2002, Mr. Sblendorio served as Senior Vice President of Business Development at The Medicines Company. Mr. Sblendorio received a B.B.A. from Pace University and an M.B.A. from Fairleigh Dickinson University. We believe that Mr. Sblendorio is qualified to serve on our board of directors because of his extensive executive leadership experience, finance and accounting background, knowledge of the life sciences industry and service on the board of directors of other life sciences companies.

### **Board Composition and Election of Directors**

Our board of directors is currently authorized to have eight members. Our board currently consists of seven members. We anticipate potentially appointing an additional independent director to our board of directors. Our board of directors is divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. The members of the classes are divided as follows:

- the class I directors are Dr. Galakatos and Dr. Ross, and their term expires at our annual meeting of stockholders to be held in 2014;
- the class II directors are Mr. Bolte and Dr. Patel, and their term expires at our annual meeting of stockholders to be held in 2015; and
- the class III directors are Dr. Dyrberg, Dr. Guyer and Mr. Sblendorio, and their term expires at our annual meeting of stockholders to be held in 2016.

Upon the expiration of the term of a class of directors, directors in that class are eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires. Our directors may be removed only for cause by the affirmative vote of the holders of 75% or more of our voting stock.

Under applicable NASDAQ rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. Our board

of directors has determined that all of our directors, other than Dr. Guyer and Dr. Patel, are independent directors, as defined by the applicable NASDAQ rules. In making such determination, the board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that the board of directors deemed relevant in determining their independence. In particular, in considering the independence of our directors, our board of directors considered the association of certain of our directors with the holders of more than 5% of our common stock as well as the effect of each of the transactions described in the "Transactions with Related Persons" section of this prospectus.

There are no family relationships among any of our directors or executive officers.

## **Board Committees**

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates under a charter that has been approved by our board.

Our board of directors has determined that all of the members of the audit committee, the compensation committee and the nominating and corporate governance committee are independent as defined under the NASDAQ rules, including, in the case of all the members of our audit committee, the independence requirements contemplated by Rule 10A-3 under the Exchange Act. In making such determination, our board of directors considered the relationships that each such director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

### ***Audit Committee***

The members of our audit committee are Mr. Sblendorio, Mr. Bolte and Dr. Galakatos. Mr. Sblendorio chairs our audit committee. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- overseeing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities and Exchange Commission, or SEC, rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Mr. Sblendorio is an "audit committee financial expert" as defined in applicable SEC rules.

#### ***Compensation Committee***

The members of our compensation committee are Dr. Galakatos, Dr. Dyrberg and Dr. Ross. Dr. Galakatos chairs our compensation committee. Our compensation committee's responsibilities include:

- reviewing and approving, or making recommendations to our board with respect to, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board with respect to director compensation;
- reviewing and discussing annually with management our compensation disclosure required by SEC rules; and
- preparing the compensation committee report required by SEC rules.

#### ***Nominating and Corporate Governance Committee***

The members of our nominating and corporate governance committee are Dr. Dyrberg, Mr. Bolte and Dr. Ross. Dr. Dyrberg chairs our nominating and corporate governance committee. Our nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become members of our board;
- recommending to our board the persons to be nominated for election as directors and to each of our board's committees;
- reviewing and making recommendations to our board with respect to our board leadership structure;
- reviewing and making recommendations to our board with respect to management succession planning;
- developing and recommending to our board corporate governance principles; and
- overseeing a periodic evaluation of our board.

#### **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.

**EXECUTIVE COMPENSATION**

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers. Our named executive officers for the year ended December 31, 2013 were David R. Guyer, M.D., our Chief Executive Officer, who is our principal executive officer, Samir C. Patel, M.D., our President, and Bruce Peacock, our Chief Financial and Business 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 our named executive officers during the years ended December 31, 2013 and December 31, 2012.

<u>Name and principal position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Option Awards \$(1)</u>	<u>Non-Equity Incentive Compensation \$(2)</u>	<u>All Other Compensation \$(3)</u>	<u>Total (\$)</u>
David R. Guyer, M.D.(4) <i>Chief Executive Officer</i>	2013	390,000	4,696,485	468,000	63,157	5,617,642
Samir C. Patel, M.D.(5) <i>President</i>	2013	448,000	1,050,177	252,000	28,966	1,779,143
	2012	434,765	77,558	110,917	26,162	649,402
Bruce Peacock(6) <i>Chief Financial and Business Officer</i>	2013	373,349	—	189,000	1,070	563,419
	2012	362,305	38,799	77,026	1,072	479,202

- (1) The amounts reported in the "Option Awards" column reflect the aggregate fair value of share-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 12 to our financial statements appearing at the end of this prospectus regarding assumptions underlying the valuation of equity awards.
- (2) The amounts reported in the "Non-Equity Incentive Plan Compensation" column represent awards to our named executive officers under our annual performance-based cash bonus program with respect to the applicable year.
- (3) The compensation included in the "All Other Compensation" column consists of premiums we paid with respect to each of our named executive officers for (a) medical, dental and vision insurance, (b) personal accident insurance, (c) life insurance, (d) long-term disability insurance, (e) short-term disability insurance, and fees related to an education assistance program. In particular, with respect to Dr. Patel, we paid medical, dental and vision insurance premiums of \$25,086 in 2012 and \$27,887 in 2013 and with respect to Dr. Guyer, we paid medical, dental and vision insurance premiums of \$17,429 in 2013. "All Other Compensation" also includes consulting fees paid to Dr. Guyer for the period prior to his appointment as our Chief Executive Officer. See Note (4) below.
- (4) Dr. Guyer also serves as a member of our board of directors but does not receive any additional compensation for his service as a director. Dr. Guyer was appointed as our Chief Executive Officer in April 2013. The salary information reflected for 2013 represents the pro rated portion of Dr. Guyer's annual salary of \$520,000 attributable to the portion of the year during which Dr. Guyer served as our Chief Executive Officer. Prior to his appointment as Chief Executive Officer, Dr. Guyer served as a member of our board of directors and as a consultant to

Ophthotech. During 2013, Dr. Guyer was paid consulting fees of \$45,000. Consulting fees paid to Dr. Guyer are reflected under "All Other Compensation".

- (5) Dr. Patel also serves as a member of our board of directors but does not receive any additional compensation for his service as a director. Dr. Patel served as our Chief Executive Officer until April 2013.
- (6) Mr. Peacock was appointed as our Chief Financial Officer in August 2013. Prior to his appointment as Chief Financial Officer, Mr. Peacock served as our Chief Business Officer, a role in which he continues to serve.

### ***Narrative Disclosure to Summary Compensation Table***

#### *Executive Compensation Program Overview*

The primary elements of our executive compensation are:

- base salary;
- annual performance-based cash bonuses;
- equity incentive awards;
- broad-based health and welfare benefits; and
- severance and change in control benefits.

#### *Base Salary*

We use base salaries to recognize the experience, skills, knowledge and responsibilities of our employees, including our named executive officers. None of our executive officers is currently party to an employment agreement that provides for automatic or scheduled increases in base salary. No formulaic base salary increases are provided to our named executive officers. However, on an annual basis, our compensation committee reviews and evaluates, with input from our chief executive officer, the need for adjustment of the base salaries of our executives.

In 2013, consistent with the terms of each named executive officer's written employment agreement, Dr. Guyer received an annual base salary of \$520,000 for the period during which he acted as Chief Executive Officer, Dr. Patel received an annual base salary of \$448,000 and Mr. Peacock received an annual base salary of \$373,349. In 2012, Dr. Patel received an annual base salary of \$434,765 and Mr. Peacock received an annual base salary of \$362,305.

For 2014, Dr. Guyer receives an annual base salary of \$545,000, Dr. Patel receives an annual base salary of \$470,000, and Mr. Peacock receives an annual base salary of \$410,000.

#### *Equity Incentive Awards*

Our equity award program is the primary vehicle for offering long-term incentives to our executives. While we do not have any equity ownership guidelines for our executives, 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. To date, we have used equity awards both to compensate our executive officers in the form of initial grants in connection with the commencement of employment, as well as to provide

additional, ongoing long-term incentives to our named executive officers as our business has developed and may continue to do so.

We have historically granted stock options with exercise prices that are set at no less than the fair market value of shares of our common stock on the date of grant as determined by contemporaneous valuations and reviewed and approved by our compensation committee or our board of directors. Vesting for grants made prior to our initial public offering varied, depending on various considerations. In the future, we generally plan that equity awards granted to our named executive officers will be subject to vesting conditions typically used in biotechnology companies similar to us in size and stage of development. Vesting and exercise rights cease shortly after termination of employment. Prior to the exercise of a stock option, the holder has no rights as a stockholder with respect to the shares subject to such option, including voting rights or the right to receive dividends or dividend equivalents.

On January 2, 2014, our board of directors granted stock options to each of our named executive officers. Each of these option awards will vest with respect to 25% of the shares subject to the option on the first anniversary of the grant date and with respect to the remaining shares in approximately equal monthly installments through the fourth anniversary of the grant date. Each of the option awards has an exercise price of \$31.29 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on the date of grant, and a grant date fair value of \$21.42 per share. The following table sets forth the number of shares of common stock issuable upon exercise of the stock options granted to our named executive officers on January 2, 2014:

<u>Name</u>	<u>Option Award (#)</u>
David R. Guyer, M.D.	175,000
Samir C. Patel, M.D.	140,000
Bruce Peacock	100,000

In April 2013, our board of directors granted stock options to Dr. Guyer in connection with his appointment as Chief Executive Officer. In May 2013, our board of directors granted stock options to Dr. Patel in recognition of his continued service as President. The following table sets forth information regarding these grants to Dr. Guyer and to Dr. Patel.

<u>Name</u>	<u>Option Award (#)</u>	<u>Exercise Price per share</u>	<u>Grant Date Fair Value</u>
David R. Guyer, M.D.	674,958	\$ 10.03	\$ 6.96
Samir C. Patel, M.D.	56,858(1)	\$ 13.22	\$ 9.24
	56,858(2)	\$ 13.22	\$ 9.24

(1) The unvested options vest monthly in equal amounts.

(2) This option is subject to performance-based vesting. The unvested options vest upon the occurrence of certain milestones.

In 2012, based upon our overall performance, we granted to Dr. Patel an option to purchase 67,796 shares of our common stock and to Mr. Peacock an option to purchase 33,898 shares of our common stock. Each of these option awards vests in approximately equal monthly installments through the fourth anniversary of the grant date. Each of the option awards has an exercise price of \$1.65 per share and a grant date fair value of \$1.14 per share.

#### *Annual Performance-Based Cash Bonus*

We have designed our annual performance-based cash bonus program to emphasize pay-for-performance and to reward our named executive officers for (1) the achievement of specified



annual corporate objectives and (2) the achievement of specified annual individual and functional performance objectives. Each executive officer is eligible to receive an annual performance-based cash bonus, which we refer to as an annual cash bonus, in an amount up to a fixed percentage of his base salary, or target bonus percentage, and each of the foregoing elements is weighted in determining the percentage of the annual cash bonus that the executive will receive. The target bonus percentages for each of our named executive officers for 2014 are as follows: Dr. Guyer, 60%; Dr. Patel, 50%; and Mr. Peacock, 45%.

Our compensation committee also has the authority to shift both corporate and individual goals to subsequent fiscal years and eliminate them from the current year's bonus calculation if it determines that circumstances that were beyond the control of the executive were the primary cause of a goal being unattainable.

Each of our compensation committee and our board of directors has authority, in its sole discretion, to adjust the bonus percentage each year in connection with its review of the executive's performance and has authority to allow an executive to receive a bonus payment in excess of his or her annual cash bonus for exceptional performance. Further, our board reviews the assessment of each executive's performance conducted by the compensation committee with respect to the annual cash bonus and retains the authority, in its sole discretion, to modify the amount of the annual cash bonus above or below the amount recommended by the compensation committee.

In 2013, consistent with the terms of each named executive officer's written employment agreement, Dr. Guyer was eligible for a target bonus equal to 60.0% of his base salary, Dr. Patel was eligible for a target bonus of 37.5% of his base salary and Mr. Peacock was eligible for a target bonus equal to 35.0% of his base salary. For 2013, Dr. Guyer was awarded a bonus in an amount equal to 90.0% of his base salary, Dr. Patel was awarded a bonus in an amount equal to 56.3% of his base salary and Mr. Peacock was awarded a bonus in an amount equal to 50.6% of his base salary. In 2012, Dr. Patel was eligible for a target bonus of 30.0% of his base salary and Mr. Peacock was eligible for a target bonus equal to 26.0% of his base salary. For 2012, Dr. Patel was awarded a bonus in an amount equal to 25.5% of his base salary and Mr. Peacock was awarded a bonus in an amount equal to 21.3% of his base salary.

#### *Benefits and Other Compensation*

We believe that establishing competitive benefit packages for our employees is an important factor in attracting and retaining highly qualified personnel. We maintain broad-based benefits that are provided to all employees, including medical, dental, group life insurance, accidental death, dismemberment insurance, long and short term disability insurance, and a 401(k) plan. We provide a match of each employee's contribution to their respective 401k retirement account up to a maximum of \$8,000. All of our executives are eligible to participate in all of our employee benefit plans, in each case on the same basis as other employees. The compensation committee in its discretion may revise, amend or add to the named executive officer's benefits and perquisites if it deems it advisable.

Prior to his appointment as our Chief Executive Officer, Dr. Guyer served as a consultant to Ophthotech. During 2013, Dr. Guyer was paid consulting fees of \$45,000. The consulting fees have been reflected in the "Summary Compensation Table" above as part of "All Other Compensation."

#### *Severance and Change in Control Benefits*

Each of our named executive officers is entitled to certain severance and change in control benefits, as described below under "—Material Terms of Employment Agreements with Named Executive Officers."

*Material Terms of Employment Agreements with Named Executive Officers*

We have written employment agreements with Dr. Guyer, Dr. Patel and Mr. Peacock. Dr. Patel's agreement provides for an employment term of one year, with the term automatically renewing for successive one-year terms, unless we or Dr. Patel give written notice of non-renewal at least 90 days prior to the renewal date. Our agreements with Dr. Guyer and Mr. Peacock do not have a stated term. The agreements with each of Dr. Guyer, Dr. Patel and Mr. Peacock provide for at-will employment. In addition, each of our executive officers are subject to invention assignment, non-disclosure, non-competition and non-solicitation agreements, either directly under their employment agreements or through separate agreements that were executed and delivered by the executives in connection with their employment agreements.

Pursuant to these agreements, each of our executive officers is entitled to receive a minimum annual base salary as follows: Dr. Guyer \$520,000; Dr. Patel \$448,000; and Mr. Peacock \$373,349.

In addition, following the end of each calendar year, each executive is eligible to receive an annual bonus. The bonus is calculated as a percentage of the executive's annual base salary. The minimum target bonus percentages for each executive officer are as follows: Dr. Guyer 60.0%; Dr. Patel 37.5%; and Mr. Peacock 35.0%. Except as otherwise provided in their respective employment agreements, each executive must be actively employed on the date the bonus is paid in order to be eligible for and receive his annual bonus.

*Potential Payments Upon Termination or Change in Control*

Upon execution and effectiveness of a separation agreement and release of claims, each named executive officer is entitled to severance payments if his employment is terminated under specified circumstances.

*Dr. Guyer.* If we terminate Dr. Guyer's employment without cause or if Dr. Guyer terminates his employment with us for good reason, each as defined in his employment agreement, Dr. Guyer is entitled to receive a lump sum payment in an amount equal to 12 months of his base salary; a pro-rated portion of his target bonus for the year in which his employment terminates; and continued coverage, at our expense, under our medical and dental benefit plans for 12 months immediately following the date of termination of his employment.

Upon the occurrence of a change in control event, as defined in our amended and restated 2007 stock incentive plan, or 2007 plan, subject to Dr. Guyer's continued employment as of the date of such event, or termination of Dr. Guyer's employment by us without cause within 75 days prior to (and in contemplation of) such event, the options awarded to Dr. Guyer in connection with his appointment as Chief Executive Officer in April 2013 become immediately exercisable in full with respect to all the unvested shares subject to such options.

*Dr. Patel.* If we terminate Dr. Patel's employment without cause or Dr. Patel terminates his employment with us for good reason, each as defined in his employment agreement, Dr. Patel is entitled to receive an amount equal to 12 months of his base salary payable in 12 equal monthly installments. If such termination occurs on a date prior to March 30, 2014, which is six months following the completion of our initial public offering, Dr. Patel will retain the right to exercise any vested options held by him on the date his employment terminates for the nine-month period following the closing of the initial public offering. If such termination occurs on or after March 30, 2014, Dr. Patel will retain the right to exercise any vested options held by him on the date his employment terminates for three months following such termination.

*Mr. Peacock.* If we terminate Mr. Peacock's employment without cause or if Mr. Peacock terminates his employment with us for good reason, each as defined in his employment agreement,

Mr. Peacock is entitled to receive an amount equal to nine months of his base salary payable in nine equal monthly installments and continued coverage, at our expense, under our medical and dental benefit plans for nine months immediately following the termination of his employment.

If we or our successor terminates Mr. Peacock's employment without cause or if Mr. Peacock terminates his employment with us or our successor for good reason, in each case within the one-year period following a change in control event, as defined in our 2007 plan, and such event also constitutes a "change in control event" within the meaning of the regulations promulgated under Section 409A of the Internal Revenue Code, as amended, or the Code, in addition to the payments and other benefits described above, Mr. Peacock is also entitled to receive an amount equal to his target bonus for the year in which his employment terminates.

Alternatively (and not in addition to the payments described above), if, following Mr. Peacock attaining the age of 63, which will occur in June 2014, he voluntarily terminates his employment on or after September 30, 2014, which is the date that is one year following the completion of our initial public offering, Mr. Peacock is entitled to receive an amount equal to 12 months of his base salary payable in 12 equal monthly installments; his target bonus for the year in which his employment terminates; the bonus he would have otherwise been entitled to receive for the year in which his employment terminates, had he remained an employee for the entire calendar year; and continued coverage, at our expense, under our medical and dental benefit plans for 12 months immediately following the termination of his employment. In addition, Mr. Peacock will be entitled to receive an offer to enter into a consulting arrangement with us following such a termination of his employment, in connection with which he will be entitled to receive, in exchange for the provision of consulting services: one twelfth of his then-current annualized base salary for each of the first three months he provides consulting services to us; 75% of such amount for each of the next three months during which he provides consulting services to us; and 50% of such amount for each of the following six months during which he provides consulting services to us. Provided Mr. Peacock is then providing consulting services to us, upon the occurrence of a change in control event, as defined in our 2007 plan, that also constitutes a "change in control event" within the meaning of the regulations promulgated under Section 409A of the Code, or in the event of our termination of the consulting arrangement without cause, Mr. Peacock is entitled to receive a lump sum payment in an amount equal to the maximum amount of payments he could have received under the consulting arrangement had he provided consulting services for a full 12 month period (less any amounts he has already received). Mr. Peacock's employment agreement provides that any fees for consulting services provided by Mr. Peacock following the first anniversary of his termination of employment will be negotiated at arm's length.

#### *Taxation*

To the extent that any payment, benefit, or distribution (or combination thereof) by us or any of our affiliates to Dr. Guyer pursuant to his employment agreement or any other agreement, plan or arrangement would be subject to the excise tax imposed by Section 4999 of the Code, Dr. Guyer is entitled to receive an amount that, after payment of all applicable taxes by Dr. Guyer, is equal to the excise tax and any other applicable interest or penalties that Dr. Guyer may owe in connection with such excise tax.

**Outstanding Equity Awards as of December 31, 2013**

The following table sets forth information regarding outstanding stock options held by our named executive officers as of December 31, 2013:

<u>Name</u>	<u>Number of Securities Underlying Unexercised Options Exercisable (#)</u>	<u>Number of Securities Underlying Unexercised Options Unexercisable (#)</u>	<u>Option Exercise Price (\$/share)</u>	<u>Option Expiration Date</u>
David R. Guyer, M.D.	112,491	562,467(1)	\$ 10.03	4/25/2023
Samir C. Patel, M.D.	235,904	—	\$ 1.59	5/17/2020
	37,216	20,411(2)	\$ 1.65	5/10/2021
	28,248	39,548(3)	\$ 1.65	4/8/2022
	8,292	48,566(4)	\$ 13.21	5/28/2023
	—	56,858(5)	\$ 13.21	5/28/2023
Bruce Peacock	72,941	—	\$ 1.65	9/27/2020
	179,270	58,205(6)	\$ 1.65	9/27/2020
	16,350	4,451(7)	\$ 1.65	5/10/2021
	1,163	5,154(8)	\$ 1.65	5/10/2021
	14,124	19,774(3)	\$ 1.65	4/8/2022

- (1) The vested options vest monthly in approximately equal amounts through April 2017.
- (2) The vested options vest monthly in approximately equal amounts through May 2015.
- (3) The vested options vest monthly in approximately equal amounts through April 2016.
- (4) The vested options vest monthly in approximately equal amounts through May 2017.
- (5) This option is subject to performance-based vesting. The vested options vest upon the occurrence of certain milestones.
- (6) The vested options vest monthly as to approximately equal amounts from January 2014 to September 2014.
- (7) The vested options vest monthly as to 497 shares in May 2014; and as to approximately equal amounts from June 2014 to December 2014.
- (8) The vested options vest monthly as to 564 shares in January 2014; 565 shares from February 2014 to May 2014; 68 shares in January 2015; 565 shares from February 2015 to April 2015; and 567 shares in May 2015.

**Additional Narrative Disclosure**

**401(k) Retirement Plan.** We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to \$17,500 in 2014, and have the amount of the reduction contributed to the 401(k) plan. Commencing January 2014, we will match 100% of an employee's contributions to the 401(k) plan up to the first 2% of the employee's salary, and 50% of the employee's contributions up to the next 4% of the employee's salary, up to a maximum amount of \$8,000 per employee.

**Pension Benefits.** We do not maintain any defined benefit pension plans.

**Nonqualified Deferred Compensation.** We do not maintain any nonqualified deferred compensation plans.

## Stock Option and Other Compensation Plans

The two equity incentive plans described in this section are our amended and restated 2007 stock incentive plan, as amended to date, or the 2007 plan, and our 2013 stock incentive plan. Prior to our initial public offering, which closed on September 30, 2013, we granted awards to eligible participants under the 2007 plan. Following the closing of our initial public offering, we grant awards to eligible participants under the 2013 stock incentive plan.

### *Amended and Restated 2007 Stock Incentive Plan*

The 2007 plan was adopted by our board of directors and approved by our stockholders in December 2007. The 2007 plan provided for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights and other stock-based awards. Our employees, officers, directors, consultants and advisors were eligible to receive awards under our 2007 plan; however, incentive stock options could only be granted to our employees.

The type of award granted under our 2007 plan and the terms of such award are set forth in the applicable award agreement.

#### *Effect of Certain Changes in Capitalization.*

Upon the occurrence of any of a stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of common stock other than an ordinary cash dividend, our board of directors shall equitably adjust:

- the number and class of securities available under the 2007 plan; and
- the number and class of securities and exercise price per share of each outstanding option.

#### *Effect of Certain Corporate Transactions*

Upon the occurrence of a merger or consolidation of the company with or into another entity, as a result of which all of the outstanding shares of our common stock are exchanged for cash, securities or other property or are cancelled, or any exchange of all of the outstanding shares of our common stock for cash, securities or other property pursuant to a share exchange transaction or upon a liquidation or dissolution of the company, our board of directors may take any one or more of the following actions:

- provide that awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a plan participant, provide that the participant's unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised by the participant within a specified period;
- provide that outstanding awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an award shall lapse, in whole or in part prior to or upon such transaction;
- in the event of such a transaction, under the terms of which holders of common stock will receive upon consummation thereof a cash payment for each share surrendered in the transaction, make or provide for a cash payment to a plan participant;
- provide that, in connection with a liquidation or dissolution of the company, awards shall convert into the right to receive liquidation proceeds; or
- any combination of the foregoing.

Our board of directors does not need to take the same action with respect to all awards and may take different actions with respect to portions of the same award.

*Effect of a Change of Control*

Pursuant to the terms of the 2007 plan, if, on or prior to the first anniversary of a change in control, the employment of a plan participant is terminated for good reason by the participant or without cause by the company, as such terms are defined in the 2007 plan:

- all unvested options then held by such participant shall immediately become exercisable in full; and
- all restricted stock then held by such participant shall immediately become free from all conditions or restrictions.

Our board of directors may at any time provide that any award will become immediately exercisable in full or in part, free from some or all restrictions or conditions, or otherwise realizable in full or in part, as the case may be.

As of January 31, 2014, there were options to purchase 2,398,778 shares of our common stock outstanding under the 2007 plan, at a weighted-average exercise price of \$7.03 per share, and options to purchase 694,223 shares of our common stock awarded under the 2007 plan had been exercised.

**2013 Stock Incentive Plan**

Our board of directors adopted and our stockholders approved the 2013 stock incentive plan in August 2013. The 2013 stock incentive plan became effective immediately prior to the closing of our initial public offering on September 30, 2013. The 2013 stock incentive plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, and other stock-based awards. The number of shares of our common stock that are reserved for issuance under the 2013 stock incentive plan is the sum of (1) the number of shares (up to 3,362,256 shares) equal to the sum of 739,317, which was the number of shares of our common stock available for issuance under the 2007 plan at the time of the completion of our initial public offering, and the number of shares of our common stock subject to outstanding awards under the 2007 plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right plus (2) an annual increase, to be added the first day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until, and including, the fiscal year ending December 31, 2023, equal to the lowest of 2,542,372 shares of our common stock, 4% of the number of shares of our common stock outstanding on the first day of the fiscal year and an amount determined by our board of directors, which, in the case of 2014, was 1,256,528 shares, or 4% of the number of shares of our common stock outstanding as of January 1, 2014. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2013 stock incentive plan. However, incentive stock options may only be granted to our employees.

Pursuant to the terms of the 2013 stock incentive plan, our compensation committee, pursuant to authority delegated to it by our board of directors, administers the plan and, subject to any limitations in the plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;

- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, measurement price, issue price and repurchase price (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years).

The compensation committee of our board of directors has also delegated authority to our Chief Executive Officer to grant awards under the 2013 stock incentive plan. Our Chief Executive Officer has the power to make awards to all of our employees, except our officers or any other employee with the title of Vice President or above (i.e., Senior Vice President, Executive Vice President or President). Our compensation committee has fixed the terms of the awards to be granted by our Chief Executive Officer, including the exercise price of such awards (which will be the fair market value of our common stock on the date of grant), and the maximum number of shares subject to awards that our Chief Executive Officer may make in a single grant to any one person in any calendar year, and the maximum number of shares subject to awards, in the aggregate, in any one year.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, our board of directors is required by the 2013 stock incentive plan to make equitable adjustments, in a manner determined by our board, to:

- the number and class of securities available and the share counting rules under the 2013 stock incentive plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share-related provisions and purchase price, if any, of any outstanding other stock-based award.

Upon a merger or other reorganization event (as defined in our 2013 stock incentive plan), our board of directors may, in its sole discretion, take any one or more of the following actions pursuant to the 2013 stock incentive plan as to some or all outstanding awards other than restricted stock:

- provide that all outstanding awards shall 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 all of the participant's unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant;
- provide that outstanding awards shall become exercisable, realizable or deliverable, or restrictions applicable to an award shall lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares 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 a 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 award; and/or

- provide that, in connection with a liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings).

Our board of directors does not need to take the same action with respect to all awards and may take different actions with respect to portions of the same award.

In the case of certain 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 with respect to outstanding awards of restricted stock will continue for the benefit of the successor company and will, unless the board of directors may otherwise determine, apply to the cash, securities or other property into which shares of our common stock are converted or exchanged 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 award of restricted stock.

At any time, our board of directors may, in its sole discretion, provide that any award under the 2013 stock incentive 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.

In addition, the 2013 stock incentive plan provides that, notwithstanding the provisions of the plan that may apply upon a reorganization event and except as otherwise provided for in the instrument evidencing an option or award of restricted stock or any other agreement between us and the participant, upon the occurrence of a change in control event (as defined in the 2013 stock incentive plan) each option shall become immediately exercisable and each award of restricted stock shall become immediately free from all conditions and restrictions, if, in either case, the employment of the participant holding such award is terminated by us (or our acquirer or successor) without cause (as defined in the 2013 stock incentive plan) or by the participant for good reason (as defined in the 2013 stock incentive plan), on or prior to the first anniversary of the date of the change in control event. Our board of directors may specify in an award at the time of grant the effect of a change in control event on any stock appreciation right, restricted stock unit or other stock-based award.

Unless our stockholders approve such action, the 2013 stock incentive plan provides that the we may not:

- amend any outstanding stock option or stock appreciation right granted under the plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right (whether or not granted under the plan) and grant in substitution therefor new awards under the plan (other than as substitute awards in the event of a merger or consolidation involving us) covering the same or a different



number of shares of common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;

- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock; or
- take any other action that constitutes a "repricing" within the meaning of the rules of the NASDAQ Stock Market.

No award may be granted under the 2013 stock incentive plan on or after August 26, 2023. Our board of directors may amend, suspend or terminate the 2013 stock incentive plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

As of January 31, 2014, there were options to purchase 1,270,873 shares of our common stock outstanding under the 2013 stock incentive plan, at a weighted-average exercise price of \$30.59 per share, and no options to purchase shares of our common stock awarded under the 2013 stock incentive plan had been exercised.

#### **Limitations on 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 and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other 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 Delaware General Corporation Law 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 Delaware General Corporation Law.

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 certain 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 our directors. These indemnification agreements may require us, among other things, to indemnify each such director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him in any action or proceeding arising out of his service as one of our directors.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities incurred in their capacity as members of our board of directors.

**Rule 10b5-1 Sales Plans**

Some of our senior employees, including our named executive officers, have adopted written plans, known as Rule 10b5-1 plans, in which they have contracted with a broker to buy or sell shares of our common stock on a periodic basis effective following the expiration of the lock-ups entered into in connection with our initial public offering. Our directors and other senior employees may also adopt such plans in the future. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or employee when entering into the plan, without further direction from the director or employee. It also is possible that the director or employee could amend or terminate any such plan when not in possession of material, nonpublic information and otherwise in accordance with our insider trading policy. In addition, our directors and employees, including our named executive officers, may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information and otherwise in accordance with our insider trading policy.

**Director Compensation*****Director Compensation Table***

The following table sets forth a summary of the compensation earned by our directors for the year ended December 31, 2013, with the exception of Dr. Guyer and Dr. Patel, who do not receive compensation for service on our board of directors and whose compensation is included in the "Summary Compensation Table" above. Our non-employee directors did not receive any compensation for their service as directors during the year ended December 31, 2012.

<u>Name</u>	<u>Fees Earned or Paid in Cash (\$)</u>	<u>Option Awards (\$)(1)</u>	<u>Total (\$)</u>
Axel Bolte	\$ —	\$ —	\$ —
Thomas Dyrberg, M.D., D.M.Sc.	12,500	489,455	501,955
Nicholas Galakatos, Ph.D.	13,000	489,455	502,455
Michael Ross, Ph.D.	10,000	489,455	499,455
Glenn Sblendorio	13,750	294,963	308,713

- (1) The amounts reported in the "Option Awards" column reflect the aggregate fair value of share-based compensation awarded during the year computed in accordance with the provisions of ASC Topic 718. See Note 12 to our financial statements appearing at the end of this prospectus regarding assumptions underlying the valuation of equity awards.

In connection with his election to our board of directors, Mr. Sblendorio received an option to purchase 15,084 shares of our common stock. In connection with the completion of our initial public offering, each of Dr. Dyrberg, Dr. Galakatos and Dr. Ross received an option to purchase 22,033 shares of our common stock and Mr. Sblendorio received an option to purchase 6,949 shares of our common stock. The stock options granted to each of these directors 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 and vest monthly in equal amounts over a three-year period.

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

- each non-employee director will receive an option to purchase 22,033 shares of our common stock upon his or her initial election or appointment to our board of directors;

- 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 9,322 shares of our common stock on the date of the first meeting of our board of directors held after each annual meeting of stockholders;
- each non-employee director will receive an annual fee of \$40,000; and
- each non-employee director who serves as chairman of a committee of our board of directors will receive additional compensation as follows:
  - chairman of the audit committee—an additional annual fee of \$15,000;
  - chairman of the compensation committee—an additional annual fee of \$12,000; and
  - chairman of the nominating and corporate governance committee—an additional annual fee of \$10,000.

Following our 2014 annual meeting of stockholders, the chairman of the audit committee will receive an annual fee of \$18,000, each additional member of the audit committee will receive an annual fee of \$8,000 and each member of the compensation committee and corporate governance committee, other than the respective chairmen, will receive an annual fee of \$5,000. In addition, following our 2014 annual meeting of stockholders, each non-employee director will receive an option to purchase 28,000 shares of our common stock upon his or her initial election or appointment to our board of directors and 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 15,000 shares of our common stock on the date of the first meeting of our board of directors held after each annual meeting of stockholders.

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. 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 through the earlier of the business day before the next annual meeting or the first anniversary of the grant date at which time they will vest in full. Stock options granted to our non-employee directors will vest in full upon the occurrence of a change in control of us.

Each annual 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 the effective date of the registration statement of which this prospectus is a part.

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

Prior to our initial public offering, other than the stock options granted to Mr. Sblendorio in connection with his election to our board of directors, we did not pay cash retainers or other compensation (other than the stock options previously granted to Mr. Sblendorio) with respect to service on our board of directors. We have historically reimbursed our directors for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors or committees of the board of directors.

## TRANSACTIONS WITH RELATED PERSONS

Since January 1, 2011, 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.

### Participation in Initial Public Offering

In our initial public offering, two of our 5% stockholders, Novo A/S and HBM Healthcare Investments (Cayman) Ltd., purchased an aggregate of 683,000 shares of our common stock. Each of those purchases was made through the underwriters at the initial public offering price of \$22.00 per share. The following table sets forth the aggregate number of shares of our common stock that these 5% stockholders purchased in our initial public offering:

<u>Name</u>	<u>Shares of Common Stock Purchased</u>	<u>Aggregate Purchase Price</u>
Novo A/S(1)	455,000	\$ 10,010,000
HBM Healthcare Investments (Cayman) Ltd.(2)	228,000	5,016,000

- (1) Novo A/S is a Danish limited liability company. The board of directors of Novo A/S, which consists of Sten Scheibye, Göran Ando, Jørgen Boe, Jeppe Christiansen, Steen Riisgaard and Per Wold-Olsen, has sole voting and investment power with respect to the shares held by Novo A/S. None of the members of the board of directors of Novo A/S has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Dyrberg, a member of our board of directors, is employed as a Senior Partner of Novo A/S. Dr. Dyrberg disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest arising as a result of his employment with Novo A/S.
- (2) The board of directors of HBM Healthcare Investments (Cayman) Ltd. has sole voting and investment power with respect to the shares by held by such entity. The board of directors of HBM Healthcare Investments (Cayman) Ltd. is comprised of Jean-Marc Le Sieur, Richard Coles, Sophia Harris, Dr. Andreas Wicki and John Urquhart, none of whom has individual voting or investment power with respect to such shares, and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Mr. Bolte, a member of our board of directors, is an advisor to HBM Partners (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM Healthcare Investments (Cayman) Ltd. Mr. Bolte has no voting or investment power over the shares held by HBM Healthcare Investments (Cayman) Ltd., and disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.

### Series C Preferred Stock Financing

In May 2013, we issued and sold an aggregate of 6,666,667 shares of our series C preferred stock at a price per share of \$2.50, for an aggregate purchase price of \$16.7 million. In August 2013, we issued and sold an aggregate of 13,333,333 additional shares of our series C preferred stock to the same purchasers at a price per share of \$2.50, for an aggregate purchase price of \$33.3 million. The following table sets forth the total number of shares of our series C preferred stock purchased by our

directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price for such shares.

<u>Name</u>	<u>Shares of Series C Preferred Stock Purchased</u>	<u>Aggregate Purchase Price</u>
Clarus Lifesciences II, LP(1)	1,097,562	\$ 2,743,905
SV Life Sciences Fund IV, L.P.(2)	56,476	141,190
SV Life Sciences Fund IV Strategic Partners, L.P.(2)	1,989,255	4,973,138
Novo A/S(3)	15,438,009	38,595,023
HBM Healthcare Investments (Cayman) Ltd.(4)	1,209,349	3,023,373
Samir C. Patel LLC(5)	136,179	340,448

- (1) Clarus Ventures II GP, L.P., as the sole general partner of Clarus Lifesciences II, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II GP, L.P. disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which Clarus Ventures II GP, L.P. does not have an actual pecuniary interest. Clarus Ventures II, LLC, as the sole general partner of Clarus Ventures II GP, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II, LLC disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which it does not have an actual pecuniary interest. Each of Nicholas Galakatos, a member of our board of directors, and Denis Henner, Robert Liptak, Nicholas Simon, Michael Steinmetz and Kurt Wheeler, as individual Managing Directors of Clarus Ventures II, LLC, individually have investment and voting control over the shares held by Clarus Lifesciences II, L.P. Each of Messrs. Galakatos, Henner, Liptak, Simon, Steinmetz and Wheeler disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. except to the extent of any pecuniary interest therein.
- (2) The general partner of SV Life Sciences Fund IV, L.P. and SV Life Sciences Fund IV Strategic Partners, L.P. is SV Life Sciences Fund IV (GP), LP. The general partner of SV Life Sciences Fund IV (GP), LP is SVLSF IV, LLC. The members of the investment committee for SVLSF IV, LLC are Kate Bingham, James Garvey, Lutz Giebel, Eugene D. Hill, III, David Milne and Michael Ross. Michael Ross, Ph.D., one of our directors, is a Managing Partner of SV Life Sciences Advisers, LLC. David R. Guyer, M.D., our Chief Executive Officer and Chairman of our board of directors, and Bruce Peacock, our Chief Financial and Business Officer, are Venture Partners of SV Life Sciences Advisers, LLC. None of Dr. Ross, Dr. Guyer or Mr. Peacock exercises investment or voting control over such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
- (3) Novo A/S is a Danish limited liability company. The board of directors of Novo A/S, which consists of Sten Scheibye, Göran Ando, Jørgen Boe, Jeppe Christiansen, Steen Riisgaard and Per Wold-Olsen, has sole voting and investment power with respect to the shares held by Novo A/S. None of the members of the board of directors of Novo A/S has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Dyrberg, a member of our board of directors, is employed as a Senior Partner of Novo A/ S. Dr. Dyrberg disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest arising as a result of his employment with Novo A/S.
- (4) The board of directors of HBM Healthcare Investments (Cayman) Ltd. has sole voting and investment power with respect to the shares by held by such entity. The board of directors of HBM Healthcare Investments (Cayman) Ltd. is comprised of Jean-Marc Le Sieur, Richard Coles, Sophia Harris, Dr. Andreas Wicki and John Urquhart, none of whom has individual voting or investment power with respect to such shares, and each disclaims beneficial ownership of such

shares except to the extent of any pecuniary interest therein. Mr. Bolte, a member of our board of directors, is an advisor to HBM Partners (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM Healthcare Investments (Cayman) Ltd. Mr. Bolte has no voting or investment power over the shares held by HBM Healthcare Investments (Cayman) Ltd., and disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.

- (5) Dr. Patel exercises voting control over shares held by Samir C. Patel LLC.

### **Royalty Financing**

In May 2013, we entered into our royalty purchase and sale agreement, or the royalty agreement, with Novo A/S, a 5% stockholder of which our director Dr. Dyrberg is an employee, pursuant to which we may obtain royalty financing in three tranches in an amount of up to \$125.0 million in return for the sale to Novo A/S of aggregate royalties at low to mid single-digit percentages of worldwide sales of Fovista, with the percentage determined by the amount of funding provided by Novo A/S. The first and second tranches of the royalty financing, in which Novo A/S purchased two low single-digit royalty interests and paid us \$83.3 million in the aggregate, closed in May 2013 and January 2014. Under the royalty agreement, Novo A/S agreed to purchase from us, and we agreed to sell to Novo A/S, an additional low single-digit royalty interest on worldwide sales of Fovista, for a purchase price of \$41.7 million. The closing of the final financing tranche is subject to the enrollment of a specified number of patients in our Phase 3 clinical trials of Fovista and our satisfying additional closing conditions and other obligations. Under specified circumstances, however, including terminations, suspensions or delays of our Phase 3 clinical trials for Fovista or transactions involving a change of control of us in which the acquiring party does not meet certain specifications, Novo A/S has the option to cancel the subsequent purchase and sale of the final royalty interest. We also have the option to cancel the subsequent purchase and sale of the final royalty interest in specified circumstances, including terminations, suspensions or delays in our Phase 3 clinical trials for Fovista, any change of control of us, or the completion of equity financings meeting specified thresholds. The royalty agreement provides that we will use the remaining proceeds we received from the first tranche of financing and future proceeds, if any, under the royalty agreement primarily to support clinical development and regulatory activities for Fovista and for certain other permitted purposes. See "Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Royalty Financing" for more information regarding this agreement.

### **Series B Preferred Stock Financing**

In December 2009, we issued and sold an aggregate of 15,000,000 shares of our series B preferred stock, at a price per share of \$1.00, for an aggregate purchase price of \$15.0 million. In addition, in March 2011, we issued and sold an aggregate of 15,000,000 additional shares of our series B preferred stock to the same purchasers at a price per share of \$1.00, for an aggregate purchase price of \$15.0 million. The following table sets forth the aggregate number of shares of our series B preferred

stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price for such shares.

Name	Shares of Series B	Aggregate
	Preferred Stock Purchased	Purchase Price
Clarus Lifesciences II, LP(1)	15,000,000	\$ 15,000,000
SV Life Sciences Fund IV, L.P.(2)	6,117,974	6,117,974
SV Life Sciences Fund IV Strategic Partners, L.P.(2)	173,692	173,692
Novo A/S(3)	5,208,334	5,208,334
HBM Healthcare Investments (Cayman) Ltd.(4)	2,083,334	2,083,334
Samir C. Patel LLC(5)	416,666	416,666

- (1) Clarus Ventures II GP, L.P., as the sole general partner of Clarus Lifesciences II, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II GP, L.P. disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which Clarus Ventures II GP, L.P. does not have an actual pecuniary interest. Clarus Ventures II, LLC, as the sole general partner of Clarus Ventures II GP, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II, LLC disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which it does not have an actual pecuniary interest. Each of Nicholas Galakatos, a member of our board of directors, and Denis Henner, Robert Liptak, Nicholas Simon, Michael Steinmetz and Kurt Wheeler, as individual Managing Directors of Clarus Ventures II, LLC, individually have investment and voting control over the shares held by Clarus Lifesciences II, L.P. Each of Messrs. Galakatos, Henner, Liptak, Simon, Steinmetz and Wheeler disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. except to the extent of any pecuniary interest therein.
- (2) The general partner of SV Life Sciences Fund IV, L.P. and SV Life Sciences Fund IV Strategic Partners, L.P. is SV Life Sciences Fund IV (GP), LP. The general partner of SV Life Sciences Fund IV (GP), LP is SVLSF IV, LLC. The members of the investment committee for SVLSF IV, LLC are Kate Bingham, James Garvey, Lutz Giebel, Eugene D. Hill, III, David Milne and Michael Ross. Michael Ross, Ph.D., one of our directors, is a Managing Partner of SV Life Sciences Advisers, LLC. David R. Guyer, M.D., our Chief Executive Officer and Chairman of our board of directors, and Bruce Peacock, our Chief Financial and Business Officer, are Venture Partners of SV Life Sciences Advisers, LLC. None of Dr. Ross, Dr. Guyer or Mr. Peacock exercises investment or voting control over such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
- (3) Novo A/S is a Danish limited liability company. The board of directors of Novo A/S, which consists of Sten Scheibye, Göran Ando, Jørgen Boe, Jeppe Christiansen, Steen Riisgaard and Per Wold-Olsen, has sole voting and investment power with respect to the shares held by Novo A/S. None of the members of the board of directors of Novo A/S has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Dyrberg, a member of our board of directors, is employed as a Senior Partner of Novo A/ S. Dr. Dyrberg disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest arising as a result of his employment with Novo A/S.
- (4) The board of directors of HBM Healthcare Investments (Cayman) Ltd. has sole voting and investment power with respect to the shares by held by such entity. The board of directors of HBM Healthcare Investments (Cayman) Ltd. is comprised of Jean-Marc Le Sieur, Richard Coles, Sophia Harris, Dr. Andreas Wicki and John Urquhart, none of whom has individual voting or investment power with respect to such shares, and each disclaims beneficial ownership of such

shares except to the extent of any pecuniary interest therein. Mr. Bolte, a member of our board of directors, is an advisor to HBM Partners (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM Healthcare Investments (Cayman) Ltd. Mr. Bolte has no voting or investment power over the shares held by HBM Healthcare Investments (Cayman) Ltd., and disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.

- (5) Dr. Patel exercises voting control over shares held by Samir C. Patel LLC.

### **Consulting Arrangement**

In connection with the initial closing of our series B preferred stock financing in December 2009, we entered into a consulting arrangement with David R. Guyer, pursuant to which Dr. Guyer provided certain consulting services to us in exchange for cash payments of \$10,833.33 per month. Dr. Guyer's consulting arrangement with us terminated in April 2013.

### **Registration Rights**

We are a party to an investors' rights agreement with certain holders of our common stock, including some of our directors, executive officers and 5% stockholders and their affiliates and entities affiliated with our officers and directors. The investors' rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

### **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 each of our directors and executive officers. See "Executive Compensation—Limitation of Liability and Indemnification" for additional information regarding these agreements.

### **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 Ophthotech 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 Chief Financial 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 chairman 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 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.

The audit committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in our best interests. The 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 such entity) that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) 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 (c) 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 charter or bylaws.

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

We did not have a written policy regarding the review and approval of related person transactions prior to our initial public offering. Nevertheless, with respect to such transactions, it was our policy for our board of directors to consider the nature of and business reason 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.

## PRINCIPAL AND SELLING STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock as of January 31, 2014 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group;
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock; and
- each of the selling stockholders.

The percentages in the column entitled "Shares Beneficially Owned Before Offering" are based on a total of 31,418,575 shares of our common stock outstanding as of January 31, 2014. The percentages in the column entitled "Shares Beneficially Owned After Offering" are based on 33,318,575 shares of our common stock to be outstanding after this offering, including the 1,900,000 shares of our common stock that we are issuing and selling and the 385,714 shares of our common stock that the selling stockholders are selling in this offering. The percentages in the column entitled "Shares Beneficially Owned After Offering Assuming Underwriters Exercise Option in Full" give further effect to the sale by the selling stockholders, assuming the underwriters exercise their option in full, of an additional 342,857 shares of our common stock. The information set forth in the columns entitled "Shares Beneficially Owned After Offering" and "Shares Beneficially Owned After Offering Assuming Underwriters Exercise Option in Full" do not give effect to the issuance of any additional shares issuable upon exercise of outstanding options or warrants as of January 31, 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 or warrants that are currently exercisable or exercisable within 60 days of January 15, 2014, are considered outstanding and beneficially owned by the person holding the options or warrants 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 the beneficial owner is *c/o* Ophthotech Corporation, One Penn Plaza, 19<sup>th</sup> Floor, New York, New York 10119.

The information in the table below with respect to each selling stockholder has been obtained from that selling stockholder. When we refer to the "selling stockholder" in this prospectus, we mean

those persons listed in the table below as offering shares, as well as the pledgees, donees, assignees, transferees, successors and others who may hold any of the selling stockholders' interest.

Name of Beneficial Owner	Shares Beneficially Owned Before Offering		Number of Shares Offered	Shares Beneficially Owned After Offering		Additional Shares to be Sold if Underwriters Exercise Option in Full	Shares Beneficially Owned after Offering Assuming Underwriters Exercise Option in Full	
	Number	%		Number	%		Number	%
<b>Named Executive Officers and Directors</b>								
David R. Guyer, M.D.(1)	201,285	*	—	201,285	*	—	201,285	*
Samir C. Patel, M.D.(2)	858,578	2.71%	—	858,578	2.55%	—	858,578	2.53%
Bruce Peacock(3)	307,062	*	—	307,062	*	—	307,062	*
Axel Bolte(4)	2,000	*	—	2,000	*	—	2,000	*
Thomas Dyrberg, M.D., D.M.Sc.(5)	3,760	*	—	3,760	*	—	3,760	*
Nicholas Galakatos, Ph.D.(6)	3,062,804	9.75%	—	3,062,804	9.19%	—	3,062,804	9.10%
Michael Ross, Ph. D(7)	3,060	*	—	3,060	*	—	3,060	*
Glenn Sblendorio(8)	4,317	*	—	4,317	*	—	4,317	*
All Executive Officers and Directors as a Group (8 persons)(9)	4,442,867	13.79%	—	4,442,867	13.02%	—	4,442,867	12.89%
<b>5% Stockholders</b>								
Clarus Lifesciences II, L.P.(10)	3,054,744	9.72%	—	3,054,744	9.17%	—	3,054,744	9.07%
Entities Affiliated with SV Life Sciences(11)	6,037,481	19.22%	372,594	5,664,887	17.00%	331,194	5,333,693	15.85%
HBM Healthcare Investments (Cayman) Limited(12)	3,653,570	11.62%	—	3,653,570	10.96%	—	3,653,570	10.85%
Novo A/S(13)	6,910,487	21.99%	—	6,910,487	20.73%	—	6,910,487	20.52%
<b>Additional Selling Stockholder</b>								
International Biotechnology Trust plc(14)	203,649	*	13,120	190,529	*	11,663	178,866	*

\* Less than one percent.

- (1) Consists of (i) 154,675 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date and (ii) 46,610 shares of common stock held by Dr. Guyer in his individual capacity.
- (2) Consists of (i) 321,051 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date; (ii) 152,543 shares of common stock held by Dr. Patel in his individual capacity; and (iii) 384,984 shares of common stock held by Samir C. Patel LLC. Dr. Patel exercises voting control over shares held by Samir C. Patel LLC.
- (3) Consists of 307,062 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date.
- (4) Consists of 2,000 shares of common stock held by Mr. Bolte in his individual capacity. Mr. Bolte is an advisor to HBM Partners (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM Healthcare Investments (Cayman) Ltd. Mr. Bolte, a member of our board of directors, has no voting or investment power over the shares held by HBM Healthcare Investments (Cayman) Ltd., and disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
- (5) Consists of (i) 3,060 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date; and (ii) 700 shares of common stock held by Dr. Dyrberg in his individual capacity. Dr. Dyrberg is employed as a Senior Partner of Novo A/S. Dr. Dyrberg disclaims beneficial ownership of shares held by Novo A/S, except to the extent of his pecuniary interest arising as a result of his employment with Novo A/S.
- (6) Consists of (i) 3,060 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date; (ii) 2,500 shares of common stock held by Dr. Galakatos in his individual capacity; (iii) 2,500 shares of common stock held by AG Peakham Trust LLC; and (iv) 3,054,744 shares of common stock held by Clarus Lifesciences II, L.P. Dr. Galakatos is a manager of AAG Peakham Trust LLC. Clarus Ventures II GP, L.P., as the sole general partner of Clarus Lifesciences II, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II GP, L.P. disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which Clarus Ventures II GP, L.P. does not have an actual pecuniary interest. Clarus Ventures II, LLC, as the sole general partner of Clarus Ventures II GP, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II, LLC disclaims beneficial ownership of all shares held by Clarus

Lifesciences II, L.P. in which it does not have an actual pecuniary interest. Each of Nicholas Galakatos, a member of our board of directors, and Denis Henner, Robert Liptak, Nicholas Simon, Michael Steinmetz and Kurt Wheeler, as individual Managing Directors of Clarus Ventures II, LLC, individually have investment and voting control over the shares held by Clarus Lifesciences II, L.P. Each of Messrs. Galakatos, Henner, Liptak, Simon, Steinmetz and Wheeler disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. except to the extent of any pecuniary interest therein. The address of Clarus Ventures II, LLC, Clarus Lifesciences II, L.P. and their affiliates is 101 Main St. #1210, Cambridge MA 02142.

- (7) Consists of 3,060 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date.
- (8) Consists of 4,317 shares of common stock underlying options that are exercisable as of January 31, 2014, or will become exercisable within 60 days after such date.
- (9) Consists of (i) 3,646,581 shares of common stock; and (ii) 796,286 shares of common stock underlying options that are exercisable as of January 15, 2014, or will become exercisable within 60 days after such date.
- (10) Consists of 3,054,744 shares of common stock held by Clarus Lifesciences II, L.P. Clarus Ventures II GP, L.P., as the sole general partner of Clarus Lifesciences II, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II GP, L.P. disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which Clarus Ventures II GP, L.P. does not have an actual pecuniary interest. Clarus Ventures II, LLC, as the sole general partner of Clarus Ventures II GP, L.P., may be deemed to beneficially own certain of the shares held by Clarus Lifesciences II, L.P. Clarus Ventures II, LLC disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. in which it does not have an actual pecuniary interest. Each of Nicholas Galakatos, a member of our board of directors, and Denis Henner, Robert Liptak, Nicholas Simon, Michael Steinmetz and Kurt Wheeler, as individual Managing Directors of Clarus Ventures II, LLC, individually have investment and voting control over the shares held by Clarus Lifesciences II, L.P. Each of Messrs. Galakatos, Henner, Liptak, Simon, Steinmetz and Wheeler disclaims beneficial ownership of all shares held by Clarus Lifesciences II, L.P. except to the extent of any pecuniary interest therein. The address of Clarus Ventures II, LLC, Clarus Lifesciences II, L.P. and their affiliates is 101 Main St. #1210, Cambridge MA 02142.
- (11) Prior to completion of this offering, consists of (i) 5,623,589 shares of common stock held by SV Life Sciences Fund IV, L.P.; (ii) 159,657 shares of common stock held by SV Life Sciences Fund IV Strategic Partners, L.P.; and (iii) 254,237 shares of common stock, held by SV Life Sciences Advisers, LLC. The general partner of SV Life Sciences Fund IV, L.P. and SV Life Sciences Fund IV Strategic Partners, L.P. is SV Life Sciences Fund IV (GP), LP. The general partner of SV Life Sciences Fund IV (GP), LP is SVLFSF IV, LLC. The members of SV Life Sciences Advisers, LLC are Kate Bingham, James Garvey, Eugene D. Hill, III, David Milne, Michael Ross, Tom Flynn and Paul LaViolette. The members of the investment committee for SVLFSF IV, LLC are Kate Bingham, James Garvey, Eugene D. Hill, III, David Milne and Michael Ross. SV Life Sciences Managers LLP is the investment manager of International Biotechnology Trust plc, the holder of 203,649 shares of common stock, and a selling stockholder. Kate Bingham, who is a member of SV Life Sciences Advisers, LLC and a member of the SVLFSF IV, LLC investment committee, is also a member of the investment committee for SV Life Sciences Managers LLP, a committee whose other members are Dr. Carl Harald Janson and Ailsa Craig. Michael Ross, Ph.D., one of our directors, is a Managing Partner of SV Life Sciences Advisers, LLC. David R. Guyer, M.D., our Chief Executive Officer and Chairman of our board of directors, and Bruce Peacock, our Chief Financial and Business Officer, are Venture Partners of SV Life Sciences Advisers, LLC. None of Dr. Ross, Dr. Guyer or Mr. Peacock exercises investment or voting control over such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of SVLFSF IV, LLC, SV Life Sciences Advisers, LLC, and their affiliates is One Boston Place, Suite 3900, Boston, MA 02108. The address of SV Life Sciences Managers LLP is 71 Kingsway, London, United Kingdom, WC2B 6ST.
- (12) Consists of (i) 3,639,902 shares of common stock; and (ii) 13,670 shares of common stock issuable upon exercise of immediately exercisable warrants, in the case of each of clauses (i) and (ii), held by HBM Healthcare Investments (Cayman) LTD. The board of directors of HBM Healthcare Investments (Cayman) Ltd. has sole voting and investment power with respect to the shares by held by such entity. The board of directors of HBM Healthcare Investments (Cayman) Ltd. is comprised of Jean-Marc Le Sieur, Richard Coles, Sophia Harris, Dr. Andreas Wicki and John Urquhart, none of whom has individual voting or investment power with respect to such shares, and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Mr. Bolte is an advisor to HBM Partners (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM Healthcare Investments (Cayman) Ltd. Mr. Bolte, a member of our board of directors, has no voting or investment power over the shares held by HBM Healthcare Investments (Cayman) Ltd., and disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for HBM Healthcare Investments (Cayman) Ltd. is Governor's Square, Suite #4-212-2, 23 Lime Tree Bay Avenue, West Bay, Grand Cayman.
- (13) Consists of (i) 6,896,819 shares of common stock; and (ii) 13,670 shares of common stock issuable upon exercise of immediately exercisable warrants, in the case of each of clauses (i) and (ii), held by Novo A/S. Novo A/S is a Danish limited liability company. The board of directors of Novo A/S, which consists of Sten Scheibye, Göran Ando, Jørgen Boe, Jeppe Christiansen, Steen Riisgaard and Per Wold-Olsen, has sole voting and investment power with respect to the shares held by Novo A/S. None of the members of the board of directors of Novo A/S has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Dyrborg, a member of our board of directors, is employed as a Senior Partner of Novo A/S.

Dr. Dyrberg disclaims beneficial ownership of shares held by Novo A/S, except to the extent of his pecuniary interest arising as a result of his employment with Novo A/S. The address for Novo A/S is Tuborg Havnevej 19, 2900 Hellerup, Denmark.

- (14) Prior to completion of this offering, International Biotechnology Trust plc holds 203,649 shares of common stock. Kate Bingham is a member of the investment committee for SV Life Sciences Managers LLP, the investment manager of International Biotechnology Trust plc, a committee whose other members are Dr. Carl Harald Janson and Ailsa Craig. Kate Bingham is also a member of the investment committee for SVLSF IV, LLC, and a member of SV Life Sciences Advisers, LLC. SV Life Sciences Advisers, LLC holds 254,237 shares of common stock. SVLSF IV, LLC is the general partner of SV Life Sciences Fund IV (GP), L.P., which is the general partner of each of SV Life Sciences Fund IV, L.P., holder of 5,623,589 shares of common stock, and SV Life Sciences Fund IV Strategic Partners, L.P., holder of 159,657 shares of common stock. The relationship between SVLSF IV, LLC, SV Life Sciences Advisers, LLC and us is further described in footnote (11) above. Kate Bingham does not exercise investment or voting control over any such shares and disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of International Biotechnology Trust plc is 71 Kingsway, London, United Kingdom, WC2B 6ST.

## DESCRIPTION OF CAPITAL STOCK

### General

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to our certificate of incorporation and the bylaws. We have filed copies of these documents with the SEC as exhibits to our registration statement of which this prospectus forms a part.

Our authorized capital stock consists of 200,000,000 shares of our common stock, \$0.001 par value per share, and 5,000,000 shares of our preferred stock, \$0.001 par value per share, all of which preferred stock is undesignated.

As of January 31, 2014, we had issued and outstanding 31,418,575 shares of our common stock held by 54 stockholders of record.

### Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of our outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

### Preferred Stock

Our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. There are not currently any shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

### Warrants

As of January 31, 2014, we had outstanding warrants to purchase 87,656 shares of our common stock at a weighted-average exercise price of \$6.32 per share, all of which were immediately exercisable.

These warrants provide for adjustments in the event of specified mergers, reorganizations, reclassifications, stock dividends, stock splits or other changes in our corporate structure.

## Options

As of January 31, 2014, we had options to purchase 3,669,651 shares of our common stock outstanding, at a weighted-average exercise price of \$15.19 per share.

## Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

### *Delaware Law*

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our stockholders that owned 15% or more of our outstanding voting stock upon the closing of our initial public offering.

### *Staggered Board; Removal of Directors*

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

### *Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations*

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by the chairman of our board of directors, our chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder

meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

### ***Super-Majority Voting***

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

### **Registration Rights**

We have entered into a third amended and restated investors' rights agreement, dated May 23, 2013, which we refer to as the investors' rights agreement, with certain holders of our common stock and warrants to purchase our common stock. Holders of a total of 19,668,672 shares of our common stock as of January 31, 2014, without giving effect to the sale of shares in this offering by the selling stockholders to the extent the underwriters exercise their option to purchase additional shares, including shares issuable upon the exercise of warrants, will have the right to require us to register these shares under the Securities Act of 1933, as amended, or Securities Act, and to participate in future registrations of securities by us, under the circumstances described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. If not otherwise exercised, the rights described below will expire five years after the closing of this offering.

#### ***Demand Registration Rights***

Beginning March 23, 2014, which is the date that is 180 days after the effective date of the registration statement for our initial public offering, subject to specified limitations set forth in the investors' rights agreement, at any time, the holders of 60% of the then outstanding shares having rights under the investors' rights agreement, which we refer to as registrable shares, may at any time demand in writing that we register all or a portion of the registrable shares under the Securities Act. We are not obligated to file a registration statement pursuant to this provision on more than two occasions, and we are not obligated to file a registration statement pursuant to this provision within 180 days of the effective date of any other registration statement that we may file.

#### ***Form S-3 Registration Rights***

In addition, at any time after we become eligible to file a registration statement on Form S-3, subject to specified limitations set forth in the investors' rights agreement, the holders of registrable shares may demand in writing that we register on Form S-3 all or a portion of the registrable shares so long as the total amount of registrable shares being registered have an aggregate offering price net of selling expenses of at least \$3 million (based on the then current market price). We are not obligated to file a Form S-3 pursuant to this provision if we have effected two or more registrations in the twelve months immediately preceding such request, and we are not obligated to file a registration statement



pursuant to this provision within 90 days of the effective date of any other registration statement that we may file.

### ***Incidental Registration Rights***

If we propose to file a registration statement under the Securities Act, other than pursuant to the demand registration rights described above, the holders of registrable shares will be entitled to notice of the registration and, subject to specified exceptions in the case of an underwritten offering, including market conditions, have the right to require us to register all or a portion of the registrable shares then held by them.

In the event that any registration in which the holders of registrable shares participate pursuant to our investors' rights agreement is an underwritten public offering, we agree to enter into an underwriting agreement containing customary representation and warranties and covenants, including without limitation customary provisions with respect to indemnification of the underwriters of such offering. Holders of registrable securities must agree to any such underwriting agreement as a condition to participation in the offering. If the total number of shares, including registrable shares, requested by holders to be included in such offering exceeds the number of shares to be sold (other than by us) that the underwriters in their reasonable discretion determine is compatible with the success of the offering, then we will be required to include in the offering only that number of such shares, including registrable shares, which we and the underwriters in their sole discretion determine will not jeopardize the success of the offering.

### ***Expenses***

Pursuant to the investors' rights agreement, we are required to pay all registration expenses, including registration and filing fees, exchange listing fees, printing expenses and accounting fees and the fees and expenses, not to exceed \$25,000, of one counsel to represent the selling stockholders, other than any underwriting discounts and commissions, that are related to any demand or incidental registration described above. The registration rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

### **NASDAQ Global Select Market**

Our common stock is listed on The NASDAQ Global Select Market under the symbol "OPHT".

## SHARES ELIGIBLE FOR FUTURE SALE

Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options or warrants and sales of shares in the public market after this offering, or the anticipation of these sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of equity securities. Our common stock is listed on The NASDAQ Global Select Market under the symbol "OPHT."

Upon the closing of this offering, we will have outstanding 33,318,575 shares of our common stock, after giving effect to the issuance by us of 1,900,000 shares of our common stock in this offering, assuming no exercise by the underwriters of their option to purchase additional shares and no exercise of options or warrants outstanding as of January 31, 2014.

Of the shares to be outstanding immediately after the closing of this offering, the 8,740,000 shares sold in our initial public offering and the 2,285,714 shares to be sold in this offering, including both the shares sold by us and any shares sold by the selling stockholders, assuming no exercise by the underwriters of their option to purchase additional shares, will be freely tradable without restriction under the Securities Act unless purchased by our "affiliates" as that term is defined in Rule 144 under the Securities Act.

Of the shares to be outstanding immediately after the closing of this offering, 694,223 additional shares of our common stock issued upon the exercise of stock options have been registered on Form S-8 or are otherwise freely tradable without restriction under the Securities Act as a result of the operation of Rule 701 thereunder, in each case, unless purchased by our "affiliates". Accordingly, these shares of our common stock will be available for sale in the open market, subject to Rule 144 volume limitations applicable to affiliates, and subject to lock-up agreements applicable to these shares.

The remaining 21,641,495 shares of our common stock outstanding after this offering, assuming no exercise by the underwriters of their option to purchase additional shares, will be "restricted securities" under Rule 144, 20,630,555 of which will be subject to the 90-day lock-up period under the lock-up agreements as described below. These restricted securities may be sold in the public market upon release or waiver of applicable lock-up agreements and only if registered or pursuant to an exemption from registration, such as Rule 144 or Rule 701 under the Securities Act.

### Rule 144

In general, under Rule 144, beginning 90 days after the date of this prospectus, any person who is not our affiliate and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell shares without restriction, subject to the availability of current public information about us. In addition, under Rule 144, any person who is not our affiliate and has not been our affiliate at any time during the preceding three months and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares immediately upon the closing of this offering without regard to whether current public information about us is available.

Beginning 90 days after the date of this prospectus, a person who is our affiliate or who was our affiliate at any time during the preceding three months and who has beneficially owned restricted securities for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 333,186 shares, immediately after this offering; and

- the average weekly trading volume of our common stock on The NASDAQ Global Select Market during the four calendar weeks preceding the filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Upon the expiration on March 23, 2014, of the 180-day lock up agreements entered into in connection with our initial public offering as described below, 2,590,478 shares of our common stock will be eligible for sale under Rule 144. Upon expiration of the 90-day lock-up agreements entered into in connection with this offering on May 12, 2014, as described below, assuming no exercise by the underwriters of their option to purchase additional shares, 19,668,672 additional shares of our common stock will be eligible for sale under Rule 144. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

#### **Rule 701**

In general, under Rule 701 of the Securities Act, any of our employees, consultants or advisors, other than our affiliates, who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement is eligible to resell these shares 90 days after the date of this prospectus in reliance on Rule 144, but without compliance with the holding period requirements of Rule 144 and without regard to the volume of such sales or the availability of public information about us. Subject to the 180-day lock-up period described below, approximately 691,681 shares of our common stock will be eligible for sale in accordance with Rule 701.

#### **Lock-Up Agreements**

##### ***Lock-Up Agreements Entered into in Connection with this Offering***

In connection with this offering, we and each of our directors and executive officers and their affiliated entities, as well as the selling stockholders, have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC, on behalf of the underwriters, we and they will not, subject to limited exceptions described in the "Underwriters" section, during the period ending 90 days after the date of this prospectus, or on May 12, 2014, either directly or indirectly:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock beneficially owned by us or them or any securities so owned convertible into or exercisable or exchangeable for common stock;
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock; or
- publicly disclose the intention to make any such offer, sale, pledge or disposition of shares of common stock.

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. Each of our directors and executive officers and their affiliated entities, as well as the selling stockholders have also agreed during such 90-day period not to make any demand for or exercise any right with respect to, the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

After giving effect to the sale of shares by the selling stockholders in this offering as a result of the underwriters exercising their option to purchase additional shares, a total of 20,731,269 outstanding shares of common stock will be subject to these lock-up agreements.

### ***Lock-Up Agreements Entered into in Connection with our Initial Public Offering***

Additionally, in connection with our initial public offering, we and each of our directors and executive officers and holders of our outstanding common stock, who collectively own 22,510,817 shares of our common stock, have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC, on behalf of the underwriters of our initial public offering, we and they will not, subject to limited exceptions described in the "Underwriters" section, during the period ending March 23, 2014, either directly or indirectly:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock beneficially owned by us or them or any securities so owned convertible into or exercisable or exchangeable for common stock;
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock; or
- publicly disclose the intention to make any such offer, sale, pledge or disposition of shares of common stock.

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. Each of our directors and executive officers and holders of our outstanding common stock have also agreed during such 180-day period not to make any demand for or exercise any right with respect to, the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

### **Registration Rights**

Upon the closing of this offering, assuming no exercise by the underwriters of their option to purchase additional shares, the holders of 20,041,266 shares of our common stock including shares issued upon conversion of our preferred stock upon completion of our initial public offering on September 30, 2013 and shares issuable upon the exercise of warrants, or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See "Description of Capital Stock—Registration Rights" for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of lock-up agreements applicable to such shares.

### **Stock Options and Form S-8 Registration Statement**

As of January 31, 2014, we had outstanding options to purchase an aggregate of 3,669,651 shares of our common stock, of which options to purchase 113,308 shares were vested. We have filed registration statements 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 the 2013 stock incentive plan and our pre-IPO stock incentive plan. See "Executive Compensation—Stock Option and Other Compensation Plans" for additional information regarding these plans. Accordingly, shares of our common stock registered under the registration statements will be available for sale in the open market, subject to Rule 144 volume limitations applicable to affiliates, and subject to any vesting restrictions and lock-up agreements applicable to these shares.

**MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S.  
HOLDERS OF COMMON STOCK**

The following is a general discussion of material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

This discussion is based on current provisions of the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation, including the Medicare contribution tax and the alternative minimum tax, that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- financial institutions;
- regulated investment companies;
- brokers or dealers in securities;
- tax-exempt organizations;
- pension plans;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- insurance companies;
- controlled foreign corporations;
- passive foreign investment companies; and
- certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other entities which are pass-through entities for U.S.

federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

**Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.**

**Dividends**

If we pay distributions on our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Disposition of Common Stock." Any such distribution would also be subject to the discussion below under the section titled "Withholding and Information Reporting Requirements—FATCA."

As discussed under "Dividend Policy," we do not expect to pay cash dividends to holders of our common stock in the foreseeable future. In the event we do pay dividends, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally, IRS Form W-8ECI). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code), subject to an applicable income tax treaty providing otherwise. Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

**Gain on Disposition of Common Stock**

A non-U.S. holder generally will not be subject to U.S. federal income tax on gain realized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and if an applicable income tax treaty so provides, the gain is attributable to a

permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, subject to an applicable income tax treaty providing otherwise, and if the non-U.S. holder is a corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

- the non-U.S. holder is a nonresident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S.-source capital losses of the non-U.S. holder, if any; or
- we are, or have been at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter), a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business.

Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes.

No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

### **Information Reporting and Backup Withholding**

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN (or other applicable Form W-8) or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading "Dividends," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

### **Federal Estate Tax**

Common stock owned or treated as owned by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax law or other treaty provides otherwise.

### **Withholding and Information Reporting Requirements—FATCA**

Recently enacted legislation, which is commonly referred to as "FATCA," will impose U.S. federal withholding tax of 30% on payments of dividends on and gross proceeds from the sale or disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Although this legislation is effective with regards to amounts paid after December 31, 2012, under final regulations issued by the U.S. Department of Treasury on January 17, 2013, and IRS Notice 2013-43 released on July 12, 2013, withholding under FATCA will only apply (1) to payments of dividends on our common stock made after June 30, 2014 and (2) to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits for such taxes.

Prospective investors should consult their own tax advisors regarding the possible impact of the FATCA rules on their investment in our common stock, and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of this 30% withholding tax under FATCA.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.



## UNDERWRITERS

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC are acting as representatives, have severally agreed to purchase, and we and the selling stockholders have agreed to sell to them, severally, the number of shares indicated below:

<u>Name</u>	<u>Number of Shares</u>
Morgan Stanley & Co. LLC	914,286
J.P. Morgan Securities LLC	914,286
Leerink Partners LLC	285,714
Stifel, Nicolaus & Company, Incorporated	171,428
Total:	<u>2,285,714</u>

The underwriters and the representatives are collectively referred to as the "underwriters" and the "representatives," respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and the selling stockholders and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' option to purchase additional shares described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of \$1.134 a share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

The selling stockholders have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 342,857 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us and the selling stockholders. These amounts are

shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional 342,857 shares of common stock from the selling stockholders.

	Per Share	Total	
		No Exercise	Full Exercise
Public offering price	\$ 31.50	\$ 71,999,991	\$ 82,799,987
Underwriting discounts and commissions to be paid by:			
Us:	\$ 1.89	\$ 3,591,000	\$ 3,591,000
The selling stockholders:	\$ 1.89	\$ 728,999	\$ 1,376,999
Proceeds, before expenses, to us	\$ 29.61	\$ 56,259,000	\$ 56,259,000
Proceeds, before expenses, to selling stockholders	\$ 29.61	\$ 11,420,992	\$ 21,572,987

The estimated offering expenses payable by us and the selling stockholders, exclusive of the underwriting discounts and commissions and the fees of counsel for the selling stockholders, which will be paid by the selling stockholders, are approximately \$800,000. We and the selling stockholders have agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority of up to \$35,000.

Our common stock is listed on The NASDAQ Global Select Market under the trading symbol "OPHT".

We, the selling stockholders, our directors and officers and our affiliated entities have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC on behalf of the underwriters, we and they will not, during the period ending 90 days after the date of this prospectus (the "restricted period"):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock beneficially owned (as such term is used in Rule 13d-3 of the Securities Exchange Act of 1934, as amended) or any securities so owned convertible into or exercisable or exchangeable for shares of common stock;
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock; or
- publicly disclose the intention to make any such offer, sale, pledge or disposition of shares of common stock.

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to us in respect of:

- a) the sale of shares to the underwriters; or
- b) the issuance by us of shares of common stock upon the exercise of an option or warrant or the conversion of a security described in this prospectus and outstanding on the date hereof, provided, that we will cause each recipient of any such issuance to execute and deliver to

Morgan Stanley & Co. LLP and J.P. Morgan Securities LLC a lock-up agreement if such recipient has not already delivered one; or

- c) any options and other awards granted under a stock incentive plan or stock purchase plan described in this prospectus (and the issuance of shares upon the exercise thereof), provided, that we will cause each recipient of any such grant to execute and deliver to Morgan Stanley & Co. LLP and J.P. Morgan Securities LLC a lock-up agreement if such recipient has not already delivered one; or
- d) the filing by us of any registration statement on Form S-8 or a successor form thereto relating to the shares of common stock granted pursuant to or reserved for issuance under a stock incentive plan or stock purchase plan described in this prospectus; or
- e) shares of common stock or other securities issued in connection with a transaction that includes a commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares of common stock issued pursuant to this clause (e) shall not exceed 5.0% of the total number of outstanding shares of common stock and (y) the recipient of any such shares of common stock and securities issued pursuant to this clause (e) during the restricted period shall enter into a lock-up agreement; or
- f) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by us regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period.

The restrictions described in the second immediately preceding paragraph do not apply to directors, officers and the selling stockholders in respect of:

- a) the sale of shares by the selling stockholders to the underwriters pursuant to the terms of the underwriting agreement; or
- b) transfers or dispositions of common stock acquired in this offering or acquired in open market transactions after the completion of this offering; or
- c) the exercise of options to purchase shares of common stock granted under a stock incentive plan or stock purchase plan which is described in this prospectus or the exercise of warrants to purchase shares of common stock described in this prospectus and outstanding as of the date of this prospectus, *provided* that the underlying common stock continues to be subject to the restrictions set forth above; or
- d) the exercise of options to purchase shares of common stock granted under a stock incentive plan or stock purchase plan described in this prospectus pursuant to an arrangement whereby we withhold shares issuable pursuant to such option in payment of the exercise price, *provided* that no filing under Section 16(a) of the Exchange Act or other public announcement, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period in connection with such option exercise, and *provided* further that the underlying common stock issued upon the exercise of such options continues to be subject to the restrictions set forth above; or
- e) transfers or dispositions to us of common stock or any security convertible into or exercisable or exchangeable for common stock pursuant to any contractual arrangement in effect on the

date of the lock-up agreement that provides for the repurchase by us of the director's, officer's or security holder's common stock or such other securities or in connection with the termination of the director's, officer's or security holder's employment with us; or

- f) transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock as a bona fide gift; or
- g) transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock by will or other testamentary document or by intestacy; or
- h) distributions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to limited partners, members, stockholders or trust beneficiaries of the directors, officers or security holders or to any investment fund or other entity controlled or managed by the directors, officers or security holders; or
- i) transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to any trust for the direct or indirect benefit of the director, officer or security holder or the immediate family of the director, officer or security holder in a transaction not involving a disposition for value,

provided that (i) in the case of any transfer or distribution pursuant to clause (f), (g), (h) or (i), each donee, transferee or distributee shall sign and deliver a lock-up letter substantially in the form of the lock-up agreement and (ii) in the case of any transfer or distribution pursuant to clause (b), (f), (h) or (i), no filing under Section 16(a) of the Exchange Act or other public announcement, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period in connection with such transfer or distribution; or

- j) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made by or on behalf of our directors, officers or security holders regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period; or
- k) transfers of shares pursuant to sales in the public market undertaken under a trading plan pursuant to Rule 10b5-1 under the Exchange Act, provided that such trading plan shall have been in effect prior to the date of this prospectus, and provided further that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding any such sales, such announcement or filing shall include a statement to the effect that sale was made pursuant to a trading plan pursuant to Rule 10b5-1 under the Exchange Act.

For purposes of the lock-up agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin.

The representatives, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

For the purposes of this offering, the representatives are waiving, solely with respect to the shares being sold in this offering, the restrictions applicable to us and the selling stockholders under the lock-up arrangements entered into in connection with our initial public offering. In connection with this offering, the lock-up arrangements described above will impact the restrictions applicable in connection

with our initial public offering such that the restricted period thereunder will continue during the period of the lock-up arrangements described above.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option to purchase additional shares. The underwriters can close out a covered short sale by exercising the option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option to purchase additional shares. The underwriters may also sell shares in excess of the option to purchase additional shares, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We, the selling stockholders and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

## Selling Restrictions

### *European Economic Area*

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

### *United Kingdom*

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 ("FSMA") received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

## LEGAL MATTERS

The validity of the shares of the common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Davis Polk & Wardwell LLP is acting as counsel for the underwriters in connection with this offering.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2012 and 2011, and for the years then ended and for the period from January 5, 2007 (Inception) to December 31, 2012, as set forth in their report. We have included our financial statements in this prospectus and elsewhere in this registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document are not necessarily complete, and, in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference to such contract, agreement or document.

You may read and copy the registration statement of which this prospectus is a part at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. You can request copies of the registration statement by writing to the Securities and Exchange Commission and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. In addition, the SEC maintains an Internet website, which is located at [www.sec.gov](http://www.sec.gov), that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. You may access the registration statement of which this prospectus is a part at the SEC's Internet website. Upon completion of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934, and we will file reports, proxy statements and other information with the SEC.

We are subject to the reporting and information requirements of the Exchange Act and, as a result, file, or will file, periodic reports, proxy statements and other information with the SEC. These periodic reports and other information are available for inspection and copying at the SEC's public reference room and the website of the SEC, in each case, referred to above. We also maintain a website at <http://www.opthotech.com> and make, or plan to make, available free of charge through this 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. The information contained on, or that can be accessed through, our website is not a part of this prospectus. The reference to our web address does not constitute incorporation by reference of the information contained in, or that can be accessed through, our website.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Index to Financial Statements**

<a href="#">Report of Independent Registered Public Accounting Firm</a>	<a href="#">F-2</a>
<a href="#">Balance Sheets as of December 31, 2012 and 2011</a>	<a href="#">F-3</a>
<a href="#">Statements of Operations for the Years Ended December 31, 2012 and 2011, and the Period From January 5, 2007 (Inception) to December 31, 2012</a>	<a href="#">F-4</a>
<a href="#">Statements of Changes in Stockholders' Deficit for the Period From January 5, 2007 (Inception) to December 31, 2012</a>	<a href="#">F-5</a>
<a href="#">Statements of Cash Flows for the Years Ended December 31, 2012 and 2011, and the Period From January 5, 2007 (Inception) to December 31, 2012</a>	<a href="#">F-6</a>
<a href="#">Notes to Financial Statements</a>	<a href="#">F-7</a>
<a href="#">Unaudited Balance Sheets as of September 30, 2013 and December 31, 2012</a>	<a href="#">F-35</a>
<a href="#">Unaudited Statements of Operations for the Nine Months Ended September 30, 2013 and 2012, and the Period From January 5, 2007 (Inception) to September 30, 2013</a>	<a href="#">F-36</a>
<a href="#">Unaudited Statements of Cash Flows for the Nine Months Ended September 30, 2013 and 2012, and the Period from January 5, 2007 (Inception) to September 30, 2013</a>	<a href="#">F-37</a>
<a href="#">Notes to Unaudited Financial Statements</a>	<a href="#">F-38</a>



**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Shareholders  
Ophthotech Corporation

We have audited the accompanying balance sheets of Ophthotech Corporation (a development stage entity) (the Company) as of December 31, 2012 and 2011, and the related statements of operations, changes in stockholders' deficit and cash flows for the years then ended and for the period from January 5, 2007 (Inception) to December 31, 2012. 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 Ophthotech Corporation at December 31, 2012 and 2011, and the results of its operations and its cash flows for the years then ended and for the period from January 5, 2007 (Inception) to December 31, 2012 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

MetroPark, New Jersey  
July 11, 2013, except as to the thirteenth paragraph of Note 17,  
as to which the date is September 9, 2013

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Balance Sheets**

(in thousands, except share and per share data)

	<u>December 31, 2012</u>	<u>December 31, 2011</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 4,304	\$ 6,396
Prepaid expenses and other current assets	44	65
Other receivables	—	1,036
Other Assets	331	—
Security deposits	158	—
Total current assets	<u>4,837</u>	<u>7,497</u>
Property and equipment, net	42	73
Other long-term assets	—	158
Total assets	<u>\$ 4,879</u>	<u>\$ 7,728</u>
<b>Liabilities, Convertible Redeemable Series A, Series A-1, Series B, Series B-1 Preferred Stock and stockholders' (deficit)</b>		
Current liabilities:		
Notes payable	11,040	—
Accrued clinical drug supplies and trial costs	1,013	1,497
Accounts payable and accrued expenses	1,391	1,626
Warrant liability	966	193
Deferred Rent	—	22
Total current liabilities	<u>14,410</u>	<u>3,338</u>
Commitments and contingencies		
Preferred Stock, Convertible and Redeemable:		
Series A—December 31, 2012 and 2011—\$0.001 par value, 73,094,000 shares authorized, 51,790,000 shares issued and outstanding (aggregate liquidation preference of \$70,564 at December 31, 2012)	69,471	65,327
Series A-1—December 31, 2012 and 2011—\$0.001 par value, 18,480,000 shares authorized, 6,000,000 shares issued and outstanding (aggregate liquidation preference of \$8,460 at December 31, 2012)	8,460	7,981
Series B—December 31, 2012—\$0.001 par value, 42,320,200 shares authorized, 30,000,000 shares issued and outstanding; December 31, 2011—\$0.001 par value, 42,000,000 shares authorized, 30,000,000 issued and outstanding (aggregate liquidation preference of \$35,868 at December 31, 2012)	35,456	33,057
Series B-1—December 31, 2012 and 2011—\$0.001 par value, 700,000 shares authorized, 500,000 shares issued and outstanding (aggregate liquidation preference of \$552 at December 31, 2012)	552	512
Total Preferred Stock, Convertible and Redeemable	<u>113,939</u>	<u>106,877</u>
Stockholders' equity deficit		
Junior Series A Convertible Preferred Stock—December 31, 2012 and 2011—\$0.001 par value, 3,000,000 shares authorized, issued and outstanding; at original issue price	3,000	3,000
Common stock—December 31, 2012—\$0.001 par value, \$0.001 par value, 155,864,851 shares authorized, 1,469,798 shares issued and outstanding; December 31, 2011—155,544,651 shares authorized, 1,451,294 shares issued and outstanding	1	1
Deficit accumulated during development stage	<u>(126,471)</u>	<u>(105,488)</u>
Total stockholders' deficit	<u>(123,470)</u>	<u>(102,487)</u>
Total liabilities and stockholders' deficit	<u>\$ 4,879</u>	<u>\$ 7,728</u>

See accompanying notes.

**OPHTHOTEC CORPORATION**  
**(A Development Stage Entity)**

**Statements of Operations**

**(in thousands, except per share data)**

	Year Ended December 31,		Period from January 5, 2007 (Inception) to December 31,
	2012	2011	2012
<b>Costs and expenses:</b>			
Research and development	\$ 6,792	\$ 13,896	\$ 74,891
General and administrative	6,889	5,738	27,349
<b>Total costs and expenses</b>	<u>13,681</u>	<u>19,634</u>	<u>102,240</u>
<b>Loss from operations</b>	(13,681)	(19,634)	(102,240)
Interest (expense) income	(507)	2	(510)
Interest and other income	—	—	481
Other loss	(374)	(30)	(371)
Change in fair value related to investor rights liability	—	—	683
Net loss before income tax benefit	(14,562)	(19,662)	(101,957)
<b>Income tax benefit</b>	—	1,029	1,327
Net loss	(14,562)	(18,633)	(100,630)
Add: accretion of preferred stock dividends	(7,063)	(6,838)	(27,155)
Net loss attributable to common stockholders	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>	<u>\$ (127,785)</u>
Net loss attributable to common stockholders per share			
Basic and diluted	<u>\$ (14.89)</u>	<u>\$ (18.27)</u>	
Weighted average common shares outstanding:			
Basic and diluted	<u>1,452</u>	<u>1,394</u>	
Unaudited basic and diluted pro forma net loss attributable to common stockholders per share	\$ (0.65)		
Unaudited basic and diluted pro forma weighted-average shares outstanding	<u>22,491</u>		

See accompanying notes.

**OPHTHOTECH CORPORATION**  
(A Development Stage Entity)

**Statements of Changes in Stockholders' Deficit**

**For the Period From January 5, 2007 (Inception) to December 31, 2012**

(in thousands)

	Junior Series A Preferred Stock		Common Stock		Additional paid-in capital	Deficit Accumulated During the Development Stage	Total
	Shares	Amount	Shares	Amount			
<b>Balance at January 5, 2007 (Inception)</b>	—	\$ —	—	\$ —	\$ —	\$ —	\$ —
Issuance of common stock	—	—	932	1	54	—	55
Issuance of Junior Series A Preferred Stock	3,000	3,000	—	—	—	—	3,000
Preferred Stock dividends	—	—	—	—	(54)	(592)	(646)
Net loss	—	—	—	—	—	(14,417)	(14,417)
<b>Balance at December 31, 2007</b>	<b>3,000</b>	<b>\$ 3,000</b>	<b>932</b>	<b>\$ 1</b>	<b>\$ —</b>	<b>\$ (15,009)</b>	<b>\$ (12,008)</b>
Issuance of common stock	—	—	97	—	11	—	11
Share-based compensation	—	—	—	—	14	—	14
Preferred Stock dividends	—	—	—	—	(25)	(2,572)	(2,597)
Net loss	—	—	—	—	—	(20,556)	(20,556)
<b>Balance at December 31, 2008</b>	<b>3,000</b>	<b>\$ 3,000</b>	<b>1,029</b>	<b>\$ 1</b>	<b>\$ —</b>	<b>\$ (38,137)</b>	<b>\$ (35,136)</b>
Issuance of common stock	—	—	107	—	13	—	13
Share-based compensation	—	—	—	—	58	—	58
Preferred Stock dividends	—	—	—	—	(71)	(4,117)	(4,188)
Net loss	—	—	—	—	—	(13,514)	(13,514)
<b>Balance at December 31, 2009</b>	<b>3,000</b>	<b>\$ 3,000</b>	<b>1,136</b>	<b>\$ 1</b>	<b>\$ —</b>	<b>\$ (55,768)</b>	<b>\$ (52,767)</b>
Issuance of common stock	—	—	290	—	39	—	39
Share-based compensation	—	—	—	—	231	—	231
Preferred Stock dividends	—	—	—	—	(270)	(5,553)	(5,823)
Net loss	—	—	—	—	—	(18,948)	(18,948)
<b>Balance at December 31, 2010</b>	<b>3,000</b>	<b>\$ 3,000</b>	<b>1,426</b>	<b>\$ 1</b>	<b>\$ —</b>	<b>\$ (80,269)</b>	<b>\$ (77,268)</b>
Issuance of common stock	—	—	25	—	4	—	4
Share-based compensation	—	—	—	—	248	—	248
Preferred Stock dividends	—	—	—	—	(252)	(6,586)	(6,838)
Net loss	—	—	—	—	—	(18,633)	(18,633)
<b>Balance at December 31, 2011</b>	<b>3,000</b>	<b>\$ 3,000</b>	<b>1,451</b>	<b>\$ 1</b>	<b>\$ —</b>	<b>\$ (105,488)</b>	<b>\$ (102,487)</b>
Issuance of common stock	—	—	19	—	2	—	2
Share-based compensation	—	—	—	—	640	—	640
Preferred Stock dividends	—	—	—	—	(642)	(6,421)	(7,063)
Net loss	—	—	—	—	—	(14,562)	(14,562)
<b>Balance at December 31, 2012</b>	<b>3,000</b>	<b>\$ 3,000</b>	<b>1,470</b>	<b>\$ 1</b>	<b>\$ —</b>	<b>\$ (126,471)</b>	<b>\$ (123,470)</b>

See accompanying notes.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Statements of Cash Flows**

(in thousands)

	Year months ended December 31,		Period from January 5, 2007 (Inception) to December 31,
	2012	2011	2012
<b>Operating Activities</b>			
Net loss	\$ (14,562)	\$ (18,633)	\$ (100,630)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation	31	32	154
Amortization of debt issuance costs	47	—	47
Accretion of debt discount	59	—	59
Non-cash change in fair value of warrant liability	366	7	382
Non-cash change in fair value of investor rights liability	—	—	(683)
Share-based compensation	640	248	1,190
Series A-1, Series B-1 and Junior Preferred Stock issued for acquired technology and licenses	—	500	9,500
Accrued interest expense converted to Series A Preferred Stock	—	—	2
Changes in operating assets and liabilities:			
Prepaid expense and other current assets	21	135	(56)
Other receivables	1,036	(738)	—
Security deposits	—	(1)	(158)
Accrued clinical drug supplies and trial costs	(484)	(822)	1,013
Accounts payable and accrued expenses	(236)	173	1,391
Deferred rent	(22)	(24)	—
Net cash used in operating activities	<u>(13,104)</u>	<u>(19,123)</u>	<u>(87,789)</u>
<b>Investing Activities</b>			
Purchase of marketable securities	—	—	(4,238)
Maturities of marketable securities	—	3,400	4,250
Purchase of property and equipment	—	(4)	(196)
Net cash provided by (used in) investing activities	<u>—</u>	<u>3,396</u>	<u>(184)</u>
<b>Financing Activities</b>			
Payment of debt issuance costs	(377)	—	(377)
Proceeds from issuance of common stock	2	4	124
Proceeds from issuance of notes payable, net	11,387	—	11,596
Proceeds from issuance of preferred stock, net	—	14,990	80,934
Net cash provided by financing activities	<u>11,012</u>	<u>14,994</u>	<u>92,277</u>
Net change in cash and cash equivalents	<u>(2,092)</u>	<u>(733)</u>	<u>4,304</u>
<b>Cash and cash equivalents</b>			
Beginning of period	6,396	7,129	—
End of period	<u>\$ 4,304</u>	<u>\$ 6,396</u>	<u>\$ 4,304</u>
<b>Supplemental disclosures of cash flow information</b>			
Accrued dividends on Series A, Series A-1, Series B and Series B-1 Preferred Stock	<u>\$ 7,063</u>	<u>\$ 6,838</u>	<u>\$ 27,155</u>
Notes payable and accrued interest converted to Series A Preferred Stock	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 212</u>

See accompanying notes.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**1. Business**

**Description of Business and Organization**

Ophthotech Corporation (the "Company" or "Ophthotech") was incorporated on January 5, 2007, in Delaware. The Company is a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the eye with a focus on developing therapeutics for age-related macular degeneration, or AMD. The Company's operations since inception have been limited to organizing and staffing the Company, acquiring rights to product candidates, business planning, raising capital and developing its product candidates. Accordingly, the Company is considered to be in the development stage as defined by Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 915, *Development Stage Entities*. The Company operates in one business segment.

Capitalized terms not otherwise defined herein are defined in their respective agreements.

**Liquidity**

The Company expects to continue to incur substantial losses over the next several years during its development phase. To fully execute its business plan, the Company will need to complete certain research and development activities and clinical trials. Further, the Company's product candidates will require regulatory approval prior to commercialization. These activities may span many years and require substantial expenditures to complete and may ultimately be unsuccessful. Any delays in completing these activities could adversely impact the Company. The Company plans to meet its capital requirements primarily through a combination of equity and debt financings, collaborations, strategic alliances and marketing distribution or licensing arrangements and in the longer term, revenue from product sales. There can be no assurance that such funds will be available, or if available, on terms favorable to the Company. The Company faces the normal risks associated with a development stage company, including but not limited to the risk that the Company's research and development activities will not be successfully completed, that adequate patent protection for the Company's technology will not be obtained, that any products developed will not obtain necessary government regulatory approval and that any approved products will not be commercially viable. In addition, the Company operates in an environment of rapid change in technology, substantial competition from pharmaceutical and biotechnology companies and is dependent upon the services of its employees and its consultants. Since inception, the Company has primarily relied upon private placements of its preferred stock and venture debt borrowings to fund operations. However, the Company's capital requirements will depend on many factors, including the success of its development and commercialization of the Company's product candidates and whether it pursues the development of additional product candidates. Even if the Company succeeds in developing and commercializing one or more of its product candidates, it may never achieve sufficient sales revenue to achieve or maintain profitability.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**2. Significant Accounting Policies**

**Basis of Presentation**

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

**Unaudited Pro Forma Information**

Unaudited pro forma net loss per share is computed using the weighted-average number of common shares outstanding and gives effect to the automatic conversion of all outstanding shares of the Company's preferred stock, into an aggregate of 21,038,477 shares of the Company's common stock, as if they had occurred during the year ended December 31, 2012 and the completion of the Company's initial public offering that occurred on September 30, 2013.

**Use of Estimates**

The preparation of financial statements and related disclosures in conformity with accounting principles generally accepted in the United States requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions that it believes are reasonable under the circumstances. The amounts of assets and liabilities reported in the Company's Balance Sheets and the amount of expenses reported for each of the periods presented are affected by estimates and assumptions, which are used for, but not limited to, the accounting for stock-based compensation and investor rights liabilities, for income taxes and accounting for research and development costs. Actual results could differ from those estimates.

**Cash and Cash Equivalents**

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. The carrying amounts reported in the Balance Sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

**Concentration of Credit Risk**

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash. The Company maintains its cash in bank accounts, which, at times, exceed federally insured limits. The Company has not recognized any losses from credit risks on such accounts during any of the periods presented. The Company believes it is not exposed to significant credit risk on cash.

**Foreign Currency Translation**

The Company maintains a bank account in a foreign currency. The Company considers the United States dollar to be the functional currency. Expenses are translated at the exchange rate on the date the expense is incurred. The effect of exchange rate fluctuations on translating foreign currency assets

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**2. Significant Accounting Policies (Continued)**

and liabilities into United States dollars is included in the Statements of Operations. Foreign exchange transaction gains and losses are included in the results of operations and are not material in the Company's financial statements.

**Financial Instruments**

The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, other receivables, accounts payable and accrued expenses, and warrants, approximate their fair value due to their short maturities. The carrying amounts of warrants approximate their fair value based upon option pricing models.

**Property and Equipment**

Property and equipment, which consist mainly of computers and other equipment, are carried at cost less accumulated depreciation. Depreciation is computed over the estimated useful lives of the respective assets, generally five to seven years, using the straight-line method.

**Research and Development**

All research and development costs are expensed as incurred. Research and development costs include costs of acquired product license and related technology rights where there is no alternative future use, prototypes used in research and development, consultant fees and amounts paid to collaborative partners. All research and development costs are charged to operations as incurred in accordance with ASC 730, *Research and Development*.

**Income Taxes**

The Company utilizes the liability method of accounting for deferred income taxes, as set forth in ASC 740-10, *Income Taxes-Overall*. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. A valuation allowance is established against deferred tax assets because the Company's management believes it cannot at this time conclude that it is more likely than not that some or all of the deferred tax assets will not be realized. The Company maintains a full valuation allowance on its deferred tax assets. Accordingly, the Company has not recorded a benefit or provision for income taxes other than for the sale of a portion of its unused New Jersey State operating loss carryforwards through a program sponsored by the State of New Jersey and the New Jersey Economic Development Authority in 2011. Since its inception, the Company has incurred losses for U.S. Federal income tax purposes, and is subject to potential tax examination from the date these losses are utilized in future tax returns.

**Share-Based Compensation**

At December 31, 2012 and 2011, the Company had one share-based employee compensation plan, which is described more fully in Note 12.



**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**2. Significant Accounting Policies (Continued)**

The Company grants stock options for a fixed number of shares to employees and non-employees with an exercise price equal to the fair value of the share at the grant date.

The Company accounts for share-based compensation in accordance with ASC 718, *Compensation—Stock Compensation*. The Company selected the Black-Scholes option pricing model as the most appropriate model for determining the estimated fair value for share-based awards. The fair value is then amortized on a straight-line basis over the requisite service periods of the awards, which is generally the vesting period. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility was calculated based on the weighted-average of historical information of similar public entities. The Company will continue to use a weighted-average approach using other similar public entity volatility information until historical volatility of the Company is relevant to measure expected volatility for future option grants.

The average expected life was determined according to the Securities and Exchange Commission ("SEC") shortcut approach as described in Staff Accounting Bulletin ("SAB") No. 110, which is the mid-point between the vesting date and the end of the contractual term.

The risk-free interest rate is based on U.S. Treasury zero-coupon bonds with a remaining term equal to the expected life assumed at the date of grant. Forfeitures are estimated based on voluntary termination behavior, as well as historical analysis of actual option forfeitures. The weighted-average assumptions used in the Black-Scholes option pricing model are as follows:

	<b>Year Ended December 31,</b>	
	<b>2012</b>	<b>2011</b>
Expected common stock price volatility	81%	79%
Risk-free interest rate	0.94% - 1.77%	1.72% - 2.38%
Expected term of options (years)	6.6	6.7
Expected annual dividend per share	\$—	\$—

**Recent Accounting Pronouncements**

In May 2011, the Financial Accounting Standards Board issued guidance that changed the requirement for presenting "Comprehensive Income" in the financial statements. The update requires an entity to present the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate but consecutive statements. The currently available option to disclose the components of other comprehensive income within the statement of stockholders' equity will no longer be available. The update is effective for fiscal years, and interim periods within those years, beginning after December 15, 2011, and should be applied retrospectively. The Company did not incur any components of comprehensive income for the periods presented and therefore did not include a statement of comprehensive income in the financial statements.

In February 2013, the FASB issued Accounting Standards Update ("ASU") 2013-02, *Comprehensive Income: Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income* ("ASU 2013-02"). ASU 2013-02 requires an entity to present the effect of certain significant

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**2. Significant Accounting Policies (Continued)**

reclassifications out of accumulated other comprehensive income on the respective line items in net income. The amendments in the ASU do not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income. ASU 2013-02 is effective prospectively for fiscal years beginning after December 15, 2012. As the ASU requires additional presentation only, there will be no impact to the Company's results of operations or financial position.

**3. Net Loss Per Common Share**

Basic and diluted net loss per common share is determined by dividing net loss applicable to common stockholders by the weighted average common shares outstanding during the period. For the periods where there is a net loss attributable to common stockholders, the outstanding shares of Preferred Stock, options, unvested restricted stock and warrants have been excluded from the calculation of diluted loss per common stockholder because their effect would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted loss per share would be the same. The following table sets forth the computation of basic and diluted net loss per share for the periods indicated.

	Year Ended December 31,	
	2012	2011
Basic and diluted net loss per common share calculation:		
Net loss	\$ (14,562)	\$ (18,633)
Accretion of preferred stock dividends	(7,063)	(6,838)
Net loss attributable to common shareholders	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>
Weighted average common shares outstanding	<u>1,452</u>	<u>1,394</u>
Net loss per share of common stock—basic and diluted	<u>\$ (14.89)</u>	<u>\$ (18.27)</u>

The following potentially dilutive securities outstanding at December, 31, 2012 and 2011, have been excluded from the computation of diluted weighted shares outstanding, as they would be anti-dilutive

	Year Ended December 31,	
	2012	2011
Redeemable convertible preferred stock	16,663	16,064
Unvested restricted stock	—	18
Options outstanding	1,344	1,113
Warrants	95	38
Total	<u>18,102</u>	<u>17,233</u>

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

#### 4. Property and Equipment

Property and equipment at December 31, 2012 and 2011, were as follows:

	<u>Useful Life</u> (Years)	<u>December 31,</u> <u>2012</u>	<u>December 31,</u> <u>2011</u>
Computer and other equipment	5	\$ 80	\$ 80
Furniture and fixtures	7	117	117
		<u>197</u>	<u>197</u>
Accumulated depreciation and amortization		(155)	(124)
Property, plant and equipment, net		<u>\$ 42</u>	<u>\$ 73</u>

For the years ended December 31, 2012 and 2011, depreciation expense was \$31 thousand and \$32 thousand, respectively.

#### 5. Financing Activities

On June 18, 2007, the Company issued promissory notes (the "Notes") totaling \$0.2 million to certain investors. The Notes carried an interest rate of 8% per annum. The Notes and related accrued interest expense were converted into Series A Preferred Stock in conjunction with the Initial Closing under the Series A Agreement described below.

On August 9, 2007, the Company entered into a Series A Preferred Stock Purchase Agreement (the "Series A Agreement") with the holders of the Notes and another investor (the "Series A Investors") which provided for the sale and issuance of the Company's Series A Preferred Stock at a price of \$1.00 per share in the following tranches: (a) 9,253,101 shares at closing (the "Initial Closing"), (b) 9,217,243 shares provided that the License Agreement described in Note 6 remained in effect within 10 days of the date of the Series A Agreement (the "First Milestone Event") and (c) 17,319,656 shares upon initiation of a Phase 1b study with respect to any of the assets acquired or licensed under the Product and Technology Agreements entered into by the Company in 2007 described in Note 6. As of December 31, 2007, the Company and the Series A Investors had completed the Initial Closing and the First Milestone Event Closing. On April 14, 2008, the Series A Agreement was amended and established the following tranches for the sale and issuance of Series A Preferred Stock to each of the Series A Investors at \$1.00 per share: (a) 6,000,000 shares provided the Collaborative License Agreement referred to above remains in effect on or before April 15, 2008 (the "Second Milestone Event"), (b) 13,000,000 shares upon initiation of a Phase 1b study with respect to any one of the assets (each such asset a "Milestone Asset") identified in the amendment to the Series A Agreement (the "Third Milestone Event"), (c) 4,319,656 shares upon initiation of a Phase 1b study with respect to a Milestone Asset other than the Milestone Asset relating to the Third Milestone Event (the "Fourth Milestone Event"), and (d) 7,000,000 shares upon initiation of a Phase 1b study with respect to a Milestone Asset other than the Milestone Asset relating to the Third Milestone Event or the Fourth Milestone Event (the "Fifth Milestone Event").

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**5. Financing Activities (Continued)**

In connection with the issuance of the Notes in June 2007, the Company issued 210,000 warrants to purchase Series A Preferred Stock with an exercise price of \$0.01 per share. The warrants expire on June 18, 2017. The warrants provide for proportionate adjustments to be made to the number of shares purchasable and the exercise price payable under the warrants in the event of certain changes to the underlying Series A Preferred Stock, including for subdivisions, combinations and stock dividends.

The Series A warrants are accounted for as a liability and are marked to market using a hybrid method of an option pricing model and a probability-weighted return methodology. The change in fair value of the Series A warrant liability is recorded within other loss. As of December 31, 2012 and 2011, the value of the Series A warrant liability was \$0.5 million and \$0.2 million, respectively, as reflected in the accompanying Balance Sheets and the change in the fair value of \$0.3 million for the year ended December 31, 2012, was recorded in the Statements of Operations.

The Company and the Series A Investors closed the Second Milestone Event on April 14, 2008, and closed the Third Milestone Event on September 19, 2008, issuing 6,000,000 and 13,000,000 shares of Series A Preferred Stock, respectively.

ASC 480, *Distinguishing Liabilities from Equity*, concluded that these rights for shares in redeemable instruments represent free-standing financial instruments and should be accounted for as liabilities under ASC 480. In accordance with ASC 480, the Company adjusts the carrying value of such rights to their estimated fair value at each reporting date. Pursuant to ASC 480, increases or decreases in the fair value of such rights are recorded in the Statements of Operations.

The estimated fair value was determined using a valuation model which considers the probability of achieving a milestone, if any, the Company's cost of capital, the estimated period the rights will be outstanding, consideration received for the instrument with the rights, the number of shares to be issued to satisfy the rights and at what price and any changes in the fair value of the underlying instrument to the rights. The recorded liability was fulfilled in May 2009 upon the exercise of the remaining rights by investors. Since such time, there have not been, and there continue not to be, any rights outstanding.

Upon the closing of an initial public offering in which all of the outstanding shares of the Company's Series A Preferred Stock and Series B Preferred Stock convert into Common Stock, the Company expects to reclassify the warrant liability to additional paid-in capital as a result of the outstanding warrants to purchase shares of Series A Preferred Stock and Series B Preferred Stock becoming, in accordance with their terms, warrants to purchase shares of Common Stock, at a weighted average exercise price of \$5.47 per share.

On September 19, 2008, the Company met the Third Milestone and issued 13,000,000 shares of Series A Preferred Stock at \$1.00 per share, resulting in net proceeds to the Company of \$13.0 million. As a result of the exercise of certain investor rights, the related liability amounting to \$0.3 million was extinguished and recorded as an increase in Preferred Stock.

On May 6, 2009, the Company met the Fourth Milestone and the Fifth Milestone and issued 11,319,656 shares of Series A Preferred Stock at \$1.00 per share, resulting in net proceeds to the

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**5. Financing Activities (Continued)**

Company of \$11.3 million. As a result of the exercise of certain investor rights, the related liability amounting to \$0.3 million was extinguished and recorded as an increase in Preferred Stock.

On October 14, 2009, the Series A Agreement was amended to allow for the sale and issuance of up to 3,000,000 additional shares of Series A Preferred Stock at an additional closing.

Consequently, on October 14, 2009, the Company issued 3,000,000 shares of Series A Preferred Stock to existing Series A stockholders at a price per share of \$1.00.

In connection with the Product and Technology Agreements entered into by the Company (see Note 6), the Company issued on August 9, 2007, 2,000,000 shares of Series A-1 Preferred Stock and 3,000,000 shares of Junior Series A Preferred Stock, with each class of Preferred Stock being recorded at a fair market value of \$1.00 per share based on the cash price paid by the Series A Investors for similar shares on the same date.

In connection with a license agreement entered into by the Company on January 4, 2008 (see Note 6), the Company issued 4,000,000 shares of Series A-1 Preferred Stock. The Series A-1 Preferred Stock was valued at \$1.00 per share. Accordingly, the Company charged \$4.0 million to research and development expense during the year ended December 31, 2008.

On December 11, 2009, the Company entered into a Series B Preferred Stock Purchase Agreement (the "Series B Agreement") with the Series A Investors and another investor (the "Series B Investors") which provided for the sale and issuance of the Company's Series B Preferred Stock at a price of \$1.00 per share in the following tranches: (a) 15,000,000 shares at closing (the "Initial B Closing") and (b) up to an additional 15,000,000 shares based on the satisfaction of the Second Closing Conditions, as defined in the Series B Agreement.

On March 1, 2011, the Company met the Second Closing Conditions, as defined in the Series B Agreement, and issued 15,000,000 shares of Series B Preferred Stock at \$1.00 per share to the existing holders of Series B Preferred Stock.

On June 20, 2012 and December 24, 2012, the Company issued secured promissory notes (the "2012 Notes") in the amount of \$7.5 million and \$4.0 million, respectively, to the same Lender. The 2012 Notes bear interest on the outstanding principal amount thereof from the Closing Date until paid in full at a rate per annum equal to the sum of (i) the greater of (A) the LIBOR Rate in effect for the applicable Interest Period and (B) 3.0%, plus (ii) the LIBOR Rate Margin adjusted on the first day of each Interest Period and fixed for the duration of each such Interest Period.

In conjunction with the secured promissory note issued on June 20, 2012, the Lender received warrants to purchase 225,000 shares of Series B Preferred Stock with an exercise price of \$1.00 per share. The warrants expire on June 20, 2022. In conjunction with the secured promissory note issued on December 24, 2012, the Lender received warrants to purchase 95,200 shares of Series B Preferred Stock with an exercise price of \$2.50 per share. The warrants expire on December 24, 2022. The warrants provide for proportionate adjustments to be made to the number of shares purchasable and

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**5. Financing Activities (Continued)**

the exercise price payable under the warrants in the event of certain changes to the underlying Series B Preferred Stock, including for subdivisions, combinations and stock dividends.

The Series B warrants are accounted for as a liability and are marked to market using a hybrid method of an option pricing model and a probability-weighted return methodology. The change in fair value of the Series B warrant liability is recorded within other loss. As of December 31, 2012, the value of the Series B warrant liability was \$0.4 million as reflected in the accompanying Balance Sheet and the change in the fair value of \$36 thousand for the year ended December 31, 2012 was recorded in the Statement of Operations.

**6. Product and Technology Agreements**

**Transferred Technology and Assumed Agreements**

Under an agreement dated July 27, 2007, the Company assumed the rights and obligations related to certain patents and know-how (the "Transferred Technology") and under certain agreements (the "Assumed Agreements") owned and/or controlled by OSI (Eyeteck), Inc. (the "Transferor") for use in the Company's activities in the research, development and commercial production of a product as defined in the agreement (the "Divestiture Agreement"). In consideration for the Transferred Technology and the Assumed Agreements, the Company made an upfront payment of \$4.0 million to the Transferor. In addition, on August 9, 2007, the Company issued to the Transferor 3,000,000 shares of Junior Series A Preferred Stock which was valued at \$1.00 per share based upon the Original Issue Price.

The Divestiture Agreement also entitles the Transferor to significant payments from the Company upon achievement of certain milestones, and to royalties on the Company's net sales of Products, as defined, and on terms set forth in the Divestiture Agreement.

The Divestiture Agreement may be terminated by either party in the event of the other party's insolvency or material breach (following a specified cure period). Unless terminated earlier by the Company or the Transferor, the Divestiture Agreement will remain in effect until the Company no longer has any financial obligations to the Transferor, after which the rights granted to the Company under the Divestiture Agreement will become perpetual and fully paid-up.

If the Company fails to satisfy its diligence obligations under the Divestiture Agreement, the Transferor may terminate the Divestiture Agreement as to particular countries with respect to which such failure has occurred, and upon such termination the Company will be obligated to transfer to the Transferor specified rights and licenses related to the product covered by the Divestiture Agreement and other related assets, and if the Company is then manufacturing such product or products, at the time of such termination, the Company may be obligated to provide transitional supply of the covered products to the Transferor, for the applicable countries.

The Assumed Agreements include a license, manufacturing and supply agreement (the "Supply Agreement") with Nektar Therapeutics, AL (the "Supplier") for a reagent linked with the active ingredient in the Company's lead product candidate. Prior to the Company's assumption of the Supply

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**6. Product and Technology Agreements (Continued)**

Agreement in 2007, the Transferor paid the Supplier approximately \$0.3 million under the Supply Agreement. The Company has paid the Supplier an aggregate of approximately \$0.8 million under the Supply Agreement, which was charged to research and development expense during the year ended December 31, 2010. Under the Supply Agreement, the Company is obligated to make certain milestone payments to the Supplier, as well as tiered royalties based on certain percentages of net sales as well as certain other payments and revenue it may receive if it licenses certain product rights to a third party. See "Note 11—Commitments and Contingencies" below.

The Supply Agreement, unless earlier terminated by either party, will expire upon the expiration of the Company's obligation to pay royalties to the Supplier on net sales of licensed products. The Supply Agreement may be terminated by either party in the event of the other party's material breach (following a specified cure period). The Company may terminate the Supply Agreement, without cause, effective at the end of a specified period following written notice to the Supplier, in which event the Company will be obligated to pay the Supplier specified termination fees and reimburse the Supplier for certain costs.

**License Agreements**

The Assumed Agreements also included an agreement with Archemix Corp. (the "Licensor") for the Company's acquisition of an exclusive royalty-bearing license over certain patent rights and technology owned and/or controlled by the Licensor (the "PDGF License") for use in the Company's activities in the research, development and commercial production of pharmaceutical products related to anti-PDGF aptamers (the "PDGF Licensed Products") as contemplated in the agreement (the "PDGF Agreement"). In addition, on July 31, 2007, the Company also entered into an agreement with the Licensor for the Company's acquisition of an exclusive royalty-bearing license over certain patent rights and technology owned and/or controlled by the Licensor (the "C5 License" and together with the PDGF License, the "Licenses") for use in the Company's activities in the research, development and commercial production of pharmaceutical products related to Zimura (the "C5 Licensed Product") as contemplated in the agreement (the "C5 License Agreement" and together with the PDGF License Agreement, the "License Agreements"). In consideration of the Licenses, the Company paid the Licensor aggregate upfront fees of \$1.0 million and, on August 9, 2007, issued to the Licensor an aggregate of 2,000,000 shares of Series A-1 Preferred Stock which was valued at \$1.00 per share based on the cash price paid by the Series A Investors for similar shares on the same date.

The Licensor is also entitled to certain regulatory milestone payments and sales milestone payments under the License Agreements.

The upfront fees totaling \$5.0 million and the value of the Junior Series A Preferred Stock and Series A-1 Preferred Stock issued totaling \$5.0 million to the Transferor and the Licensor, under the Divestiture Agreement and the License Agreement, respectively, were charged to research and development expense during the year ended December 31, 2007.

On January 4, 2008, the Company entered into an agreement with certain collaborative partners whereby the Company acquired an exclusive license to develop, market and promote products

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**6. Product and Technology Agreements (Continued)**

containing or comprising certain material upon which the collaborative partners have sole and exclusive worldwide rights to develop, market and sell. Upon the execution of the license agreement, the Company issued 4,000,000 shares of Series A-1 Preferred Stock to such partners. The Series A-1 Preferred Stock was valued at \$1.00 per share based upon the Original Issue Price. Accordingly, the Company charged research and development expense for \$4.0 million. Under the license agreement, the corroborative partners are entitled to certain development and sales milestone payments plus royalties on net sales. On May 3, 2012, the Company terminated such agreement.

On September 12, 2011, the License Agreements, were amended to cover expanded licenses for all indications outside of the ophthalmic field (as defined in the amended license agreements (the "Amended License Agreements")). Upon the execution of the Amended License Agreements, the Company issued 500,000 shares of Series B-1 Preferred Stock to the Licensor. The Series B-1 Preferred Stock was valued at \$1.00 per share based upon the Original Issue Price, which was still deemed to be fair value as of the date of this transaction. Accordingly, the Company charged research and development expense for \$0.5 million.

Unless earlier terminated, the amended PDGF Agreement will expire upon the later of 10 years after the first commercial sale in any country of the last PDGF Licensed Product and the expiration of the last-to-expire valid claim of the PDGF licensed patents that covers a PDGF Licensed Product. Unless earlier terminated, the amended C5 Agreement will expire upon the later of 12 years after the first commercial sale in any country of the last C5 Licensed Product, the expiration of the last-to-expire valid claim of the C5 licensed patents, and the date on which no further payments of sublicensing income, if any, are to be received by the Company.

Either of the Amended License Agreements may be terminated by either party in the event of the other party's material breach (following a specified cure period). The Licensor may also terminate each of the Amended License Agreements, or may convert the Company's exclusive licenses to non-exclusive licenses, if the Company challenges or assists a third party in challenging the validity or enforceability of any of the patents licensed under the applicable Amended License Agreement. The Company may terminate each of the Amended License Agreements at any time and for any or no reason effective at the end of a specified period following written notice to the Licensor.

**7. Capital Structure**

**Authorized Capital Stock**

In connection with the issuance of the notes on June 20, 2012, the Company amended its certificate of incorporation to increase the authorized shares of capital stock to the following: 155,769,651 shares of common stock and 73,094,000 shares of Series A Preferred Stock, 18,480,000 shares of Series A-1 Preferred Stock, 3,000,000 shares of Junior Series A Preferred Stock, 42,225,000 shares of Series B Preferred Stock, and 700,000 shares of Series B-1 Preferred Stock, each with a par value of \$0.001 per share.



**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**7. Capital Structure (Continued)**

In connection with the issuance of the notes on December 24, 2012, the Company amended its certificate of incorporation to increase the authorized shares of capital stock to the following: 155,864,851 shares of common stock and 73,094,000 shares of Series A Preferred Stock, 18,480,000 shares of Series A-1 Preferred Stock, 3,000,000 shares of Junior Series A Preferred Stock, 42,320,200 shares of Series B Preferred Stock, and 700,000 shares of Series B-1 Preferred Stock, each with a par value of \$0.001 per share. Such authorized amounts remained the same at December 31, 2012.

**Common Stock**

The Company's common stock has a par value of \$0.001 per share. The voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock. Each holder of common stock is entitled to vote on all matters and is entitled to one vote for each share held.

***Restricted Stock***

Of the 1,469,798 shares of common stock issued and outstanding at December 31, 2012, 677,964 shares were issued to officers of the Company. Such shares of stock are subject to restrictions on transfer and a risk of forfeiture as set forth in the respective restricted stock agreements between the Company and the owners of such shares. At December 31, 2012, all shares were 100% vested and no longer subject to forfeiture.

**Preferred Stock**

***Voting Rights***

Each holder of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock is entitled to vote on all matters and is entitled to one vote equal to the number of shares of common stock into which such shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock could be converted. Except as provided by law or by the other provisions of the Certificate of Incorporation, holders of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock vote together with the holders of common stock as a single class.

The Junior Series A Preferred Stock is non-voting and is not entitled to receive notice of, or vote at, any meetings of the stockholders of the Company.

***Dividend Rights***

The holders of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock, in preference to the holders of common stock, are entitled to receive dividends as described below. Such dividends accrue from day to day, whether or not declared and are cumulative. The dividends are payable only when, as and if declared by the Board of Directors. No

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**7. Capital Structure (Continued)**

dividends were declared for the years ended December 31, 2012 and 2011, or for the period from January 5, 2007 (inception) to December 31, 2012.

For any shares of Series A Preferred Stock and Series A-1 Preferred Stock outstanding as of the Series B Original Issue Date (as defined in the Series B Purchase Agreement), during the period from and after the issuance of each such share through but excluding the Series B Original Issue Date, cash dividends accrued with respect to such shares at a rate of \$0.08 per share. From and after the Series B Original Issue Date, cash dividends continue to accrue with respect shares of Series A Preferred Stock and Series A-1 Preferred Stock that were outstanding as of the Series B Original Issue Date at a rate of \$0.04 per share per annum.

For any shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock or Series B-1 Preferred Stock issued on or after the Series B Original Issue Date, during the period from and after the issuance of each such share, cash dividends accrue with respect to each outstanding share at a rate of \$0.04 per share per annum.

For all outstanding shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock, during the period from and after the later of the Series B Original Issue Date or the issuance of each such share, stock dividends accrue with respect to each outstanding share at a rate of 0.04 of a share per annum.

The dividend rights of the holders of Junior Series A Preferred Stock are subject to and qualified by the rights, powers and preferences of the holders of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock.

***Liquidation Preference of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock***

The liquidation rights of the holders of Junior Series A Preferred Stock are subject to and qualified by the rights, powers and preferences of the holders of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock.

Upon the liquidation of the Company, before any distribution shall be made to the holders of the Junior Series A Preferred Stock or common stock, the holders of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock, are entitled to be paid out of the assets of the Company, for each outstanding share and for each share accrued as stock dividends an amount equal to the original issue price of one dollar (the "Series A Original Issue Price", the "Series A-1 Original Issue Price", the "Series B Original Issue Price", or the "Series B-1 Original Issue Price", as applicable) plus any accrued cash dividends unpaid, whether or not declared, together with any other dividends declared but unpaid (the "Series A Preferential Payment Amount", the "Series A-1 Preferential Payment Amount", the "Series B Preferential Payment Amount", or the "Series B-1 Preferential Payment Amount", as applicable). The holders of the Junior Series A Preferred Stock then outstanding are then entitled to be paid out of the assets of the Company, before any distribution to the holders of the Company's common stock, an amount equal to the original issue price of one dollar

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**7. Capital Structure (Continued)**

plus any dividends declared but unpaid (the "Junior Series A Preferred Stockholders Preferential Payment Amount").

After the payment of the Series A, Series A-1, Series B, Series B-1 and Junior Series A Preferential Payment Amounts, the remaining assets shall be distributed pro rata based on the number of shares to the holders of the Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock (after giving effect to the payment of any accrued stock dividends to the holders of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock) and common stock as if the Series A Preferred Stock, the Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock had been converted to common stock immediately prior to such dissolution, liquidation or winding up of the Company (as-if-converted basis), provided however that (i) if the Series A Preferential Payment Amount per share plus the payment received after the pro rata distribution or Series A-1 Preferential Payment Amount per share plus the payment received after the pro rata distribution, as the case may be, exceeds two times the Series A Original Issue Price or the Series A-1 Original Issue Price, as applicable (the "Series A Maximum Participation Amount"), the amount such holder of the Series A Preferred Stock or Series A-1 Preferred Stock shall receive shall be the greater of (a) the Series A Maximum Participation Amount or (b) the amount such holder of Series A Preferred Stock and Series A-1 Preferred Stock would receive on an as-if-converted basis, (ii) if the Series B Preferential Payment Amount per share plus the payment received after the pro rata distribution, exceeds 2.65 times the Series B Original Issue Price (the "Series B Maximum Participation Amount"), the amount such holder of the Series B Preferred Stock and Series B-1 Preferred Stock shall receive shall be the greater of (a) the Series B Maximum Participation Amount or (b) the amount such holder of Series B Preferred Stock and Series B-1 Preferred Stock would receive on an as-if-converted basis.

Under the Company's certificate of incorporation, any merger, acquisition or consolidation involving the Company, or the sale, lease, transfer, exclusive license or other disposition in a single transaction or series of related transactions of all or substantially all of the assets of the Company that would have resulted in a change in control of the Company, shall be considered a liquidation event ("Deemed Liquidation Event"), unless the holders of at least a majority of the outstanding shares of Series A Preferred Stock and holders of at least 60% of the outstanding shares of Series B Preferred Stock elect otherwise. Because in a Deemed Liquidation Event, the holders of shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock retain their preferential rights as described above, the Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock have been presented outside of stockholders' deficit in the accompanying Balance Sheets. In a Deemed Liquidation Event, the Junior Series A Preferred Stockholder is treated the same as common stock.

***Optional Conversion***

Subject to and in compliance with the provisions of the Certificate of Incorporation, each share of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock, and Junior Series A Preferred Stock are convertible, at the option of the holder

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**7. Capital Structure (Continued)**

thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of common stock as is determined by dividing the Series A, Series A-1, Series B and Series B-1 Original Issue Price by the Series A, Series A-1, Series B and Series B-1 Conversion Price in effect at the time of conversion. The Series A, Series A-1, Series B and Series B-1 Conversion Price is initially equal to \$1.00. Such respective initial conversion prices, and the rate at which shares of respective classes of Preferred Stock may be converted into shares of common stock, are subject to adjustment as provided in the Certificate of Incorporation. Immediately prior to an optional conversion, all accrued stock dividends, accrued but unpaid, whether or not declared, shall be deemed issued in respect of the shares of preferred stock.

***Adjustment for Stock Splits and Combinations***

If the Company shall effect a stock split or combination with respect to the common stock, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price and Series B-1 Conversion Price shall be proportionately adjusted so that the number of shares of common stock issuable on conversion of each outstanding share of the relevant series is increased or decreased in proportion to the corresponding increase or decrease in the aggregate number of shares of common stock outstanding as a result of the stock split or combination, as applicable.

Any such adjustment becomes effective at the close of business on the date the stock split or combination becomes effective.

***Mandatory Conversion***

All outstanding shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock and Junior Series A Preferred Stock are subject to automatic conversion into shares of common stock, at the then effective applicable conversion rate, upon the closing of an underwritten public offering of shares of common stock to the public at a specified minimum price per share (subject to adjustment as a result of any stock dividend, stock split, combination or similar recapitalization of the common stock), resulting in at least \$40.0 million of proceeds, net of underwriting discount and commissions, to the Company. In addition, (a) all outstanding shares of Series A Preferred Stock and Series A-1 Preferred Stock are subject to conversion into shares of common stock, at the then effective applicable conversion rate at such date and time, or upon the occurrence of such event as may be, specified by vote or written consent of the holders of at least majority of the then outstanding shares of Series A Preferred Stock and (b) all outstanding shares of Series B Preferred Stock and Series B-1 Preferred Stock are subject to conversion into shares of common stock, at the then effective applicable conversion rate at such date and time, or upon the occurrence of such event as may be, specified by vote or written consent of the holders of at least 60% of the then outstanding shares of Series B Preferred Stock. Immediately prior to a mandatory conversion, all accrued stock dividends, accrued but unpaid, whether or not declared, shall be deemed issued in respect to the shares of preferred stock.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**7. Capital Structure (Continued)**

In the event that any holder of shares of Series A Preferred Stock or Series B Preferred Stock does not participate in a qualified financing (defined as any transaction involving the issuance or sale of additional shares of common stock after the Series B Original Issue Date that would result in the reduction of the Series B Conversion Price pursuant to the terms of the Certificate of Incorporation or any bridge financing, unless the holders of at least a majority of the Series A Preferred Stock and at least 60% of the Series B Preferred Stock elect that such transaction not be treated as a qualified financing) by purchasing, in the aggregate, such holder's pro rata amount, then each share of Series A Preferred Stock and Series B Preferred Stock held by such holder shall automatically, and without any further action on the part of such holder, be converted into one share of common stock.

**8. Income Taxes**

The Company utilizes the liability method of accounting for deferred income taxes. Under this method, deferred tax liabilities and assets are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. A valuation allowance is established against deferred tax assets because, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company's policy is to record interest and penalties on uncertain tax positions as income tax expense. As of December 31, 2012, the Company does not believe any material uncertain tax positions are present. Accordingly, interest and penalties have not been accrued due to an uncertain tax position and the fact the Company has reported tax losses since inception.

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. A reconciliation of the statutory U.S. federal rate to the Company's effective tax rate is as follows:

	<b>For the years ended</b>	
	<b>December 31,</b>	
	<b>2012</b>	<b>2011</b>
Percent of pre-tax income:		
U.S. federal statutory income tax rate	35.0%	35.0%
State taxes, net of federal benefit	0.0%	3.4%
Permanent items	(1.0)%	(0.6)%
Research and development credit	1.0%	0.7%
Change in valuation allowance	(35.0)%	(33.3)%
Effective income tax rate	<u>0.0%</u>	<u>5.2%</u>

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

(tabular dollars and shares in thousands, except per share data)

December 31, 2012

**8. Income Taxes (Continued)**

Significant components of the Company's deferred tax assets/liabilities for 2012 and 2011 consist of the following:

	December 31,	
	2012	2011
<b>Deferred tax assets/liabilities</b>		
Federal net operating loss carryforwards	\$ 29,464	\$ 24,325
State and local net operating loss carryforwards	4,825	3,487
License and technology payments	5,566	6,099
Share-based compensation	476	220
Depreciation	(11)	(27)
Federal research and development credit carryforwards	1,562	1,417
State research and development credit carryforwards	781	708
Deferred income tax assets	42,663	36,229
Valuation allowance	(42,663)	(36,229)
Net deferred tax assets (liabilities)	—	—

In assessing the reliability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Due to the Company's history of losses, and lack of other positive evidence, the Company has determined that it is more likely than not that its deferred tax assets will not be realized, and therefore, the deferred tax assets are fully offset by a valuation allowance at December 31, 2012 and 2011.

The following table summarizes carryforwards of net operating losses and tax credits as of December 31, 2012:

	Amount	Expiration
Federal net operating losses	\$ 84,200	2032
Research and development credits	\$ 1,600	2032

The federal, state, and local net operating loss carryforwards will start to expire in 2027.

For the year ended December 31, 2011, the Company sold a portion of its unused New Jersey State operating loss carryforwards through a program sponsored by the State of New Jersey and the New Jersey Economic Development Authority. On January 24, 2012, the Company received cash proceeds of \$1.0 million, net of fees of \$34 thousand, resulting in the recognition of a tax benefit for the year ended December 31, 2011. Such amount is reflected in other receivables in the accompanying Balance Sheet as of December 31, 2011. The Company did not participate in the program during 2012.

Utilization of the net operating losses 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 due to changes in ownership of the Company that have occurred previously or that could occur in the

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**8. Income Taxes (Continued)**

future. These ownership changes may limit the amount of net operating losses and general business tax credits carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period.

The Company believes that it had undergone at least one ownership change during 2007, but has not completed a study to determine the impact of the ownership change on its ability to utilize the aforementioned carryforwards. The amount of net operating losses and credits incurred during the year of ownership change amounted to \$4.5 million and \$0.1 million, respectively. As such, the net operating losses and credits at the time of the ownership change would have been no greater than \$4.5 million and \$0.1 million, respectively. Accordingly, the Company's ability to utilize its carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. Therefore, the Company may not be able to take full advantage of these carryforwards for federal or state income tax purposes. No other ownership changes have been identified in any years subsequent to 2007.

**9. Operating Leases**

The Company leases office spaces located in Princeton, New Jersey and New York, New York under operating lease arrangements. The Company's Princeton, New Jersey office space lease expires on September 30, 2013, whereas the Company's New York, New York office space lease expired on September 30, 2012. Effective October 1, 2012, the Company's lease for the New York office is month-to-month. Future minimum rental commitments under noncancelable operating leases in effect as of December 31, 2012, are as follows:

2013	\$ 90
Thereafter	—
<b>Total</b>	<b><u>\$ 90</u></b>

Rent expense is calculated on the straight-line basis and amounted to \$0.4 million for each of the years ended December 31, 2012 and 2011, respectively. As of December 31, 2011, the excess of the amount recognized as expense over the amount paid amounted to \$22 thousand and was recorded as a deferred rent liability in the accompanying Balance Sheets. As of December 31, 2012, there was no deferred rent liability.

**10. Security Deposits**

Security deposits consist of amounts required to secure the Company's performance of its obligations under the operating leases for its New Jersey and New York offices. As of December 31, 2012, such amount was approximately \$0.2 million and reflected in the Balance Sheet as Security Deposits. As of December 31, 2011, such amount was approximately \$0.2 million and reflected in the Balance Sheet as Other long-term assets.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

(tabular dollars and shares in thousands, except per share data)

December 31, 2012

**11. Commitments and Contingencies**

From time to time, the Company may be subject to claims or liabilities that arise in the ordinary course of its business activities.

The following table summarizes the Company's contractual obligations as of December 31, 2012:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(\$ in thousands)				
Operating Leases(1)	\$ 90	\$ 90	\$ —	\$ —	\$ —
Debt Obligations(2)	11,500	2,889	8,611	—	—
<b>Total(3)</b>	<b>\$ 11,590</b>	<b>\$ 2,979</b>	<b>\$ 8,611</b>	<b>\$ —</b>	<b>\$ —</b>

- (1) Operating lease obligations reflect our obligation to make payments in connection with the lease for the Company's office space.
- (2) Debt obligations reflect the Company's obligation to make monthly principal payments under the loan and security agreement for its venture facility that the Company entered into in June 2012 and amended in December 2012 and in March 2013.
- (3) This table does not include (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known with certainty, (b) any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known and (c) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above.

Under various agreements, the Company will be required to pay royalties and make milestone payments. These agreements include the following:

- Under an acquisition agreement with OSI (Eyetechn), Inc. for rights to particular anti-PDGF aptamers, including Fovista, the Company is obligated to pay to OSI Pharmaceuticals one-time payments of \$12.0 million in the aggregate upon marketing approval in the United States and the European Union, of a covered anti-PDGF product. The Company is also obligated to pay to OSI Pharmaceuticals a royalty at a low single-digit percentage of net sales of any covered anti-PDGF product it successfully commercializes.
- Under a license agreement with Archemix Corp., or Archemix, with respect to pharmaceutical products comprised of or derived from anti-PDGF aptamers, the Company is obligated to make payments to Archemix of up to an aggregate of \$16.5 million in additional payments if it achieves specified clinical and regulatory milestones with respect to Fovista, including a payment of \$2.5 million that will be triggered by the initiation of its planned Phase 3 clinical program of Fovista. In addition, the Company is obligated to make payments to Archemix up to an aggregate of \$3.0 million if it achieves specified commercial milestones with respect to Fovista and, for each other anti-PDGF aptamer product that it may develop under the agreement, up to an aggregate of approximately \$18.8 million if it achieves specified clinical and regulatory milestones and up to an aggregate of \$3.0 million if it achieves specified commercial milestones. From inception through December 31, 2012, the Company has made approximately \$2.3 million in payments resulting from this agreement.
- Under a license agreement with Archemix with respect to pharmaceutical products derived from anti-C5 aptamers, for each anti-C5 aptamer product that the Company may develop under the



**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**11. Commitments and Contingencies (Continued)**

agreement, including Zimura, it is obligated to make payments to Archemix of up to an aggregate of \$57.5 million if it achieves specified development, clinical and regulatory milestones and, as to all anti-C5 products under the agreement collectively, up to an aggregate of \$22.5 million if it achieves specified commercial milestones. From inception through December 31, 2012, the Company has made \$2.0 million in payments resulting from this agreement.

- Under a license, manufacturing and supply agreement with Nektar Therapeutics, or Nektar, for specified pegylation reagents used to manufacture Fovista, the Company is obligated to pay Nektar up to an aggregate of \$5.5 million in additional payments if it achieves specified clinical and regulatory milestones, including a payment of \$1.0 million that will be triggered by the initiation of its planned Phase 3 clinical program of Fovista. In addition, the Company is obligated to pay Nektar an additional payment of \$3.0 million if it achieves a specified commercial sale milestone. The Company is obligated to pay Nektar tiered royalties at low to mid single-digit percentages of net sales of any licensed product it successfully commercializes, with the royalty percentage determined by its level of licensed product sales, the extent of patent coverage for the licensed product and whether it has granted a third party commercialization rights to the licensed product. The Company has agreed to pay Nektar a low double-digit percentage of any upfront payment it receives in connection with granting any third party commercialization rights to a licensed product, less certain milestone events the Company has previously paid to Nektar, and a higher double-digit percentage of other specified amounts it receives in connection with any such commercialization agreement, subject to agreed minimum and maximum amounts. From inception through December 31, 2012, the Company has made approximately \$0.8 million in payments resulting from this agreement.

We also have employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

In addition, in the course of normal business operations, we have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. We can elect to discontinue the work under these agreements at any time. We could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require upfront payments and even long-term commitments of cash.

**12. Stock Option and Compensation Plans**

The Company adopted its 2007 Stock Incentive Plan (the "Plan") for employees and consultants for the purpose of advancing the interests of the Company stockholders by enhancing its ability to attract, retain and motivate persons who are expected to make important contributions to the Company.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

(tabular dollars and shares in thousands, except per share data)

December 31, 2012

**12. Stock Option and Compensation Plans (Continued)**

The following table sets forth the activity under the Company's Option Plan:

	Shares Available for Grant	Number of Shares	Options Outstanding	
			Weighted- Average Exercise Price	Weighted- Average Fair Value Per Share
	(shares in thousands)			
Balance, December 31, 2010	260	953		
Increase to Option pool	—	—		
Options granted	(184)	184	\$ 1.65	\$ 1.18
Options exercised	—	(24)	\$ 0.17	\$ 0.12
Options forfeited	—	—		
Balance, December 31, 2011	76	1,113		
Increase to Option pool	314	—		
Options granted	(250)	250	\$ 3.12	\$ 1.65
Options exercised	—	(18)	\$ 0.12	\$ 1.59
Options forfeited	1	(1)		
Balance, December 31, 2012	141	1,344	\$ 1.65	\$ 1.30

The aggregate intrinsic value of options outstanding as of December 31, 2012 was \$11.3 million. The aggregate intrinsic value is calculated as the difference between the Company's estimated stock price of \$10.03 on December 31, 2012, and the exercise price of the option, multiplied by the number of options.

In determining this exercise price, the Company considered input from management and the valuation of the common stock. The Company determined the value of common stock based on the probability weighted expected return method, or PWERM, described in the AICPA Practice Aid. The Company considered but did not use the market approach because the early stage of its development and the absence of clinical trial data from the lead candidate made comparisons to public companies difficult. Similarly, the Company did not use the income approach because of the uncertain outcomes of the ongoing and future clinical trials. Under a PWERM analysis, the value of a company's common stock is estimated based upon an analysis of current and future enterprise values, assuming three possible liquidity scenarios: an initial public offering ("IPO"), a recapitalization of the company and a sale of the company. After considering the various potential liquidity scenarios and the likely timing, the Company used a pre-money enterprise value assigned to each scenario based on recent trends in capital markets. To determine the price per share of the common stock, the Company divided the resulting enterprise value for each liquidity scenario by the number of common shares that would be outstanding under each scenario. The common stock price for each scenario was then assigned a probability based on management's estimates.

***Employees Options***

Employee options outstanding at December 31, 2012 and 2011, had a weighted average remaining contractual life of approximately 7.8 and 8.3 years, respectively. As of December 31, 2012, the number

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**12. Stock Option and Compensation Plans (Continued)**

of vested and non-vested shares granted was 1,158,456 and 465,700, respectively, at a weighted average exercise price of \$1.36 per share. As of December 31, 2011, the number of vested and non-vested shares granted was 949,259 and 519,976, respectively, at a weighted average exercise price of \$1.18 per share.

In general, the options vest at 25% of the original number of shares after one year of service with the Company. Thereafter, the remaining 75% vest at 2.08% per month over the next three years. Only vested options can be exercised and can be exercised up to ten years from the grant date. Upon change in control of the Company, all unvested options vest immediately. Vested options can be exercised up to ten years from the grant date.

For the years ended December 31, 2012 and 2011, the Company incurred share-based compensation expense in the amounts of \$0.5 million and \$0.2 million, respectively. For the period from January 5, 2007 (inception) to December 31, 2012, share-based compensation expense was \$0.9 million. As of December 31, 2012, there was \$0.6 million of total unrecognized share-based compensation. Such costs are expected to be recognized over a weighted average period of approximately 2.7 years.

On December 30, 2012, the Board of Directors modified the vesting terms related to an employee's unvested shares so that all unvested shares immediately vested as of the employee's death on October 29, 2012. As a result of the modification, the Company recorded an additional \$0.3 million in share-based compensation expense.

***Non-employee Options***

Non-employee options outstanding at December 31, 2012 and 2011 had a weighted average remaining contractual life of approximately 6.9 and 7.0 years, respectively. As of December 31, 2012, the number of vested and non-vested shares granted was 183,808 and 55,304, respectively, at a weighted average exercise price of \$0.59 per share. As of December 31, 2011, the number of vested and non-vested shares granted was 161,082 and 31,963, respectively, at a weighted average exercise price of \$0.41 per share.

For the years ended December 31, 2012 and 2011, the Company granted a total of 41,946 and 3,812 stock options, respectively, to its Consultants. In general, the grants vest ratably over a three-year period and have a life of 10 years. Stock options issued to nonemployees uses the fair value method of accounting as prescribed under ASC 505, *Equity-Based Payments to Non-Employees*, and are periodically revalued as the options vest and are recognized as expense over the related service period.

For the years ended December 31, 2012 and 2011, the Company incurred share-based compensation expense in the amount of \$0.1 million for each respective year. As of December 31, 2012, there was \$0.4 million of total unrecognized share-based compensation, respectively. Such costs are expected to be recognized over a weighted average period of approximately 3.0 years.

**13. Employee Benefit Plan**

Through a professional employer organization, the Company maintains a defined contribution 401(k) plan available to employees. Employee contributions are voluntary and are determined on an

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**13. Employee Benefit Plan (Continued)**

individual basis, limited by the maximum amounts allowable under federal tax regulations. The Company does not match any of the employee contributions.

**14. Fair Value Measurements**

ASC 820, *Fair Value Measurements and Disclosures*, defines fair value as the price that would be received to sell an asset, or paid to transfer a liability, in the principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value standard also establishes a three-level hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The valuation hierarchy is based upon the transparency of inputs to the valuation of an asset or liability on the measurement date. The three levels are defined as follows:

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market.
- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability.
- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability.

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis at December 31, 2012.

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>Assets</b>			
Investments in money markets*	\$ 524	\$ —	\$ —
<b>Liabilities</b>			
Series A Warrant Liability	\$ —	\$ —	\$ 523
Series B Warrant Liability	\$ —	\$ —	\$ 443

\* Investments in money markets are reflected in cash and cash equivalents in the accompanying Balance Sheets.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**14. Fair Value Measurements (Continued)**

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis at December 31, 2011.

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>Assets</b>			
Investments in money markets*	\$ 4,874	\$ —	\$ —
<b>Liabilities</b>			
Series A Warrant Liability	\$ —	\$ —	\$ 193

\* Investments in money markets are reflected in cash and cash equivalents in the accompanying Balance Sheets.

**Level 3 Valuation**

The warrant liability is recorded in its own line item on the Company's Balance Sheets. The warrant liability is marked-to-market each reporting period with the change in fair value recorded to other loss in the Statement of Operations until the warrants are exercised, expire or other facts and circumstances lead the warrant liability to be reclassified as an equity instrument.

The fair value of the warrant liability is estimated using a hybrid method that integrates a scenario based PWERM model and an option pricing model. The three scenarios used for the PWERM model include dissolution, acquisition and an initial public offering. The variables used in the models include the expected volatility based on similar public companies, the preferred stock value, risk free interest rates and the estimated time to a liquidity event. The range of risk free interest rates and volatility included in each model are predicated on the length of time to reach the expected outcome employed in each scenario. The range of fair value used in each model relates to the enterprise value calculated for each of the expected outcome scenarios. For example, the enterprise value for a dissolution scenario is significantly less than the enterprise value for an initial public offering.

The significant assumptions used in preparing the option pricing model for valuing the Company's warrants for the Series A preferred shares as of December 31, 2011, include (i) volatility (64.7%), (ii) risk free interest rate (0.06% - 0.12%), (iii) strike price (\$0.01), (iv) fair value of Series A preferred shares (\$0.18 - \$1.51), (v) expected life (0.5 years to 1.0 years) and (vi) expected outcome probability weighting of three outcome scenarios: merger (50%); technology sale (20%) and dissolution (30%).

The significant assumptions used in preparing the option pricing model for valuing the Company's warrants for the Series A preferred shares as of December 31, 2012, include (i) volatility (47.2% - 85.3%), (ii) risk free interest rate (0.05% - 0.62%), (iii) strike price (\$0.01), (iv) fair value of Series A preferred shares (\$1.22 - \$4.34), (v) expected life (0.25 years to 4.5 years) and (vi) expected outcome probability weighting of three outcome scenarios: merger (65%); dissolution (20%) and an initial public offering (15%).

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**14. Fair Value Measurements (Continued)**

The significant assumptions used in preparing the option pricing model for valuing the Company's warrants for the Series B preferred shares as of December 31, 2012, include (i) volatility (47.2% - 80.1%), (ii) risk free interest rate (0.05% - 1.68%), (iii) strike prices (\$1.00 - \$2.50), (iv) fair value of Series B preferred shares (\$1.18 - \$4.22), (v) expected life (0.25 years to 9.5 years) and (vi) expected outcome probability weighting of three outcome scenarios: merger (65%); dissolution (20%) and an initial public offering (15%).

The table presented below is a summary of changes in the fair value of the Company's Level 3 valuation for the Series A and Series B warrant liabilities for periods ending December 31, 2012 and 2011:

	Level 3	
	Series A Warrant Liability	Series B Warrant Liability
Balance at December 31, 2010	\$ 186	\$ —
Change in fair value of warrant liability	7	—
Balance at December 31, 2011	193	—
Warrants issued in connection with venture debt facility	—	407
Change in fair value of warrant liability	330	36
Balance at December 31, 2012	<u>\$ 523</u>	<u>\$ 443</u>

No other changes in valuation techniques or inputs occurred during the year ended December 31, 2012. No transfer of assets between Level 1 and Level 2 of the fair value hierarchy occurred during the year ended December 31, 2012.

**15. Notes Payable**

On June 20, 2012, and December 24, 2012, the Company issued secured promissory notes (the "2012 Notes") in the amount of \$7.5 million and \$4.0 million, respectively, to the same Lender. The 2012 Notes bear interest on the outstanding principal amount thereof from the Closing Date until paid in full at a rate per annum equal to the sum of (i) the greater of (A) the LIBOR Rate in effect for the applicable Interest Period and (B) 3.0%, plus (ii) the LIBOR Rate Margin adjusted on the first day of each Interest Period and fixed for the duration of each such Interest Period.

**OPHTHOTECH CORPORATION**  
(A Development Stage Entity)

**Notes to Financial Statements (Continued)**

(tabular dollars and shares in thousands, except per share data)

December 31, 2012

**16. Selected Quarterly Financial Information (unaudited)**

The following is a summary of the quarterly results of operations for the years ended December 31, 2012 and 2011 (in thousands, except per share amounts):

	2012			
	March 31	June 30	September 30	December 31
Revenues	\$ —	\$ —	\$ —	\$ —
Research and development	1,621	1,578	1,595	1,998
General and administrative	1,388	1,694	2,259	1,548
Loss from operations	(3,009)	(3,272)	(3,854)	(3,546)
Net loss attributable to common shareholders	\$ (4,765)	\$ (5,326)	\$ (5,928)	\$ (5,606)
Basic and diluted earnings per common share	\$ (3.31)	\$ (3.68)	\$ (4.07)	\$ (3.82)

	2011			
	March 31	June 30	September 30	December 31
Revenues	\$ —	\$ —	\$ —	\$ —
Research and development	3,531	3,316	3,627	3,422
General and administrative	1,194	1,396	1,321	1,827
Loss from operations	(4,725)	(4,712)	(4,948)	(5,249)
Net loss attributable to common shareholders	\$ (6,213)	\$ (6,441)	\$ (6,765)	\$ (6,052)
Basic and diluted earnings per common share	\$ (4.56)	\$ (4.65)	\$ (4.81)	\$ (4.27)

**17. Subsequent Events**

On March 15, 2013, the Company issued a secured promissory note in the amount of \$1.5 million (the "2013 Note") to the holder of the 2012 Notes. The 2013 Note carries interest at a rate per annum equal to the sum of (i) the greater of (A) the LIBOR Rate in effect for the applicable Interest Period and (B) 3.0%, plus (ii) the LIBOR Rate Margin adjusted on the first day of each Interest Period and fixed for the duration of each such Interest Period.

In conjunction with the issuance of the 2013 Note, the Lender received warrants to purchase 35,700 shares of Series B Preferred Stock with an exercise price of \$2.50 per share. The warrants expire on March 15, 2023 and provide for proportionate adjustments to be made to the number of shares purchasable and the exercise price payable under the warrants in the event of certain changes to the underlying Series B Preferred Stock, including for subdivisions, combinations and stock dividends.

On April 25, 2013, the Company amended its certificate of incorporation to increase the authorized shares of capital stock to the following: 187,918,509 shares of common stock and 73,094,000 shares of Series A Preferred Stock, 18,480,000 shares of Series A-1 Preferred Stock, 3,000,000 shares of Junior Series A Preferred Stock, 42,391,600 shares of Series B Preferred Stock, 700,000 shares of Series B-1 Preferred Stock, and 28,000,000 shares of Series C Preferred Stock, each with a par value of \$0.001 per share.

On May 23, 2013, the Company entered into a Purchase and Sale Agreement (the "Purchase and Sale Agreement") with Novo A/S, providing for the Company to sell, and Novo A/S to purchase, the right, title, and interest in a portion of the revenues from the sale of (a) Fovista, (b) Fovista-Related

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**17. Subsequent Events (Continued)**

Products, and (c) Other Products (as defined in the Purchase and Sale Agreement), calculated as low to mid single-digit percentages of net sales.

The Purchase and Sale Agreement provides for up to three separate purchases for a purchase price of \$41.7 million each, at a first, second and third closing, for an aggregate purchase price of \$125.0 million. In each purchase, Novo A/S acquires rights to a low single-digit percentage of net sales. Following the purchase of all royalty interests under the Purchase and Sale Agreement, Novo A/S will have a right to receive royalties on net sales at a mid-single digit percentage.

On May 23, 2013, the Company received cash proceeds of \$41.7 million for the royalty entitlement related to the first closing on the date of the Purchase and Sale Agreement. Receipt of cash proceeds for the second and third purchases is contingent upon certain triggers and conditions detailed in the Purchase and Sale Agreement, none of which occurred prior to the Company's initial public offering.

The royalty payment period covered by the Purchase and Sale Agreement begins on commercial launch and ends, on a product by product and country by country basis, on the latest to occur of (i) the 12th anniversary of the commercial launch, (ii) the expiration of certain patent rights and (iii) the expiration of the regulatory exclusivity for each product in each country.

Under the terms of the Purchase and Sale Agreement, the Company is not required to reimburse or otherwise compensate Novo A/S through any means other than the agreed royalty entitlement. In addition, the Company does not, under the terms of the Purchase and Sale Agreement, have the right or obligation to prepay Novo A/S in connection with a change of control of the Company or otherwise.

The Purchase and Sale Agreement requires the establishment of a Joint Oversight Committee in the event that Novo A/S does not continue to have a representative on the Company's board of directors. The Joint Oversight Committee would have responsibilities that include "discussion and review" of all matters related to Fovista research, development, regulatory approval and commercialization, but there is no provision either implicit or explicit that gives the Joint Oversight Committee or its members decision-making authority.

On May 23, 2013, the Company entered into a Series C Preferred Stock Purchase Agreement (the "Series C Agreement") with certain of its existing investors for the sale and issuance of an aggregate of 20,000,000 shares of the Company's Series C Preferred Stock at a price of \$2.50 per share. In connection with entering into the Series C Agreement, the Company issued 6,666,667 shares of Series C Preferred Stock at \$2.50 per share in a closing that occurred on May 23, 2013, simultaneous with entry into the Series C Agreement. In connection with entering into the Series C Agreement, the minimum public offering price per share in an underwritten public offering of common stock required for the automatic conversion of outstanding shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Junior Series A Preferred Stock was adjusted to \$14.75 per share (subject to further adjustment as a result of any stock dividend, stock split, combination or similar recapitalization of the common stock).

On May 23, 2013, the Company repaid the outstanding principal, interest and related prepayment fees on the 2012 Notes and 2013 Note.

The Company has determined that in accordance with ASC 470-20-20, at the time of the initial closing under the Series C Agreement on May 23, 2013, there was a firm commitment from the Series C Preferred Stock investors with respect to the significant terms of the financing, including the



**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Notes to Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**December 31, 2012**

**17. Subsequent Events (Continued)**

quantity of shares to be issued, the fixed price of the shares and the timing of the transaction. In addition, the Company has concluded that the Series C Agreement and the Company's certificate of incorporation includes a disincentive feature for non-performance that was sufficiently large enough to make investor performance at subsequent closings probable. As such, the Company's measurement of any beneficial conversion feature occurred at the time of the initial closing. Based on a \$10.03 per share valuation of the Company's common stock as of the date of the initial closing of the sale of the Series C Preferred Stock, as well as the fact that the Series C Preferred Stock include a common stock conversion price of \$14.75 per share (implying a one-to-one conversion into shares of common stock), the Company determined that there was no beneficial conversion feature associated with the issuance of its Series C Preferred Stock.

The Company filed a registration statement on Form S-1 with the SEC relating to the initial public offering of its common stock. In connection with the Company's initial public offering:

- (i) The Company effected a one-for-5.9000 reverse stock split of its common stock on September 9, 2013. All share and per share amounts related to common stock, options and warrants included in these financial statements and notes to financial statements have been restated to reflect the reverse stock split. The conversion ratios of the Company's preferred stock have also been adjusted to reflect the reverse stock split.
- (ii) The Company's board of directors adopted and the Company's stockholders approved the 2013 stock incentive plan ("2013 Plan"), which became effective immediately prior to the closing of the Company's initial public offering. The 2013 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, and other stock-based awards. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2013 Plan.

**OPHTHOTECH CORPORATION**  
(A Development Stage Entity)

**Balance Sheets**

(in thousands, except share and per share data)

	September 30, 2013 (unaudited)	December 31, 2012
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 236,079	\$ 4,304
Prepaid expenses and other current assets	2,096	44
Other Assets	—	331
Security deposits	158	158
Total current assets	238,333	4,837
Property and equipment, net	32	42
Other long-term assets	11	—
Total assets	<u>\$ 238,376</u>	<u>\$ 4,879</u>
<b>Liabilities, Convertible Redeemable Series A, Series A-1, Series B, Series B-1 Preferred Stock and stockholders' equity (deficit)</b>		
Current liabilities:		
Accrued clinical drug supplies and trial costs	\$ 3,477	1,013
Accounts payable and accrued expenses	4,431	1,391
Notes payable	—	11,040
Warrant liability	—	966
Total current liabilities	7,908	14,410
Royalty purchase liability	41,667	—
Total liabilities	49,575	14,410
Preferred Stock, Convertible and Redeemable:		
Series A—\$0.001 par value, 73,094,000 shares authorized, 51,790,000 shares issued and outstanding at December 31, 2012	—	69,471
Series A-1—\$0.001 par value, 18,480,000 shares authorized, 6,000,000 shares issued and outstanding at December 31, 2012	—	8,460
Series B—\$0.001 par value, 42,320,200 shares authorized, 30,000,000 shares issued and outstanding at December 31, 2012	—	35,456
Series B-1—\$0.001 par value, 700,000 shares authorized, 500,000 shares issued and outstanding at December 31, 2012	—	552
Total Preferred Stock, Convertible and Redeemable	—	113,939
Stockholders' equity (deficit)		
Junior Series A Convertible Preferred Stock—\$0.001 par value, 3,000,000 shares authorized, issued and outstanding at December 31, 2012	—	3,000
Preferred stock—\$0.001 par value, 5,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock—\$0.001 par value, 200,000,000 shares authorized, 31,250,817 shares issued and outstanding at September 30, 2013; 155,864,851 shares authorized, 1,469,798 shares issued and outstanding at December 31, 2012	31	1
Additional paid-in capital	351,431	—
Deficit accumulated during development stage	(162,661)	(126,471)
Total stockholders' equity (deficit)	188,801	(123,470)
Total liabilities and stockholders' equity (deficit)	<u>\$ 238,376</u>	<u>\$ 4,879</u>

See accompanying unaudited notes.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Entity)**

**Statements of Operations**

**(Unaudited)**

**(in thousands, except share and per share data)**

	Nine Months Ended September 30,		Period from January 5, 2007 (Inception) to September 30, 2013
	2013	2012	
<b>Costs and expenses:</b>			
Research and development	\$ 17,836	\$ 4,794	\$ 92,727
General and administrative	9,145	5,341	36,494
<b>Total costs and expenses</b>	<u>26,981</u>	<u>10,135</u>	<u>129,221</u>
<b>Loss from operations</b>	(26,981)	(10,135)	(129,221)
Interest expense	(1,454)	(256)	(1,964)
Interest and other income	—	—	481
Loss on extinguishment of debt	(1,091)	—	(1,091)
Other loss	(1,231)	(340)	(1,602)
Change in fair value related to investor rights liability	—	—	683
<b>Net loss before income tax benefit</b>	<u>(30,757)</u>	<u>(10,731)</u>	<u>(132,714)</u>
<b>Income tax benefit</b>	—	—	1,327
Net loss	(30,757)	(10,731)	(131,387)
Add: accretion of preferred stock dividends	(5,891)	(5,288)	(33,046)
<b>Net loss attributable to common stockholders</b>	<u>\$ (36,648)</u>	<u>\$ (16,019)</u>	<u>\$ (164,433)</u>
Net loss attributable to common stockholders per share:			
Basic and diluted	<u>\$ (23.21)</u>	<u>\$ (11.07)</u>	
Weighted average common shares outstanding:			
Basic and diluted	<u>1,579</u>	<u>1,447</u>	

See accompanying unaudited notes.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Statements of Cash Flows**

(Unaudited)

(in thousands)

	Nine months ended September 30,		Period from January 5, 2007 (Inception) to September 30, 2013
	2013	2012	
<b>Operating Activities</b>			
Net loss	\$ (30,757)	\$ (10,731)	\$ (131,387)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation	14	24	169
Amortization of debt issuance costs	88	24	135
Accretion of debt discount	87	30	146
Non-cash change in fair value of warrant liability	1,231	332	1,612
Non-cash change in fair value of investor rights liability	—	—	(683)
Loss on extinguishment of debt	1,091	—	1,091
Share-based compensation	1,607	283	2,797
Series A-1, Series B-1 and Junior Preferred Stock issued for acquired technology and licenses	—	—	9,500
Accrued interest expense converted to Series A Preferred Stock	—	—	2
Changes in operating assets and liabilities:			
Prepaid expense and other current assets	(2,052)	27	(2,107)
Other receivables	—	1,036	—
Security deposits	(11)	—	(170)
Accrued clinical drug supplies and trial costs	2,464	(1,039)	3,477
Accounts payable and accrued expenses	3,040	787	4,431
Deferred rent	—	(22)	—
Net cash used in operating activities	<u>(23,198)</u>	<u>(9,249)</u>	<u>(110,987)</u>
<b>Investing Activities</b>			
Purchase of marketable securities	—	—	(4,238)
Maturities of marketable securities	—	—	4,250
Purchase of property and equipment	(5)	—	(201)
Net cash used in investing activities	<u>(5)</u>	<u>—</u>	<u>(189)</u>
<b>Financing Activities</b>			
Payment of debt issuance costs	(43)	(263)	(421)
Proceeds from issuance of common stock	—	2	124
Proceeds from initial public offering, net	175,555	—	175,555
Proceeds from issuance of notes payable, net	—	—	210
(Repayment of) proceeds from issuance of venture debt facility, net	(11,900)	7,460	(512)
Proceeds from issuance of preferred stock, net	49,699	—	130,632
Proceeds from royalty purchase agreement	41,667	—	41,667
Net cash provided by financing activities	<u>254,978</u>	<u>7,199</u>	<u>347,255</u>
Net change in cash and cash equivalents	<u>231,775</u>	<u>(2,050)</u>	<u>236,079</u>
<b>Cash and cash equivalents</b>			
Beginning of period	4,304	6,396	—
End of period	<u>\$ 236,079</u>	<u>\$ 4,346</u>	<u>\$ 236,079</u>
<b>Supplemental disclosures of cash flow information</b>			
Conversion of preferred stock to common stock up completion of IPO	\$ 174,310	\$ —	\$ 174,310
Accreted dividends on Series A, Series A-1, Series of B, B-1 and Series C Preferred Stock	<u>\$ 5,891</u>	<u>\$ 5,288</u>	<u>\$ 33,046</u>
Notes payable and accrued interest converted to Series A Preferred Stock	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 212</u>

See accompanying unaudited notes.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements**

**(tabular dollars and shares in thousands, except per share data)**

**1. Business**

**Description of Business and Organization**

Ophthotech Corporation (the "Company" or "Ophthotech") was incorporated on January 5, 2007, in Delaware. The Company is a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the eye with a focus on developing therapeutics for age-related macular degeneration, or AMD. The Company's operations since inception have been limited to organizing and staffing the Company, acquiring rights to product candidates, business planning, raising capital and developing its product candidates. Accordingly, the Company is considered to be in the development stage as defined by Financial Accounting Standards Board Accounting Standards Codification ("ASC") 915, *Development Stage Entities*. The Company operates in one business segment.

Capitalized terms not otherwise defined herein are defined in their respective agreements.

**Liquidity**

Since the Company's inception, it has incurred significant operating losses. The Company reported a net loss of \$30.8 million for the nine months ended September 30, 2013 and \$10.7 million for the nine months ended September 30, 2012. As of September 30, 2013, the Company had a deficit accumulated during the development stage of \$162.7 million. To date, the Company has not generated any revenues and has financed its operations primarily through private placements of its preferred stock, venture debt borrowings, its royalty purchase and sale agreement with Novo A/S and its initial public offering ("IPO"), which closed on September 30, 2013. The Company issued and sold an aggregate of 8,740,000 shares of common stock in its IPO at a public offering price of \$22.00 per share, including 1,140,000 shares pursuant to the exercise by the underwriters of an over-allotment option. The Company received net proceeds from the IPO of \$175.6 million, after deducting underwriting discounts and commissions and other offering expenses. The Company has devoted substantially all of its financial resources and efforts to research and development and expects to continue to incur significant expenses and increasing operating losses over the next several years. The Company's net losses may fluctuate significantly from quarter to quarter and year to year.

To fully execute its business plan, the Company will need to complete certain research and development activities and clinical trials. Further, the Company's product candidates will require regulatory approval prior to commercialization. These activities may span many years and require substantial expenditures to complete and may ultimately be unsuccessful. Any delays in completing these activities could adversely impact the Company. The Company plans to meet its capital requirements primarily through a combination of equity and debt financings, collaborations, strategic alliances and marketing distribution or licensing arrangements and in the longer term, revenue from potential product sales. There can be no assurance that such funds will be available, or if available, on terms favorable to the Company. The Company faces the normal risks associated with a development stage company, including but not limited to the risk that the Company's research and development activities will not be successfully completed, that adequate patent protection for the Company's technology will not be obtained, that any products developed will not obtain necessary government regulatory approval and that any approved products will not be commercially viable. In addition, the Company operates in an environment of rapid change in technology, substantial competition from pharmaceutical and biotechnology companies and is dependent upon the services of its employees and

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**1. Business (Continued)**

its consultants. The Company's capital requirements will depend on many factors, including the success of its development and commercialization of its product candidates and whether it pursues the development of additional product candidates. Even if the Company succeeds in developing and commercializing one or more of its product candidates, it may never achieve sufficient sales revenue to achieve or maintain profitability.

**2. Summary of Significant Accounting Policies**

The Company's complete listing of significant accounting policies are described in Note 2 of the notes to the audited financial statements as of December 31, 2012, included in this prospectus.

**Basis of Presentation**

The accompanying unaudited financial information as of September 30, 2013, for the nine months ended September 30, 2013 and 2012, and for the period from January 5, 2007 (Inception) to September 30, 2013 has been prepared by the Company, pursuant to the rules and regulations of the Securities and Exchange Commission. Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. generally accepted accounting principles have been condensed or omitted pursuant to such rules and regulations. The December 31, 2012 balance sheet was derived from the Company's audited financial statements. These interim financial statements should be read in conjunction with the 2012 audited annual financial statements and notes thereto in the final prospectus dated September 25, 2013 related to the Company's initial public offering.

In the opinion of management, the unaudited financial information as of September 30, 2013, for the nine months ended September 30, 2013 and 2012, and for the period from January 5, 2007 (Inception) to September 30, 2013, reflects all adjustments, which are normal recurring adjustments, necessary to present a fair statement of financial position, results or operations and cash flows. The results of operations for the nine months ended September 30, 2013 and 2012, are not necessarily indicative of the operating results for the full fiscal year or any future period.

**Use of Estimates**

The preparation of financial statements and related disclosures in conformity with accounting principles generally accepted in the United States requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions that it believes are reasonable under the circumstances. The amounts of assets and liabilities reported in the Company's Balance Sheets and the amount of expenses reported for each of the periods presented are affected by estimates and assumptions, which are used for, but not limited to, accounting for share-based compensation and accounting for research and development costs. Actual results could differ from those estimates.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**2. Summary of Significant Accounting Policies (Continued)**

**Cash and Cash Equivalents**

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. The carrying amounts reported in the Balance Sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

**Concentration of Credit Risk**

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash and cash equivalents. The Company maintains its cash in bank accounts, which, at times, exceed federally insured limits. The Company also maintains cash equivalents in money market funds that invest primarily in U.S. Treasury securities. The Company has not recognized any losses from credit risks on such accounts during any of the periods presented. The Company believes it is not exposed to significant credit risk on its cash and cash equivalents.

**Foreign Currency Translation**

The Company maintains a bank account in a foreign currency. The Company considers the U.S. dollar to be its functional currency. Expenses are translated at the exchange rate on the date the expense is incurred. The effect of exchange rate fluctuations on translating foreign currency assets and liabilities into U.S. dollars is included in the Statements of Operations. Foreign exchange transaction gains and losses are included in the results of operations and are not material in the Company's financial statements.

**Financial Instruments**

The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, accounts payable and accrued expenses approximate their respective fair value due to their short maturities.

**Property and Equipment**

Property and equipment, which consist mainly of computers and other equipment, are carried at cost less accumulated depreciation. Depreciation is computed over the estimated useful lives of the respective assets, generally five to seven years, using the straight-line method.

**Research and Development**

Research and development expenses consist of costs associated with the development and clinical testing of Fovista, an anti-PDGF aptamer the Company is developing for use in combination with anti-VEGF drugs for treatment of wet age-related macular degeneration, or wet AMD, and the Company's other product candidates. Research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, ("CROs") and other vendors, contract manufacturing organizations and consultants; and

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**2. Summary of Significant Accounting Policies (Continued)**

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense.

Research and development costs also include costs of acquired product licenses and related technology rights where there is no alternative future use, prototypes used in research and development, consultant fees and amounts paid to collaborative partners.

All research and development costs are charged to operations as incurred in accordance with ASC 730 *Research and Development*. The Company accounts for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made.

The Company anticipates that its research and development expenses will increase substantially as compared to prior periods in connection with initiating and conducting its pivotal Phase 3 clinical program for Fovista and if such trials are successful, seeking marketing approval for Fovista.

The Company does not currently utilize a formal time allocation system to capture expenses on a project-by-project basis because it records expenses by functional department. Accordingly, the Company does not allocate expenses to individual projects or product candidates, although it does allocate some portion of its research and development expenses by functional area and by compound.

**Income Taxes**

The Company utilizes the liability method of accounting for deferred income taxes, as set forth in ASC 740-10, *Income Taxes-Overall*. Under this method, deferred tax liabilities and assets are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. A valuation allowance is established against net deferred tax assets because, based on the weight of available evidence, it is more likely than not that some or all of the net deferred tax assets will not be realized. The Company maintains a full valuation allowance on its deferred tax assets. Accordingly, the Company has not recorded a benefit or provision for income taxes other than for the sale of a portion of its unused New Jersey State operating loss carryforwards through a program sponsored by the State of New Jersey and the New Jersey Economic Development Authority in 2011. The Company's U.S. federal net operating losses have occurred since inception and as such, tax years subject to potential tax examination could apply from that date because carrying-back net operating loss opens the relevant year to audit.

**Share-Based Compensation**

The Company follows the provisions of the ASC 718, *Compensation—Stock Compensation* which requires the measurement and recognition of compensation expense for all share-based payment awards made to employees and non-employee directors, including employee stock options. Share-based compensation expense is based on the grant date fair value estimated in accordance with the provisions of ASC 718 and is generally recognized as an expense over the requisite service period.



**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**2. Summary of Significant Accounting Policies (Continued)**

For stock options granted as consideration for services rendered by non-employees, the Company recognizes expense in accordance with the requirements of ASC 505-50, *Equity Based Payments to Non-Employees*. Non-employee option grants that do not vest immediately upon grant are recorded as an expense over the vesting period of the underlying stock options. At the end of each financial reporting period prior to vesting, the value of these options, as calculated using the Black-Scholes option-pricing model, will be re-measured using the fair value of the Company's common stock and the non-cash expense recognized during the period will be adjusted accordingly. Since the fair value of options granted to non-employees is subject to change in the future, the amount of the future expense will include fair value re-measurements until the stock options are fully vested.

Prior to the Company's initial public offering, the Company 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 its common stock.

Due to the lack of trading history, the Company's computation of stock-price volatility is based on the volatility rates of comparable publicly held companies over a period equal to the expected term of the options granted by the Company. The Company's computation of expected term was determined using the "simplified" method which is the midpoint between the vesting date and the end of the contractual term. The Company believes that it does not have sufficient reliable exercise data in order to justify the use of a method other than the "simplified" method of estimating the expected exercise term of employee stock option grants. The Company has paid no dividends to stockholders. The risk-free interest rate is based on the zero-coupon U.S. Treasury yield at the date of grant for a term equivalent to the expected term of the option.

Share-based compensation expense includes stock options granted to employees and non-employees and has been reported in the Company's statements of operations as follows:

	Nine months ended September 30,	
	2013	2012
Research and development	\$ 1,052	\$ 182
General and administrative	555	101
Total	<u>\$ 1,607</u>	<u>\$ 283</u>

The Company had no shares of unvested restricted common stock granted to employees at September 30, 2013 or at December 31, 2012, respectively.

**Reclassification**

Certain amounts in prior periods have been reclassified to conform to the current year presentation. Such reclassifications did not have a material effect on the Company's financial condition or results of operations as previously reported.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**2. Summary of Significant Accounting Policies (Continued)**

**JOBS Act**

As an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012, the 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. The Company has elected to delay the adoption of such new or revised accounting standards. As a result of this election, the Company's financial statements may not be comparable to the financial statements of other public companies.

**3. Capitalization**

On September 9, 2013, the Company effected a one-for-5.9 reverse stock split of its common stock. All share and per share data (except par value) related to common stock, options and warrants included in these financial statements and accompanying notes have been adjusted to reflect the reverse stock split for all periods presented.

On September 30, 2013, the Company closed its initial public offering of 8,740,000 shares of common stock at a price of \$22.00 per share. The net proceeds to the Company were \$175.6 million, after deducting underwriters' commissions and other offering expenses. In connection with the closing of the IPO, all of the Company's shares of redeemable convertible preferred stock outstanding at the time of the offering were automatically converted into 21,038,477 shares of common stock.

In August 2013, the Company's Board of Directors and stockholders approved a restated certificate of incorporation which became effective following the closing of the Company's IPO on September 30, 2013. The restated certificate of incorporation increased the number of authorized shares of common stock to 200,000,000 and decreased the number of authorized shares of preferred stock to 5,000,000.

**4. Net Loss Per Common Share**

Basic and diluted net loss per common share is determined by dividing net loss applicable to common stockholders by the weighted average common shares outstanding during the period. For the periods where there is a net loss attributable to common shareholders, the outstanding shares of preferred stock, stock options, unvested restricted stock, and warrants have been excluded from the calculation of diluted loss per common shareholder because their effect would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted loss per share would be

**OPHTHOTECH CORPORATION**  
(A Development Stage Company)

**Notes to Unaudited Financial Statements (Continued)**

(tabular dollars and shares in thousands, except per share data)

**4. Net Loss Per Common Share (Continued)**

the same. The following table sets forth the computation of basic and diluted net loss per share for the periods indicated:

	Nine months ended September 30,	
	2013	2012
Basic and diluted net loss per common share calculation:		
Net loss	\$ (30,757)	\$ (10,731)
Accretion of preferred stock dividends	(5,891)	(5,288)
Net loss attributable to common shareholders	<u>\$ (36,648)</u>	<u>\$ (16,019)</u>
Weighted average common shares outstanding	<u>1,579</u>	<u>1,447</u>
Net loss per share of common stock—basic and diluted	<u>\$ (23.21)</u>	<u>\$ (11.07)</u>

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding for the periods presented, as they would be anti-dilutive:

	As of September 30,	
	2013	2012
Redeemable convertible preferred stock	—	16,513
Options outstanding	2,620	1,301
Warrants	101	78
Total	<u>2,721</u>	<u>17,892</u>

**5. Fair Value Measurements**

ASC 820, *Fair Value Measurements and Disclosures*, defines fair value as the price that would be received to sell an asset, or paid to transfer a liability, in the principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value standard also establishes a three-level hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The valuation hierarchy is based upon the transparency of inputs to the valuation of an asset or liability on the measurement date. The three levels are defined as follows:

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market.
- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability.
- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**5. Fair Value Measurements (Continued)**

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of September 30, 2013:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>Assets</b>			
Investments in U.S. Treasury money market funds*	\$ 234,843	\$ —	\$ —
<b>Liabilities</b>			
Series A Warrant Liability	\$ —	\$ —	\$ —
Series B Warrant Liability	\$ —	\$ —	\$ —

\* Investments in U.S. Treasury money market funds are reflected in cash and cash equivalents in the accompanying Balance Sheets.

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2012:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>Assets</b>			
Investments in money market funds*	\$ 524	\$ —	\$ —
<b>Liabilities</b>			
Series A Warrant Liability	\$ —	\$ —	\$ 523
Series B Warrant Liability	\$ —	\$ —	\$ 443

\* Investments in money markets funds are reflected in cash and cash equivalents in the accompanying Balance Sheets.

**Level 3 Valuation**

The warrant liability was recorded in its own line item on the Company's Balance Sheets. The warrant liability was marked-to-market each reporting period with the change in fair value recorded to other loss in the Statement of Operations. The fair value of the warrant liability was estimated using a hybrid method between a probability-weighted expected return method, or PWERM, model and an option pricing model, which includes variables such as the expected volatility based on guideline public companies, the preferred stock value, and the estimated time to a liquidity event.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**5. Fair Value Measurements (Continued)**

The significant assumptions used in preparing the option pricing model for valuing the Company's warrants for the Series A preferred shares as of December 31, 2012, include (i) volatility (47.2% - 85.3%), (ii) risk free interest rate (0.05% - 0.62%), (iii) strike price (\$0.01), (iv) fair value of Series A preferred shares (\$1.22 - \$4.34), (v) expected life (0.25 years to 4.5 years) and (vi) expected outcome probability weighting of three outcome scenarios: merger (65%); dissolution (20%) and an initial public offering (15%).

The significant assumptions used in preparing the option pricing model for valuing the Company's warrants for the Series B preferred shares as of December 31, 2012, include (i) volatility (47.2% - 80.1%), (ii) risk free interest rate (0.05% - 1.68%), (iii) strike prices (\$1.00 - \$2.50), (iv) fair value of Series B preferred shares (\$1.18 - \$4.22), (v) expected life (0.25 years to 9.5 years) and (vi) expected outcome probability weighting of three outcome scenarios: merger (65%); dissolution (20%) and an initial public offering (15%).

The table presented below is a summary of changes in the fair value of the Company's Level 3 valuation for the Series A and Series B warrant liabilities for the period ended September 30, 2013:

	Level 3	
	Series A Warrant Liability	Series B Warrant Liability
Balance at December 31, 2012	523	443
Warrants issued in connection with venture debt facility	—	32
Change in fair value of warrant liability	379	852
Conversion of warrant liability to equity	(902)	(1,327)
Balance at September 30, 2013	<u>\$ —</u>	<u>\$ —</u>

Upon completion of the Company's IPO on September 30, 2013, the underlying preferred stock was converted to common stock and the preferred stock warrants became exercisable for common stock. The fair value of the warrant liability was re-measured immediately prior to the completion of the Company's IPO, and the fair value of the warrant liability at that time was reclassified to additional paid-in capital. Based on the initial public offering price of \$22.00 per share, the fair value of the warrant liability that was reclassified to additional paid-in capital was \$2.2 million. The Company recorded a related charge of approximately \$1.0 million and \$1.2 million as other loss in its results of operations for the three and nine months ended September 30, 2013, respectively.

**6. Notes Payable**

In June 2012, December 2012 and March 2013, the Company issued secured promissory notes (the "Notes") in the amount of \$7.5 million and \$4.0 million and \$1.5 million, respectively, to the same lender. The Notes bore interest on the outstanding principal amount thereof from the Closing Date until paid in full at a rate per annum equal to the sum of (i) the greater of (A) the LIBOR Rate in effect for the applicable Interest Period and (B) 3.0%, plus (ii) the LIBOR Rate Margin adjusted on the first day of each Interest Period and fixed for the duration of each such Interest Period.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**6. Notes Payable (Continued)**

As of December 31, 2012, the Company classified the debt with the lender as a current liability since the Company intended to pay down the balance in its entirety within twelve months. The Company repaid in full the outstanding principal, interest and related prepayment fees in May 2013. The repayment of the Notes resulted in a loss on extinguishment of debt in the amount of \$1.1 million for the nine months ended September 30, 2013. In addition, the Company made payments of \$0.8 million which, in accordance with the Notes, were required upon the earlier of the maturity date or the prepayment date of the Notes. These payments were recorded as interest expense for the nine months ended September 30, 2013.

**7. Stock Option and Compensation Plans**

The Company adopted its 2007 Stock Incentive Plan (the "2007 Plan") for employees and consultants for the purpose of advancing the interests of the Company stockholders by enhancing its ability to attract, retain and motivate persons who are expected to make important contributions to the Company. The 2007 Plan provided for the granting of stock option awards, restricted stock awards, and other stock-based and cash-based awards. Following the effectiveness of the 2013 Stock Incentive Plan described below in connection with the closing of the Company's initial public offering, the Company is no longer granting additional awards under the 2007 Plan.

During the nine months ended September 30, 2013, the Company's Board of Directors and stockholders increased the number of shares authorized under the 2007 Plan by 1,878,343 shares. The Company's board of directors also adopted and the Company's stockholders also approved the 2013 stock incentive plan (the "2013 Plan"), which became effective immediately prior to the closing of the Company's initial public offering. The 2013 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, and other stock-based awards. Upon effectiveness of the 2013 Plan, the number of shares of the Company's common stock that were reserved for issuance under the 2013 Plan was the sum of (1) such number of shares (up to approximately 3,359,641 shares) as is equal to the sum of 739,317 shares (the number of shares of the common stock then available for issuance under the 2007 Plan), and such number of shares of the Company's common stock that are subject to outstanding awards under the 2007 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (2) an annual increase, to be added the first day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until, and including, the fiscal year ending December 31, 2023, equal to the lowest of 2,542,372 shares of the Company's common stock, 4% of the number of shares of the Company's common stock outstanding on the first day of the fiscal year and an amount determined by our board of directors. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2013 Plan. However, incentive stock options may only be granted to employees of the Company.

As of September 30, 2013, the Company had approximately 2,620,000 stock options outstanding under the 2007 Plan and approximately 739,000 shares available for grant under the 2013 Plan.

The Company recognized share-based compensation of approximately \$1.6 million for the nine months ended September 30, 2013 and approximately \$0.3 million during the nine months ended September 30, 2012. As of September 30, 2013, there was approximately \$11.6 million of total

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**7. Stock Option and Compensation Plans (Continued)**

unrecognized share-based compensation expense that is expected to be recognized over a weighted average period of approximately 3.4 years.

The intrinsic value of the Company's approximately 1,091,000 vested options as of September 30, 2013 was \$30.8 million, based on a per share price of \$29.71, the closing price of the Company's stock at September 30, 2013, and a weighted average exercise price of \$1.36 per share. The intrinsic value of the Company's approximately 1,529,000 unvested options as of September 30, 2013 was \$30.5 million, based on a per share price of \$29.71, the closing price of the Company's stock at September 30, 2013, and a weighted average exercise price of \$9.76 per share.

**8. Royalty Agreement and Series C Agreement**

In May 2013, the Company entered into a Purchase and Sale Agreement (the "Purchase and Sale Agreement") with Novo A/S, providing for the Company to sell, and Novo A/S to purchase, the right, title, and interest in a portion of the revenues from the sale of (a) Fovista, (b) Fovista-Related Products, and (c) Other Products (as defined in the Purchase and Sale Agreement), calculated as low to mid-single digit percentages of net sales.

The Purchase and Sale Agreement provides for up to three separate purchases for a purchase price of \$41.7 million each, at a first, second and third closing, for an aggregate purchase price of \$125.0 million. In each purchase, Novo A/S acquires rights to a low single digit percentage of net sales. If all royalty interests under the Purchase and Sale Agreement are purchased, Novo A/S will have a right to receive royalties on net sales at a mid-single digit percentage.

In May 2013, the Company received cash proceeds of \$41.7 million for the royalty entitlement related to the first closing on the date of the Purchase and Sale Agreement. Receipt of cash proceeds for the second and third purchases is contingent upon certain triggers and conditions detailed in the Purchase and Sale Agreement, none of which have occurred prior to this filing.

The royalty payment period covered by the Purchase and Sale Agreement begins on commercial launch and ends, on a product-by-product and country-by-country basis, on the latest to occur of (i) the 12th anniversary of the commercial launch, (ii) the expiration of certain patent rights and (iii) the expiration of the regulatory exclusivity for each product in each country.

Under the terms of the Purchase and Sale Agreement, the Company is not required to reimburse or otherwise compensate Novo A/S through any means other than the agreed royalty entitlement. In addition, the Company does not, under the terms of the Purchase and Sale Agreement, have the right or obligation to prepay Novo A/S in connection with a change of control of the Company or otherwise.

The proceeds from the first financing tranche under the Purchase and Sale Agreement were recorded as a liability on the Company's Balance Sheet as of September 30, 2013, in accordance with ASC 730. Because there is a significant related party relationship between the Company and Novo A/S, the Company is treating its obligation to make royalty payments under the Purchase and Sale Agreement as an implicit obligation to repay the funds advanced by Novo A/S. As the Company makes royalty payments in accordance with the Purchase and Sale Agreement, it will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, the Company will impute interest accordingly on a prospective basis based on such estimates, which would result in a corresponding increase in the liability balance.

**OPHTHOTECH CORPORATION**  
**(A Development Stage Company)**

**Notes to Unaudited Financial Statements (Continued)**

**(tabular dollars and shares in thousands, except per share data)**

**8. Royalty Agreement and Series C Agreement (Continued)**

The Purchase and Sale Agreement requires the establishment of a Joint Oversight Committee in the event that Novo A/S does not continue to have a representative on the Company's board of directors. The Joint Oversight Committee would have responsibilities that include "discussion and review" of all matters related to Fovista research, development, regulatory approval and commercialization, but there is no provision either implicit or explicit that gives the Joint Oversight Committee or its members decision-making authority.

Also in May 2013, the Company entered into a Series C Preferred Stock Purchase Agreement (the "Series C Agreement") with certain of its existing investors for the sale and issuance, upon the satisfaction of certain conditions, of an aggregate of 20,000,000 shares of the Company's Series C Preferred Stock at a price of \$2.50 (\$14.75 on a post-reverse stock split basis) per share. The Company issued 6,666,667 shares of Series C Preferred Stock at \$2.50 (\$14.75 on a post-reverse stock split basis) per share in a closing that occurred in May 2013, simultaneous with entry into the Series C Agreement. In August 2013, the Company amended the Series C Agreement to provide for the acceleration of the sale and issuance of the remaining 13,333,333 shares issuable thereunder, the purchase and sale of which closed on August 7, 2013 at \$2.50 (\$14.75 on a post-reverse stock split basis) per share for aggregate proceeds of \$33.3 million. There are no further rights or obligations for the issuance of Series C Preferred Stock under the Series C Agreement.

As the Series C Agreement was entered into in conjunction with the Purchase and Sale Agreement, the Company's management considered whether the consideration received for the issuance of Series C Preferred Stock or the consideration received for the sale of the royalty entitlement at the first closing under the Purchase and Sale Agreement should be allocated in the Company's financial statements in a manner different than the prices stated in the respective agreements. The Company's management, with the assistance of an outside valuation specialist, determined that the \$2.50 (\$14.75 on a post-reverse stock split basis) per share price approximated the fair value of a share of Series C Preferred Stock, and therefore concluded that the consideration received under the agreements should be allocated in accordance with the terms of the respective agreements. In connection with entering into the Series C Agreement, the minimum public offering price per share in an underwritten public offering of common stock required for the automatic conversion of outstanding shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Junior Series A Preferred Stock pursuant to the Company's certificate of incorporation was adjusted to \$14.75 per share (subject to further adjustment as a result of any stock dividend, stock split, combination or similar recapitalization of the common stock).

The Company has determined that in accordance with ASC 470-20-20, at the time of the initial closing under the Series C Agreement on May 23, 2013, there was a firm commitment from the Series C Preferred Stock investors with respect to the significant terms of the financing, including the quantity of shares to be issued, the fixed price of the shares and the timing of the transaction. In addition, the Company has concluded that the Series C Agreement and the Company's certificate of incorporation includes a disincentive feature for non-performance that was sufficiently large enough to make investor performance at subsequent closings probable. As such, the Company's measurement of any beneficial conversion feature occurred at the time of the initial closing. Based on a \$10.03 per share valuation of the Company's common stock as of the date of the initial closing of the sale of the



**OPHTHOTECH CORPORATION**  
(A Development Stage Company)

**Notes to Unaudited Financial Statements (Continued)**

(tabular dollars and shares in thousands, except per share data)

**8. Royalty Agreement and Series C Agreement (Continued)**

Series C Preferred Stock, as well as the fact that the Series C Preferred Stock featured a common stock conversion price of \$14.75 per share (implying a one-to-one conversion into shares of common stock), the Company determined that there was no beneficial conversion feature associated with the issuance of its Series C Preferred Stock.

The proceeds received from Novo A/S under the Purchase and Sale Agreement will be reported as revenue for income tax purposes. Notwithstanding the Company's receipt of \$41.7 million in proceeds under the Purchase and Sale Agreement in May 2013, the Company has forecasted a tax loss for the 2013 tax year. Based upon the Company's cumulative history of losses and expected future losses, the Company recorded a full valuation allowance against all net federal and state deferred tax assets.

**9. Selected Quarterly Financial Information (unaudited)**

The following is a summary of the quarterly results of operations for 2013 and 2012 (in thousands, except per share amounts):

	2013		
	March 31	June 30	September 30
Revenues	\$ —	\$ —	\$ —
Research and development	2,390	4,345	11,101
General and administrative	1,738	3,241	4,166
Loss from operations	(4,128)	(7,586)	(15,267)
Net loss attributable to common shareholders	\$ (6,361)	\$ (11,863)	\$ (18,424)
Basic and diluted earnings per common share	\$ (4.33)	\$ (8.07)	\$ (10.26)

	2012		
	March 31	June 30	September 30
Revenues	\$ —	\$ —	\$ —
Research and development	1,621	1,578	1,595
General and administrative	1,388	1,694	2,259
Loss from operations	(3,009)	(3,272)	(3,854)
Net loss attributable to common shareholders	\$ (4,765)	\$ (5,326)	\$ (5,928)
Basic and diluted earnings per common share	\$ (3.31)	\$ (3.68)	\$ (4.07)

**10. Subsequent Events**

On January 23, 2014, in connection with its royalty agreement with Novo A/S, the Company received approximately \$41.7 million in exchange for a low single-digit royalty interest in future potential worldwide sales of Fovista. The receipt of this second financing tranche under the royalty agreement was triggered as a result of the Company reaching an initial enrollment milestone of a specified number of patients in its Phase 3 clinical program for Fovista. The closing of a third potential financing tranche of approximately \$41.7 million is subject to the further enrollment milestone of a specified number of patients in the Company's Phase 3 clinical program for Fovista, and the Company satisfying additional closing conditions and other obligations.

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