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**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2013

or

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

For the transition period from _____ to _____

Commission file number 001-36080

OPHTHOTECH CORPORATION

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

20-8185347
(I.R.S. Employer
Identification No.)

One Penn Plaza, 19th Floor
New York, NY
(Address of principal executive
offices)

10119
(Zip Code)

(212) 845-8200

(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, \$0.001 par value	The NASDAQ Stock Market LLC

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes o No

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

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

Large accelerated filer o

Accelerated filer o

Non-accelerated filer
(Do not check if a smaller reporting company)

Smaller reporting company o

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

As of June 28, 2013, the last business day of the registrant's most recently completed second fiscal quarter, the registrant's common stock was not publicly traded. The registrant's common stock began trading on the NASDAQ Global Select Market on September 25, 2013. As of December 31, 2013, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately \$327.5 million, based on the closing price of the registrant's common stock on December 31, 2013.

The number of shares outstanding of the registrant's class of common stock, as of February 28, 2014: 33,318,575

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2014 Annual Meeting of Shareholders, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2013.

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FORWARD-LOOKING STATEMENTS

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

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

- 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;

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

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

PART I

Item 1. Business

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 FovistaTM in 2016. We are also developing our product candidate ZimuraTM, 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 anti-VEGF 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 anti-VEGF 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 activated initial trial sites in the third trial in this Phase 3 clinical program in the United States in 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 2013, annual worldwide sales of Lucentis and Eylea for all indications totaled approximately \$6.1 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

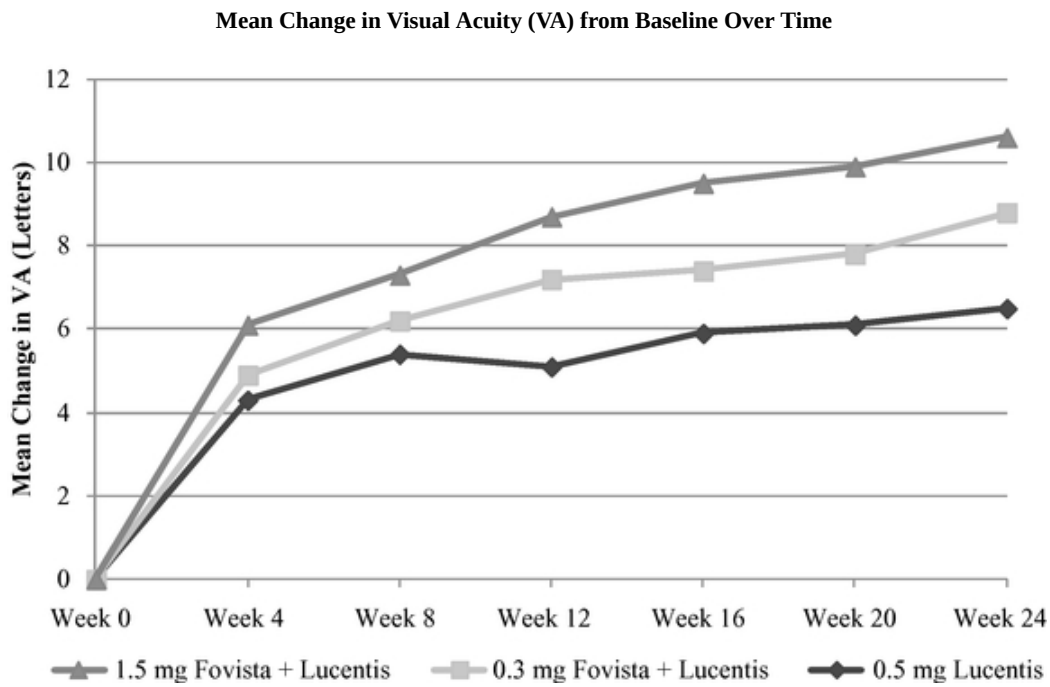
In our completed Phase 2b clinical trial, the combination of 1.5 mg of Fovista and Lucentis demonstrated statistically significant superiority compared to Lucentis monotherapy based on the primary endpoint of mean change in visual acuity from baseline at 24 weeks, providing a 62% comparative benefit 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:

- While 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 2bn clinical trial, 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, or CATT, published in 2013 in the *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 are also conducting a third clinical trial which is evaluating 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 severe form of dry AMD. 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.

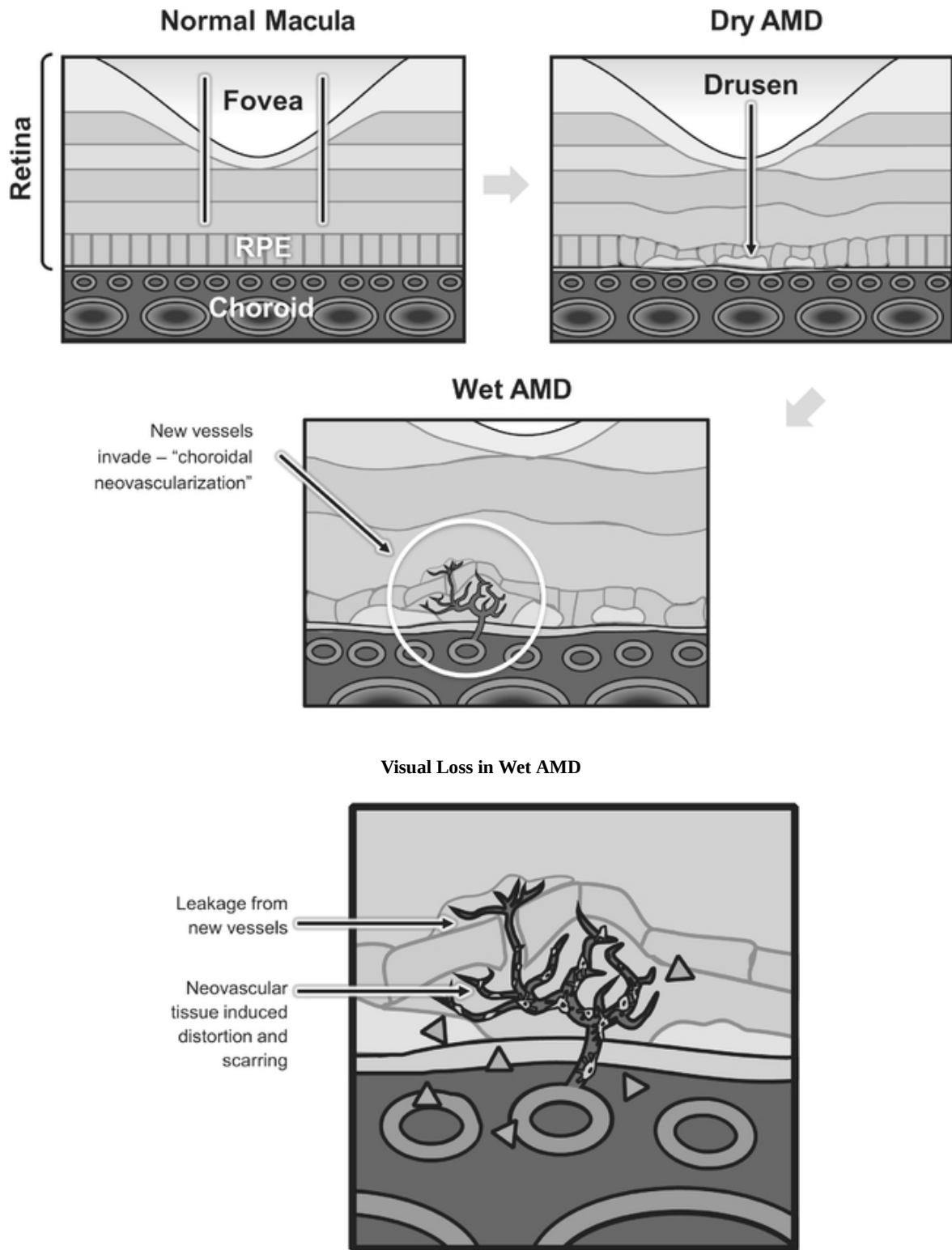
Wet AMD traditionally has been divided into subtypes based on the pattern of the abnormal new blood vessels using the diagnostic imaging technique fluorescein angiography or cross sectional location of the abnormal new blood vessels using the diagnostic imaging technique spectral domain optical coherence tomography, or SD-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 SD-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 vessels. 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 SD-OCT models to image the abnormal new blood vessels and the associated leakage in wet AMD patients. SD-OCT utilizes specialized light scattering through the biological tissues and obtains high-resolution retinal tissue images using a specialized camera. SD-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. SD-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.

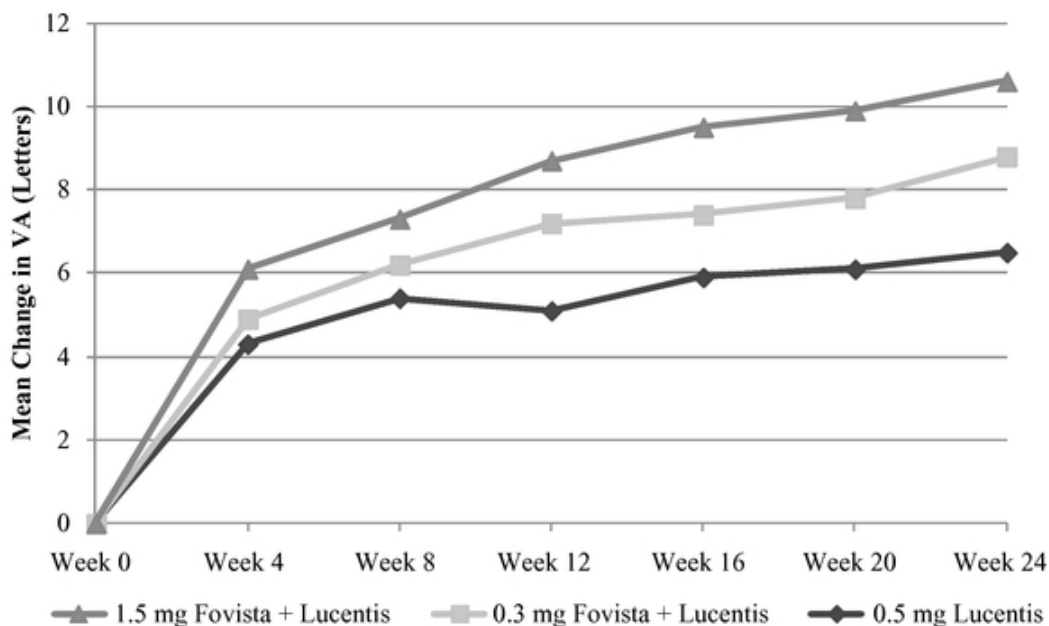
Retinal specialists have historically used fluorescein angiography to determine the extent and location of abnormal new blood vessels relative to the RPE. Currently, there is a shift among retinal specialists to using SD-OCT to image abnormal new blood vessels and associated leakage in wet AMD patients.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



Visual Loss in Wet AMD

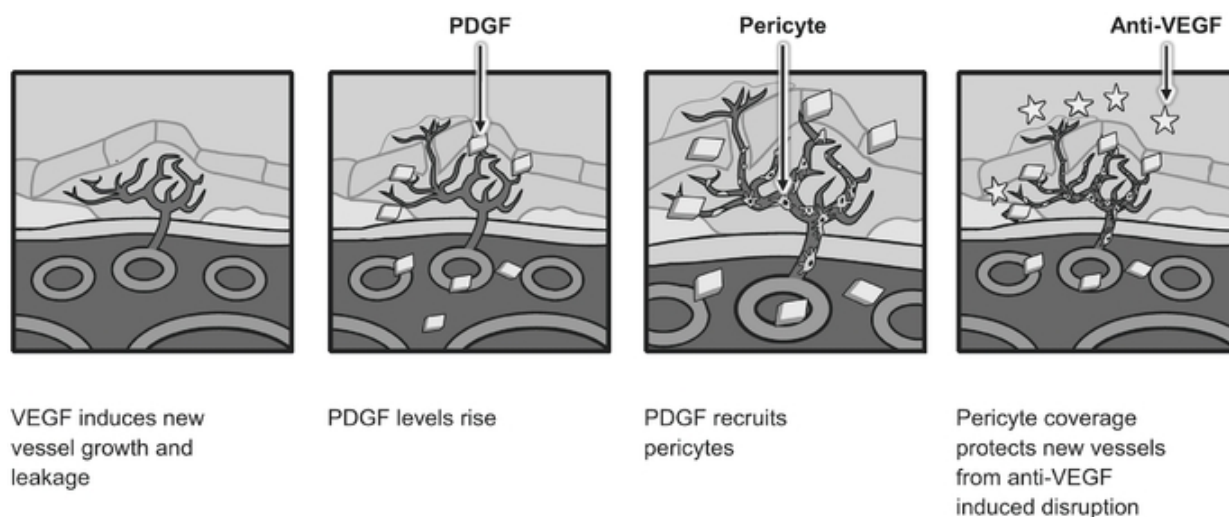
Mean Change in Visual Acuity (VA) from Baseline Over Time



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.

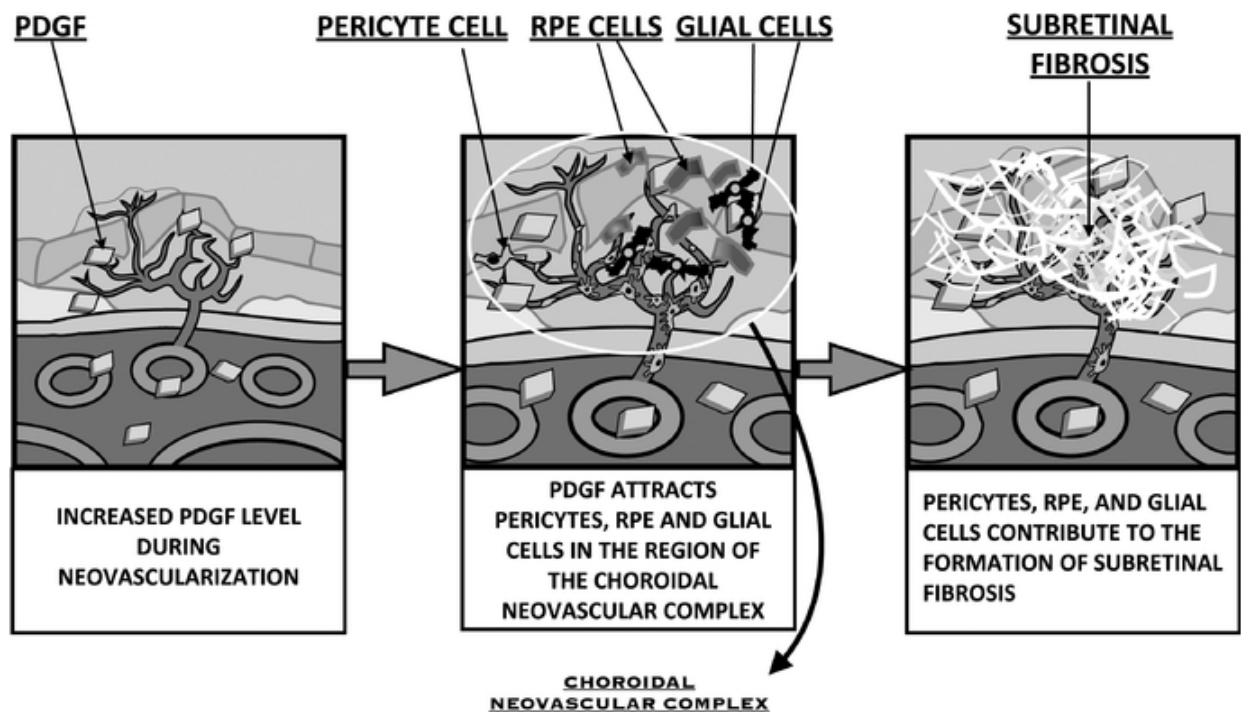
The following diagrams show cross-sections of the back of an eye and the chemical and cellular processes associated with the progression to neovascularization in wet AMD:



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 2013, annual worldwide sales of Lucentis and Eylea for all indications totaled approximately \$6.1 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 and distributors 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 CATT study 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- α and PDGFR- β .

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 PDGFR- β . 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.

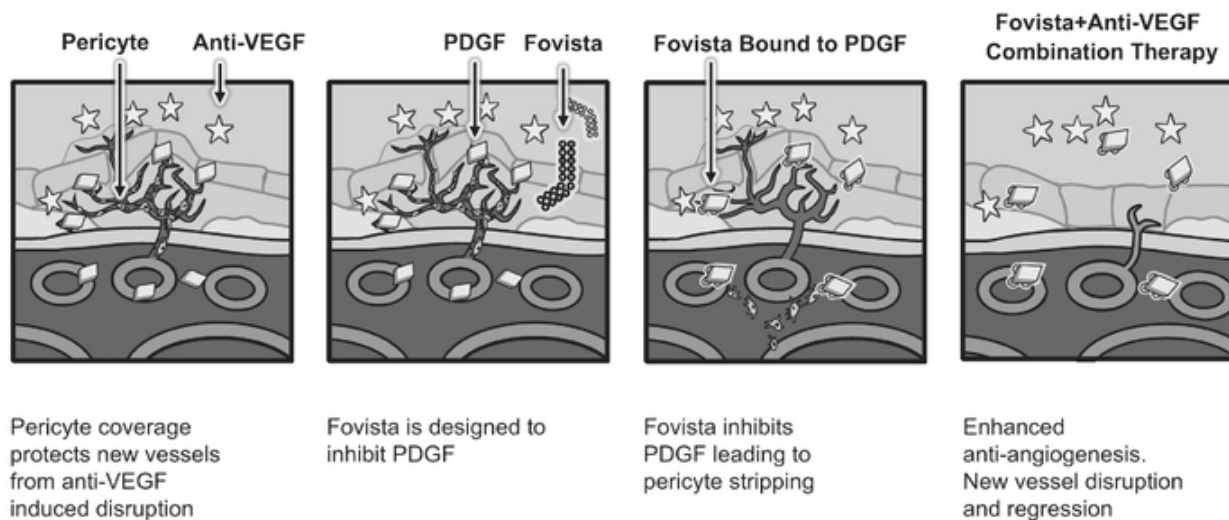
We have measured Fovista's inhibition of both PDGF-BB and PDGF-AB binding to both their receptors, PDGFR- α and PDGFR- β , by widely accepted scientific methods. In *in vitro* assays, Fovista strongly inhibits both PDGF-BB and PDGF-AB from binding to their receptors with potency equal to an antibody that directly blocks the PDGFR- α and PDGFR- β 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*, entitled "Histopathologic and Ultrastructural Features of Surgically Excised Subfoveal Choroidal Neovascular Lesions," 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 an article entitled "Intraocular Injection of an Aptamer that binds PDGF-B: A Potential Treatment for Proliferative Retinopathies" showing 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:

Regression of Neovascularization



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 are evaluating Fovista in combination with Lucentis and the other of which is evaluating Fovista in combination with each of Avastin or Eylea. All three of these Phase 3 clinical trials 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 activated initial trial sites in the third trial in this Phase 3 clinical program in the United States in 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 second quarter of 2014.

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 SD-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 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.

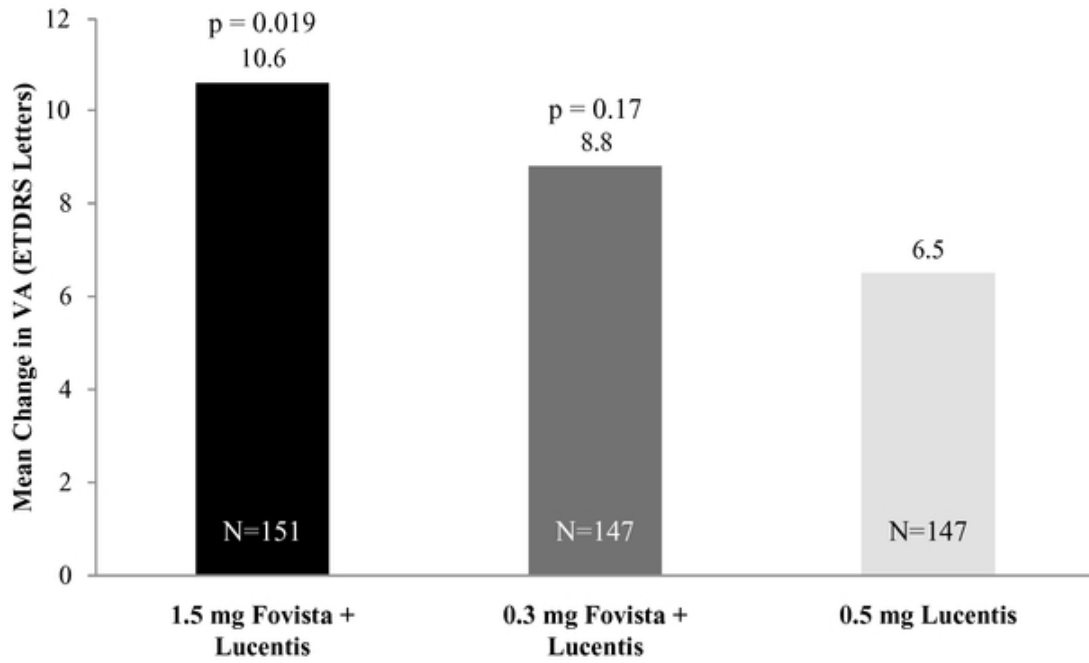
Measures of Mean Visual Acuity—Primary Efficacy Endpoint

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.

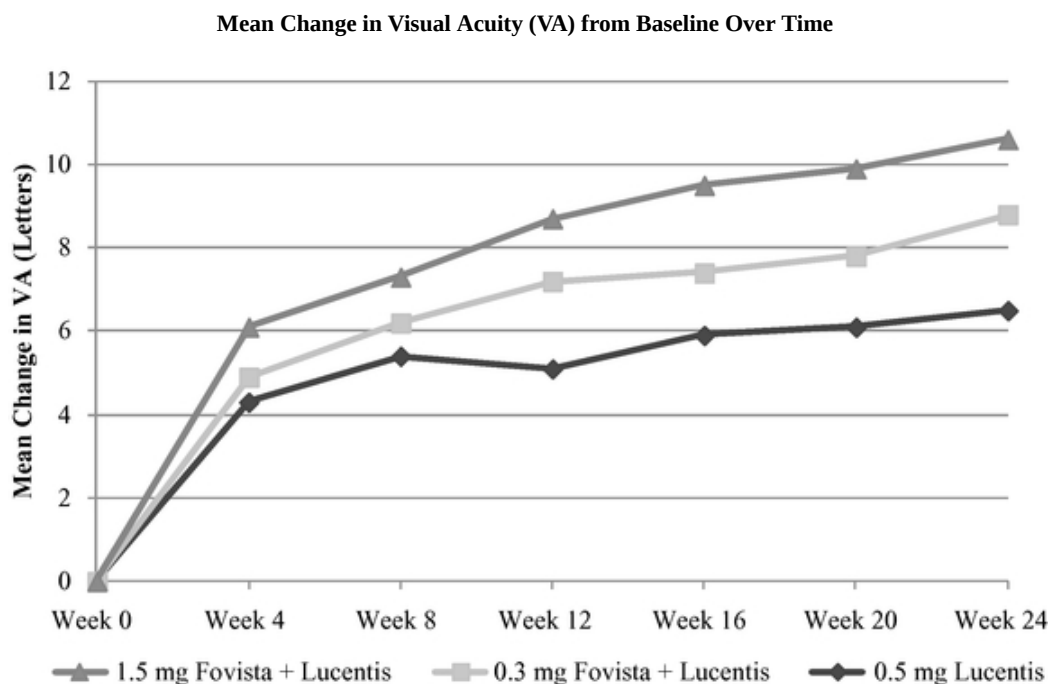
The graph below sets forth the results of the pre-specified primary endpoint in this Phase 2b clinical trial.

Mean Change in Visual Acuity (VA) from Baseline at 24 Weeks



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.



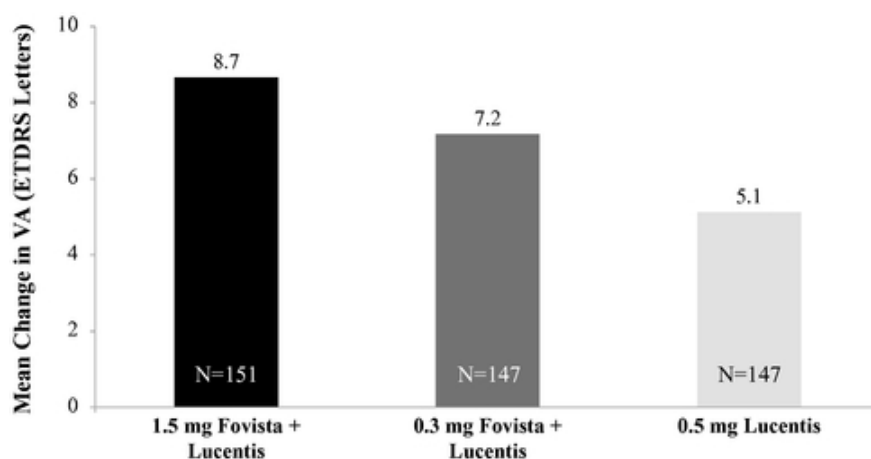
We believe that the divergence of the efficacy curves suggests an increasing relative benefit in visual outcome for the combination of 1.5 mg of Fovista and Lucentis over time compared to Lucentis monotherapy. If we observe a similar pattern of visual benefit in our Phase 3 clinical program, we believe 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.

Mean Change in Visual Acuity (VA) from Baseline 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

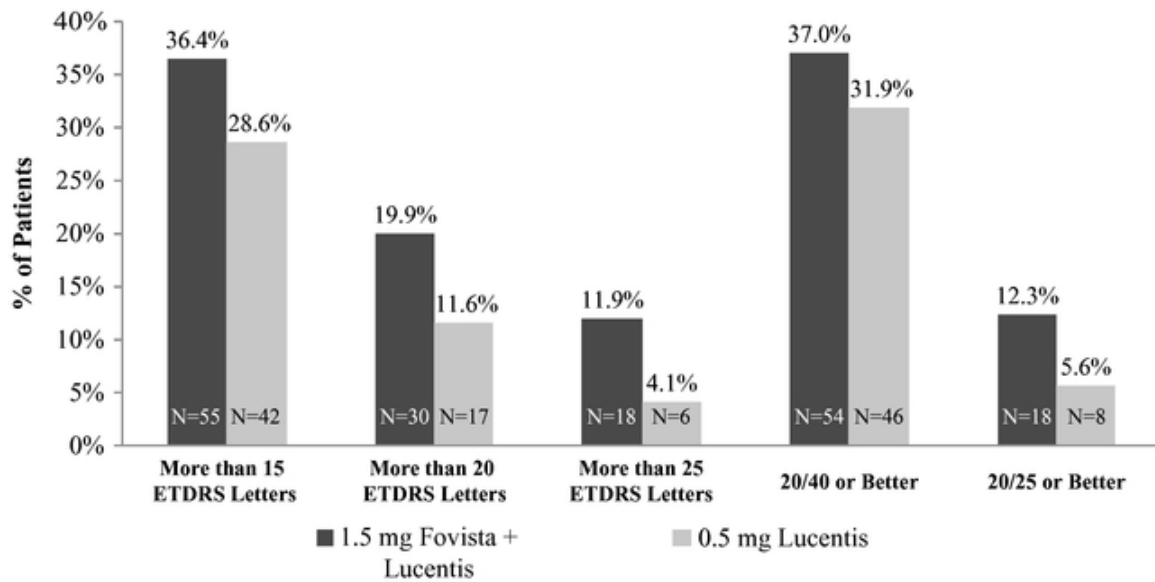
<u>Arm</u>	<u># (%) of Patients Gaining ³ 15 letters at Week 12</u>	<u># (%) of Patients Gaining ³ 15 letters at Week 24</u>
1.5 mg		
Fovista + Lucentis	48 (31.8)%	59 (39.1)%
0.3 mg		
Fovista + Lucentis	31 (21.1)%	49 (33.3)%
0.5 mg Lucentis	33 (22.4)%	50 (34.0)%

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.

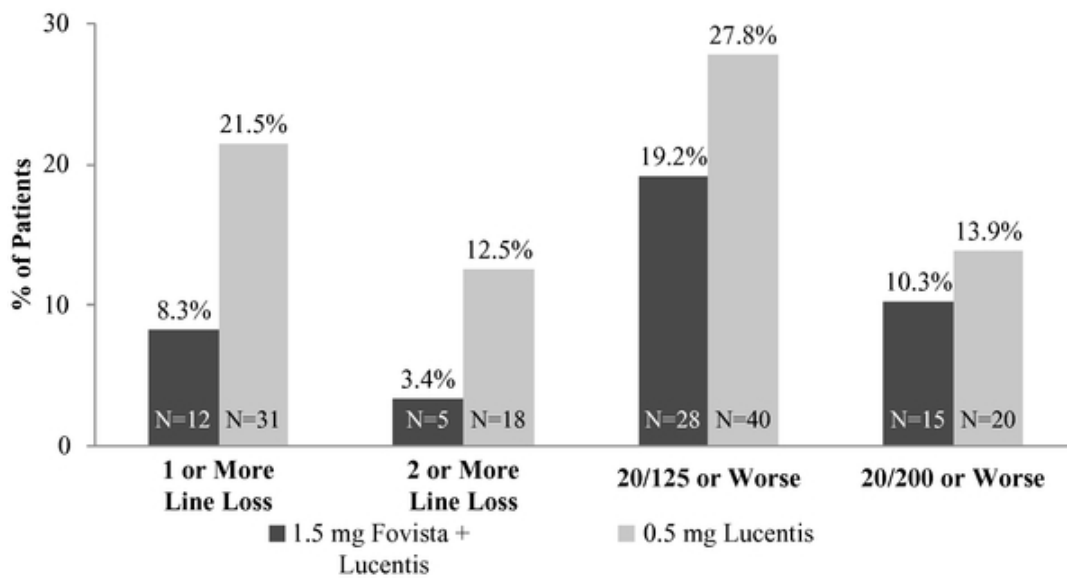
Retrospective Analysis of Visual Gain. We observed differences in the proportion of patients that showed improvement when measured by the number of lines of improvement in visual acuity from baseline, referred to as final visual acuity, favoring the combination of 1.5 mg of Fovista and Lucentis compared 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

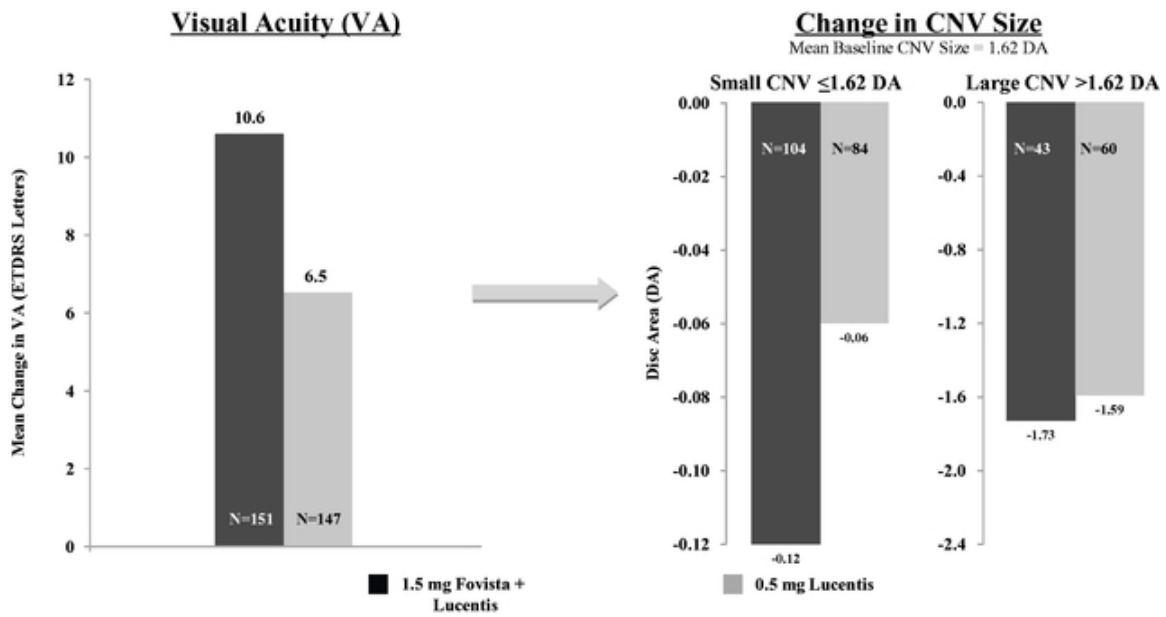
We performed retrospective analyses of anatomical changes, based on choroidal neovascularization and subretinal hyper-reflective material, that were not pre-specified primary or secondary endpoints in the trial design. Although a retrospective analysis performed after unblinding trial results can result 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.

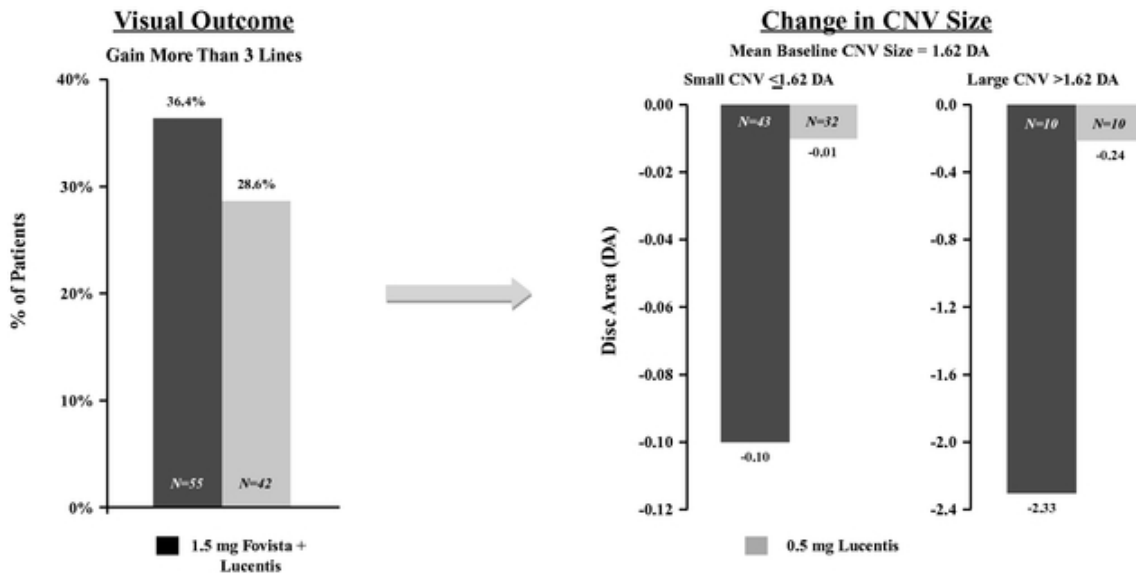
Patients in both the large CNV size patient subgroup and small CNV size patient subgroup showed greater reductions in the size of choroidal neovascularization from baseline when treated with the combination of 1.5 mg of Fovista and Lucentis as compared to patients in the applicable subgroup receiving 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**



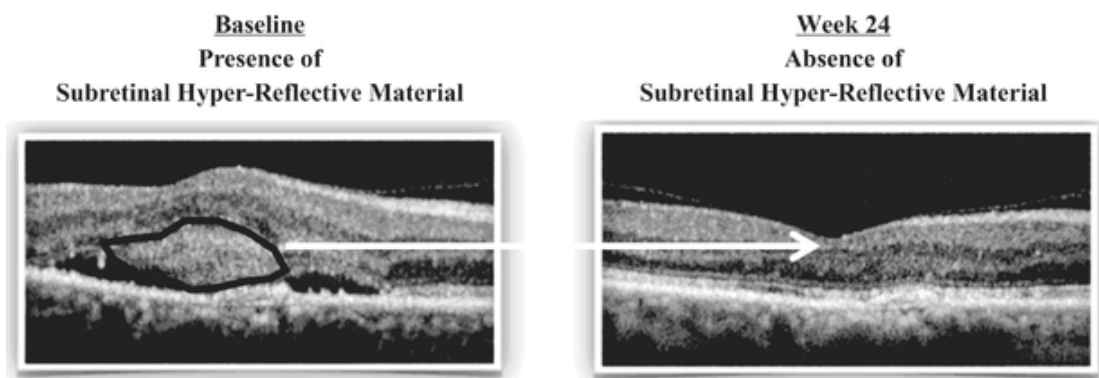
Retrospective Analysis of Subretinal Hyper-Reflective Material. We performed a retrospective review of SD-OCT images of patients who participated in the trial without regard to baseline size of choroidal

neovascularization. SD-OCT is the imaging technique most widely used today in clinical practice for the evaluation of wet AMD. Unlike fluorescein angiograms, SD-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 SD-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 SD-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 SD-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 SD-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



	Presence of Subretinal Hyper-Reflective Material at Baseline	Absence of Subretinal Hyper-Reflective Material at Week 24
All Patients		
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)
Patients With Significant Visual Gain (>3-Lines)		
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 SD-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
Patients With One or More Systemic Serious Adverse Events	11 (7.4)%	13 (8.7)%	9 (5.9)%
MedDRA System Organ Class(1)			
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)%
Any Antiplatelet Trialists' Collaboration (APTC) Event			
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
Ocular Serious Adverse Events	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
Patients with One or More Adverse Events	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 is evaluating 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 activated initial trial sites in the third trial in this Phase 3 clinical program in the United States in 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, have begun to obtain approvals to proceed and have begun dosing patients in certain of those countries. We plan to submit applications seeking to initiate the third trial of Fovista administered in combination with Avastin or Eylea in the second 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 have had 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.

In the fourth quarter of 2013, the CHMP 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 Phase 3 clinical trials for Fovista, 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 would 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.

In the first quarter of 2014, we received a written response from the CHMP on these issues. The CHMP is in agreement with our plan to use the less frequent dosing schedule approved for Eylea in the European Union as the dosing schedule in our Phase 3 clinical trial evaluating Fovista administered in combination with Eylea so that no bridging study will be needed for this combination. The CHMP has also agreed with our plan for monthly dosing for the first 12 months of each of our Phase 3 clinical trials evaluating Fovista administered in combination with Lucentis and, to slightly modify the dosing

regimen in the second 12 months for one of these two trials so that it is consistent with the less frequent dosing schedule approved for Lucentis in the European Union. The dosing schedule for the second 12 months in the other study evaluating Fovista administered with Lucentis remains unchanged. Accordingly, the CHMP has informed us that no bridging study will be needed and 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, remains unchanged.

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 currently 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 SD-OCT, the patient also will be treated at that alternate month visit. We will, however, submit to the relevant regulatory authorities, amendments to the protocols for these trials to change certain aspects of the trial design as a result of our agreement with the CHMP regarding the dosing regimens in these trials described above. We may also make further changes with respect to the second 12 months of the trials. Any such changes will be made 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, further 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, except for the dosing schedule in the second twelve months. 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 following intravitreal injections of 0.5 mg of Lucentis.

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 following intravitreal injections of 1.25 mg of Avastin; or
 - sham injections 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. However, 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. 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 SD-OCT of each patient's affected eye. The reading center will use SD-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 SD-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 SD-OCT in the United States and the European Union as the standard for retinal imaging for wet AMD. SD-OCT utilizes specialized light scattering through the biological tissues and obtains high-resolution retinal tissue images using a specialized camera. SD-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 SD-OCT machines have markedly improved the resolution of retinal imaging. SD-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 SD-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 SD-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 SD-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 SD-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. SD-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. SD-OCT is the current standard of imaging of wet AMD patients and we believe that the use of SD-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 SD-OCT assessment. If we determine that the potential Fovista label may exclude its use for the treatment of patients with certain SD-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 SD-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 have supplied 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 include the previously untested combinations of Fovista with Avastin or Eylea. 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 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 mm² for the 24 patients receiving the 0.3 mg dose and 0.78 mm²

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 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 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 peptide 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 that entered clinical development in February 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.
- Santen has a dual inhibitor of VEGF and PDGF in Phase 1/2a clinic development.
- 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 α_2 -adrenergic receptor agonist, which has completed a Phase 2 clinical trial.
- Pfizer has a humanized monoclonal antibody that binds amyloid- β (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 February 28, 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 (Eyeteck)

In July 2007, we entered into a divestiture 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, under which we acquired specified technology, rights, and other assets owned or controlled by Eyeteck relating to particular anti-PDGF aptamers, including Fovista, and assumed Eyeteck's liabilities and obligations under specified agreements between Eyeteck and Archemix Corp., or Archemix, and between Eyeteck 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 Eyeteck a \$4.0 million upfront payment and issued Eyeteck 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 February 28, 2014, we had 38 full-time employees, including a total of five employees with M.D. or Ph.D. degrees. Of our workforce, 20 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.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2007. Our principal executive offices are located at One Penn Plaza, 19th Floor, New York, NY 10119, and our telephone number is (212) 845-8200. Our Internet website is <http://www.opthotech.com>.

Available Information

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

Item 1A. Risk Factors.

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

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 \$51.1 million for the year ended December 31, 2013, \$14.6 million for the year ended December 31, 2012 and \$18.6 million for the year ended December 31, 2011. As of December 31, 2013, we had a deficit accumulated during the development stage of \$183.1 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 our initial public offering, which we closed in September 2013 and a follow-on public offering, which we closed in February 2014. 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

received net proceeds from the follow-on public offering of \$55.5 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 (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. 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;
- obtaining adequate coverage and reimbursement for our product candidates, if approved, from governmental and third-party payors;
- 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 our stockholders to lose all or part of their investment.

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

We are an early-stage company. We were incorporated and commenced active operations in 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 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 Phase 3 clinical program for Fovista in 2016. As of December 31, 2013, our cash and cash equivalents were \$210.6 million which, together with \$41.7 million received under our royalty agreement with Novo A/S in January 2014, net proceeds of \$55.5 million from the follow-on public offering of common stock that we completed in February 2014 and our potential future funding of \$41.7 million under our royalty agreement with Novo A/S, we believe will be sufficient 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 this 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 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, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as holders of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our pledge of 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.

We have broad discretion in the use of our available cash and other sources of funding and may not use them effectively.

Our management has broad discretion in the use of our available cash and other sources of funding 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 in a manner that does not produce income or that loses value.

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 activated initial trial sites in the third trial in this Phase 3 clinical program in the United States in 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, have begun to obtain approvals to proceed, and have begun dosing patients in certain of those countries. We plan to submit applications seeking to initiate the third trial of Fovista administered in combination with Avastin or Eylea in the second 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 have had 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. 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.

In the fourth quarter of 2013, 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 Phase 3 clinical trials for Fovista, 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 would 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.

In the first quarter of 2014, we received written confirmation from the CHMP on these issues. The CHMP is in agreement with our plan to use the less frequent dosing schedule approved for Eylea in the European Union as the dosing schedule in our Phase 3 clinical trial evaluating Fovista administered in combination with Eylea so that no bridging study will be needed for this combination. The CHMP has also agreed with our plan for monthly dosing for the first 12 months of each of our Phase 3 clinical trials evaluating Fovista administered in combination with Lucentis and, to slightly modify the dosing regimen in the second 12 months for one of these trials so that it is consistent with the less frequent dosing schedule approved for Lucentis in the European Union. The dosing schedule for the second 12 months for one of these trials in the other study evaluating Fovista administered with Lucentis remains unchanged. Accordingly, the CHMP has informed us that no bridging study will be needed and 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, remains unchanged. 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 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, Santen, 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 February 28, 2014, we hired more than half of our 38 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

Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.

As of February 28, 2014, our executive officers, directors and principal stockholders and their affiliates, in the aggregate, beneficially owned shares representing approximately 61% 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 our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- 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.

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 the ability of our stockholders to sell their shares.

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

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, our stockholders may not be able to sell their shares of common stock at or above the price at which they purchased their shares. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of 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.

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 February 28, 2014, we had outstanding 33,318,575 shares of common stock. Of these shares, 21,816,564 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, a description of which, including certain exceptions thereto, is available in the registration statement filed in connection with such offering. These shares will be able to be sold beginning on March 24, 2014. Additionally, 19,516,995 of those shares are subject to lock-up agreements entered into in connection with our recent follow-on public offering but will be able to be sold beginning on May 12, 2014. Any of our remaining shares that are not restricted securities under Rule 144 under the Securities Act or subject to lock-up agreements, including, for example, shares sold in our initial public offering or this offering, may be resold in the public market without restriction unless purchased by our affiliates. Moreover, holders of an aggregate of 19,337,482 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. As of February 28, 2014, we had outstanding options to purchase an aggregate of approximately 3,754,000 share of our common stock, of which options to purchase approximately 1,046,000 were vested. These shares can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates and the applicable lock-up agreements entered into in connection with our public offerings.

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

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

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

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

In addition, the JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have 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 our stockholders' sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our properties 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.

Item 3. Legal Proceedings

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures

None.

PART II

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

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>
2013		
Third Quarter (September 25, 2013 to September 30, 2013)	\$ 31.99	\$ 23.00
Fourth Quarter	\$ 36.60	\$ 22.61

Holders

As of February 28, 2014, there were approximately 57 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of our common stock, shares of our preferred stock and warrants to purchase shares of our preferred stock issued, and stock options and restricted stock awards granted, by us during the year ended December 31, 2013 that were not registered under the Securities Act of 1933, as amended, or the Securities Act, and that have not otherwise been described in a Quarterly Report on Form 10Q. Also included is the consideration, if any, received by us for such shares and options and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of securities

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.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The recipients of securities in the transactions described above represented that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could

hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions.

(b) Stock option grants

During the period between January 1, 2013 and June 30, 2013 and the period between October 1, 2013 and October 16, 2013, we issued to certain employees, directors and consultants options to purchase an aggregate of 874,086 shares of our common stock under our equity compensation plans with exercise prices ranging from \$13.22 to \$29.00 per share. During these periods, options to purchase 23,966 shares of our common stock were exercised or forfeited for aggregate consideration of \$25,363. 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 our equity compensation plans.

The issuances of stock options and the shares of our common stock issuable upon the exercise of the options described in this section (b) prior to October 16, 2013, were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Issuance of warrants

In connection with a venture debt facility, which we fully repaid in May 2013, we issued to the lender, on March 15, 2013, a warrant to purchase 35,700 shares of our series B preferred stock, at an exercise price of \$2.50 per share.

The issuance of this warrant was made in reliance on the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The lender represented that it was an accredited investor and was acquiring the warrant for its own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that it could bear the risks of the investment and could hold the warrant for an indefinite period of time and appropriate legends were affixed to the instruments representing such warrant issued in such transactions. Such recipient either received adequate information about us or had, through its relationship with us, access to such information.

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

Purchase of Equity Securities

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

Use of Proceeds from Registered Securities

On September 30, 2013, we closed our initial public offering of 8,740,000 shares of our common stock, including 1,140,000 shares of our common stock pursuant to the exercise by the underwriters of an over-allotment option, at a public offering price of \$22.00 per share for an aggregate offering price

of approximately \$192.3 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-190643), which was declared effective by the SEC on September 24, 2013.

We received aggregate net proceeds from the offering of \$175.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

As of December 31, 2013, we have used approximately \$5.1 million of the net proceeds from the offering as follows:

- approximately \$3.9 million to fund certain costs of our Phase 3 clinical program for Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD, which costs consists of external research and development expenses and clinical development related employee expenses; and
- approximately \$1.2 million for working capital and other general corporate purposes.

We have not used any of the net proceeds from the offering to make payments, directly or indirectly, to any director or officer of ours, or any of their associates, to any person owning 10 percent or more of our common stock or to any affiliate of ours. We have invested the remaining net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act.

Item 6. Selected Financial Data

The following selected financial data should be read together with our financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2013, 2012 and 2011 and the balance sheet data as of December 31, 2013, 2012, and 2011 from our audited financial statements included elsewhere in this Annual Report on Form 10-K, which have been audited by Ernst & Young LLP, an independent registered accounting firm. 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,		
	2013	2012 (in thousands)	2011
Statement of Operations Data:			
Revenue	\$ —	\$ —	\$ —
Operating Expenses:			
Research and development	33,215	6,792	13,896
General and administrative	14,210	6,889	5,738
Total operating expenses	47,425	13,681	19,634
Loss from operations	(47,425)	(13,681)	(19,634)
Interest (expense) income	(1,454)	(507)	2
Loss on extinguishment of debt	(1,091)	—	—
Other loss	(1,175)	(374)	(30)
Net loss before income tax benefit	(51,145)	(14,562)	(19,662)
Income tax benefit	—	—	1,029
Net loss	(51,145)	(14,562)	(18,633)
Add: accretion of preferred stock dividends	(5,891)	(7,063)	(6,838)
Net loss attributable to common stockholders	\$ (57,036)	\$ (21,625)	\$ (25,471)
Net loss attributable to common stockholders per share:			
Basic and diluted	\$ (6.34)	\$ (14.89)	\$ (18.27)
Weighted average common shares outstanding:			
Basic and diluted	9,003	1,452	1,394

	As of December 31,		
	2013	2012 (in thousands)	2011
Balance sheet data:			
Cash and cash equivalents	\$ 210,596	\$ 4,304	\$ 6,396
Total assets	\$ 217,682	\$ 4,879	\$ 7,728
Royalty purchase liability	\$ 41,667	\$ —	\$ —
Preferred stock	\$ —	\$ 113,939	\$ 106,876
Additional paid-in capital	\$ 352,739	\$ —	\$ —
Deficit accumulated during the development stage	\$ (183,050)	\$ (126,471)	\$ (105,488)
Total stockholders' equity (deficit)	\$ 169,720	\$ (123,470)	\$ (102,487)

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

The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of

important factors that could cause actual results to 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 \$51.1 million for the year ended December 31, 2013, \$14.6 million for the year ended December 31, 2012, and \$18.6 million for the year ended December 31, 2011. As of December 31, 2013, we had a deficit accumulated during the development stage of \$183.1 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, our initial public offering, which we closed in September 2013 and a follow-on public offering of common stock, which we closed in February 2014. 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 received net proceeds from the follow-on public offering of \$55.5 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 initiated our pivotal Phase 3 clinical program for Fovista in August 2013. As our patient enrollment increases, we expect our expenses to increase substantially as compared to prior periods. Our expenses will also increase as we expand or further development of 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. 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 December 31, 2013, we have incurred approximately \$108.1 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, 2013, 2012 and 2011:

	Years ended December 31,		
	2013	2012	2011
	(in thousands)		
Fovista	26,206	3,619	9,864
Zimura	15	36	547
Volociximab	14	23	457
Personnel related	4,770	2,749	2,813
Share-based compensation	2,062	343	120
Other	148	22	95
	<u>\$ 33,215</u>	<u>\$ 6,792</u>	<u>\$ 13,896</u>

We recorded research and development expenses from inception to December 31, 2013 of \$55.4 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 Phase 3 clinical program for Fovista in 2016. As of December 31, 2013, our cash and cash equivalents were \$210.6 million which, together with \$41.7 million received under our royalty agreement with Novo A/S in January 2014, net proceeds of \$55.5 million from the follow-on public offering of common stock that we completed in February 2014 and our potential future funding of \$41.7 million under our royalty agreement with Novo A/S, we believe will be sufficient 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 \$1.2 million and \$0.3 million as other loss in our results of operations for the years ended December 31, 2013 and 2012, 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 in our Audited Financial Statements at the end of this Annual Report on Form 10-K. However, we believe that the following accounting policies are the most critical to aid our stockholders 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 sheet. 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, 2013, we had approximately \$86.0 million of federal net operating loss carry-forwards. We also had federal and state research and development tax credit carry-forwards of approximately \$3.0 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, 2013 and 2012. 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 an offering of our common stock 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.

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, 2013, 2012 and 2011:

	Years ended December 31,		
	2013	2012	2011
Expected common stock price volatility	83%	81%	79%
Risk-free interest rate	0.89% - 2.94%	0.94% - 1.77%	1.72% - 2.38%
Expected term of options (years)	6.1	6.6	6.7
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 December 31, 2013, actual forfeitures have not been material.

Share-based compensation expense associated with stock options granted to employees and non-employees was \$2.9 million for the year ended December 31, 2013, \$0.6 million for the year ended December 31, 2012 and \$0.2 million for the year ended December 31, 2011. As of December 31, 2013, we had \$16.5 million of total unrecognized share-based compensation expense, which we expect to recognize over a weighted-average remaining vesting period of approximately 3.3 years. We expect our share-based compensation for stock options granted to employees and non-employees 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, 2013, 2012 and 2011 we allocated share-based compensation as follows:

	Years ended December 31,		
	2013	2012	2011
	(in thousands)		
Research and development	\$ 2,062	\$ 412	\$ 159
General and administrative	809	228	89
Total	<u>\$ 2,871</u>	<u>\$ 640</u>	<u>\$ 248</u>

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 estimated fair market value per share of our common stock was determined by our board of directors 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.

In determining the exercise prices of the options 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.

As of December 31, 2013, we had outstanding options to purchase an aggregate of approximately 2,708,000 shares of our common stock, of which options to purchase approximately 984,000 were vested. The intrinsic value of our approximately 984,000 vested options as of December 31, 2013 was \$29.1 million, based on a per share price of \$32.35, 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 \$2.78 per share. The intrinsic value of our approximately 1,724,000 unvested options as of December 31, 2013 was \$33.1 million, based on a per share price of \$32.35 and a weighted average exercise price of \$13.19 per share. As of February 28, 2014, we had outstanding options to purchase an aggregate of approximately 3,754,000 shares of our common stock, of which options to purchase approximately 1,046,000 were vested.

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 2010 valuation, we utilized a discount for marketability of 40%. We lowered this discount for marketability to 30% for our December 2011 valuation, 26% for our November 2012 valuation, 25% for our May 2013 and 9% for our August 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.

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. There are, however, no standards for which adoption has been delayed adoption that would have a significant impact on the our financial statements.

Results of Operations**Comparison of Years Ended December 31, 2013 and 2012**

	Year Ended December 31,		Increase (Decrease)
	2013	2012	
	(in thousands)		
Statement of Operations Data:			
Revenue	\$ —	\$ —	\$ —
Operating Expenses:			
Research and development	33,215	6,792	26,423
General and administrative	14,210	6,889	7,321
Total operating expenses	47,425	13,681	33,744
Loss from operations	(47,425)	(13,681)	33,744
Interest expense, net	(1,454)	(507)	947
Loss on extinguishment of debt	(1,091)	—	1,091
Other loss	(1,175)	(374)	801
Net loss before income tax benefit	(51,145)	(14,562)	36,583
Income tax provision	—	—	—
Net loss	(51,145)	(14,562)	36,583
Add: accretion of preferred stock dividends	(5,891)	(7,063)	(1,172)
Net loss attributable to common stockholders	<u>\$ (57,036)</u>	<u>\$ (21,625)</u>	<u>\$ 35,411</u>

Revenue

We did not recognize any revenue for the year ended December 31, 2013 or for the year ended December 31, 2012.

Research and Development Expenses

Our research and development expenses were \$33.2 million for the year ended December 31, 2013, an increase of \$26.4 million compared to \$6.8 million for the year ended December 31, 2012. The increase was primarily due to milestone payments, manufacturing activity and clinical trial startup costs as we commenced our Phase 3 clinical program for Fovista in August 2013.

General and Administrative Expenses

Our general and administrative expenses for the year ended December 31, 2013 were \$14.2 million, an increase of \$7.3 million compared to \$6.9 million for the year ended December 31, 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 year ended December 31, 2013 was \$1.5 million compared to \$0.5 million for the year ended December 31, 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 year ended December 31, 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 related to the venture debt facility.

Other Loss

Other loss was \$1.2 million for the year ended December 31, 2013 compared to \$0.4 million for the year ended December 31, 2012. The \$0.8 million increase was primarily due to the change in fair value of the preferred stock warrant liability. These warrants were converted into warrants to purchase common stock upon the closing of our initial public offering.

Comparison of Years Ended December 31, 2012 and 2011

	Year Ended December 31,		Increase (Decrease)
	2012	2011	
	(in thousands)		
Statement of Operations Data:			
Revenue	\$ —	\$ —	\$ —
Operating Expenses:			
Research and development	6,792	13,896	(7,104)
General and administrative	6,889	5,738	1,151
Total operating expenses	13,681	19,634	(5,953)
Loss from operations	(13,681)	(19,634)	(5,953)
Interest (expense) income	(507)	2	509
Loss on extinguishment of debt	—	—	—
Other loss	(374)	(30)	344
Net loss before income tax benefit	(14,562)	(19,662)	(5,100)
Income tax benefit	—	1,029	(1,029)
Net loss	(14,562)	(18,633)	(6,129)
Add: accretion of preferred stock dividends	(7,063)	(6,838)	225
Net loss attributable to common stockholders	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>	<u>\$ (5,904)</u>

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, and was de minimis 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, an increase of \$0.3 million compared the year ended December 31, 2011. The increase was primarily due to the change in fair value of the preferred stock warrants liability.

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 and a recent follow-on public offering of common stock, which we completed in February 2014. 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. In February 2014, we issued and sold 1,900,000 shares of common stock and selling shareholders sold 728,571 shares of common stock, 342,857 of which were sold by the selling stockholders upon the full

exercise by the underwriters of their option to purchase additional shares, in a follow-on public offering at a public offering price of \$31.50 per share. We received net proceeds of \$55.5 million after deducting underwriting discounts and commissions and other offering expenses payable by us. We did not receive any proceeds from the sale of shares by the selling stockholders in the follow-on public offering.

Cash Flows

As of December 31, 2013, we had cash and cash equivalents totaling \$210.6 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, 2013 and 2012:

	Years ended December 31,		
	2013	2012	2011
	(in thousands)		
Net cash (used in) provided by:			
Operating Activities	\$ (48,775)	\$ (13,104)	\$ (19,123)
Investing Activities	(5)	—	3,396
Financing Activities	255,072	11,012	14,994
Net change in cash and cash equivalents	<u>\$ 206,292</u>	<u>\$ (2,092)</u>	<u>\$ (733)</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 increase in net cash used in the year ended December 31, 2013 compared to the year ended December 31, 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.

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

Cash Flows from Investing Activities

Net cash used in investing activities for the years ended December 31, 2013 and 2012 was de minimis in both periods.

Cash Flows from Financing Activities

Net cash provided by financing activities was \$255.1 million for the year ended December 31, 2013 and \$11.0 million for the year ended December 31, 2012. Net cash provided by financing activities for the year ended December 31, 2013 consisted primarily of proceeds of \$175.6 million from our initial public offering in September 2013, net proceeds of \$49.7 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 year ended December 31, 2012 consisted 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. We initiated our pivotal Phase 3 clinical program for Fovista in August 2013. We plan to enroll a total of 1,866 patients for this program, the majority of which we expect to enroll in 2014 and 2015. In addition, we also expect our expenses to increase as we 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 (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.

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. As of December 31, 2013, our cash and cash equivalents were \$210.6 million which, together with \$41.7 million received under our royalty agreement with Novo A/S in January 2014, net proceeds of \$55.5 million from the follow-on public offering of common stock that we completed in February 2014 and our potential future funding of \$41.7 million under our royalty agreement with Novo A/S, we believe will be sufficient 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 this 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, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect their 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 December 31, 2013:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
			(\$ in thousands)		
Operating Leases(1)	\$ 5,047	\$ 777	\$ 1,769	\$ 1,761	\$ 740
Total(2)	\$ 5,047	\$ 777	\$ 1,769	\$ 1,761	\$ 740

- (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 as of December 31, 2013, due to the fact that the royalty payment period was 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 (Eyetechnology), Inc., or Eyetechnology, 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 December 31, 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 December 31, 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 December 31, 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 \$0.4 million. 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 \$0.1 million 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 \$0.1 million, 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 \$0.2 million over the term of the lease.

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.

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

We are exposed to market risk related to changes in interest rates. We had cash and cash equivalents of \$210.6 million as of December 31, 2013, 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 December 31, 2013, substantially all of our total liabilities were denominated in the U.S. dollar.

Item 8. Financial Statements and Supplementary Data

Our financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-32 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2013. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2013, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for "emerging growth companies".

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting occurred during the three months ended December 31, 2013 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors and Executive Officers

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Compliance with Section 16(a) of the Exchange Act

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Code of Ethics

We have adopted a code of business conduct and ethics that applies to our directors and officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions) as well as our other employees. A copy of our code of business conduct and ethics is available on our website. We intend to post on our website all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or the NASDAQ Global Market concerning any amendment to, or waiver of, our code of business conduct and ethics.

Director Nominees

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Audit Committee

We have separately designated a standing Audit Committee established in accordance with Section 3(a)(58)(A) of the Exchange Act. Additional information regarding the Audit Committee that is required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Audit Committee Financial Expert

Our board of directors has determined that Glenn Sblendorio is the "audit committee financial expert" as defined by Item 407(d)(5) of Regulation S-K of the Exchange Act and are "independent" under the rules of the NASDAQ Global Market.

Item 11. Executive Compensation

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item will be set forth in our Proxy Statement for the 2014 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

The following financial statements are filed as part of this Annual Report on Form 10-K:

	<u>Page</u>
Report of Independent Registered Public Accounting Firm	F-2
Balance Sheets	F-3
Statements of Operations	F-4
Statements of Changes in Stockholders' Deficit	F-5
Statements of Cash Flows	F-6
Notes to Financial Statements	F-7

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our financial statements or notes thereto.

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following our financial statements. The Exhibit Index is incorporated herein by reference.

OPHTHOTECH CORPORATION

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm	F-2
Balance Sheets as of December 31, 2013 and 2012	F-3
Statements of Operations for the Years Ended December 31, 2013, 2012 and 2011, and the Period From January 5, 2007 (Inception) to December 31, 2013	F-4
Statements of Changes in Stockholders' Equity (Deficit) for the Period From January 5, 2007 (Inception) to December 31, 2013	F-5
Statements of Cash Flows for the Years Ended December 31, 2013, 2012 and 2011, and the Period From January 5, 2007 (Inception) to December 31, 2013	F-6
Notes to Financial Statements	F-7

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, 2013 and 2012, and the related statements of operations, changes in stockholders' deficit and cash flows for each of the three years in the period ended December 31, 2013 and for the period from January 5, 2007 (Inception) to December 31, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ophthotech Corporation at December 31, 2013 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013 and the period from January 5, 2007 (Inception) to December 31, 2013, in conformity with US generally accepted accounting principles.

/s/ Ernst & Young LLP

MetroPark, New Jersey

March 11, 2014

Ophthotech Corporation
(A Development Stage Entity)

Balance Sheets

(in thousands, except share and per share data)

	<u>December 31, 2013</u>	<u>December 31, 2012</u>
Assets		
Current assets		
Cash and cash equivalents	\$ 210,596	\$ 4,304
Prepaid expenses and other current assets	6,804	44
Other Assets	—	331
Security deposits	—	158
Total current assets	<u>217,400</u>	<u>4,837</u>
Property, plant and equipment, net	27	42
Security deposits	255	—
Total assets	<u>\$ 217,682</u>	<u>\$ 4,879</u>
Liabilities, Convertible Redeemable Series A, Series A-1, Series B, Series B-1 Preferred Stock and stockholders' equity (deficit)		
Current liabilities		
Accrued clinical drug supplies and trial costs	\$ 2,485	1,013
Accounts payable and accrued expenses	3,810	1,391
Notes payable	—	11,040
Warrant liability	—	966
Total current liabilities	<u>6,295</u>	<u>14,410</u>
Royalty purchase liability	<u>41,667</u>	<u>—</u>
Total liabilities	<u>47,962</u>	<u>14,410</u>
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	<u>—</u>	<u>113,939</u>
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, 31,413,208 shares issued and outstanding at December 31, 2013; 155,864,851 shares authorized, 1,469,798 shares issued and outstanding at December 31, 2012	31	1
Additional paid-in capital	352,739	—
Deficit accumulated during development stage	<u>(183,050)</u>	<u>(126,471)</u>
Total stockholders' equity (deficit)	<u>169,720</u>	<u>(123,470)</u>
Total liabilities and stockholders' equity (deficit)	<u>\$ 217,682</u>	<u>\$ 4,879</u>

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

Ophthotech Corporation
(A Development Stage Entity)

Statement of Operations

(in thousands, except per share data)

	Years Ended December 31,			Period from January 5, 2007 (Inception) to December 31, 2013
	2013	2012	2011	
Costs and expenses:				
Research and development	\$ 33,215	\$ 6,792	\$ 13,896	\$ 108,107
General and administrative	14,210	6,889	5,738	41,559
Total costs and expenses	<u>47,425</u>	<u>13,681</u>	<u>19,634</u>	<u>149,666</u>
Loss from operations	(47,425)	(13,681)	(19,634)	(149,666)
Interest (expense) income	(1,454)	(507)	2	(1,482)
Loss on extinguishment of debt	(1,091)	—	—	(1,091)
Other loss	(1,175)	(374)	(30)	(1,546)
Change in fair value related to investor rights liability	—	—	—	683
Net loss before income tax benefit	(51,145)	(14,562)	(19,662)	(153,102)
Income tax benefit	—	—	1,029	1,327
Net loss	(51,145)	(14,562)	(18,633)	(151,775)
Add: accretion of preferred stock dividends	(5,891)	(7,063)	(6,838)	(33,046)
Net loss attributable to common stockholders	<u>\$ (57,036)</u>	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>	<u>\$ (184,821)</u>
Net loss attributable to common stockholders per share:				
Basic and diluted	<u>\$ (6.34)</u>	<u>\$ (14.89)</u>	<u>\$ (18.27)</u>	
Weighted average common shares outstanding:				
Basic and diluted	<u>9,003</u>	<u>1,452</u>	<u>1,394</u>	

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

Ophthotech Corporation
(A Development Stage Entity)

Statement of Stockholders' Equity (Deficit)

For the Period from January 5, 2007 (Inception) to December 31, 2013

(in thousands)

	Junior Series A Preferred Stock		Common Stock		Additional paid-in capital	Deficit Accumulated During the Development Stage	Total
	Shares	Amount	Shares	Amount			
Balance at January 5, 2007 (Inception)	—	\$ —	—	\$ —	—	—	—
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)
Balance at December 31, 2007	3,000	\$ 3,000	932	\$ 1	—	\$ (15,009)	\$ (12,008)
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)
Balance at December 31, 2008	3,000	\$ 3,000	1,029	\$ 1	—	\$ (38,137)	\$ (35,136)
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)
Balance at December 31, 2009	3,000	\$ 3,000	1,136	\$ 1	—	\$ (55,768)	\$ (52,767)
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)
Balance at December 31, 2010	3,000	\$ 3,000	1,426	\$ 1	—	\$ (80,269)	\$ (77,268)
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)
Balance at December 31, 2011	3,000	\$ 3,000	1,451	\$ 1	—	\$ (105,488)	\$ (102,487)
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)
Balance at December 31, 2012	3,000	\$ 3,000	1,470	\$ 1	—	\$ (126,471)	\$ (123,470)
Issuance of common stock upon conversion of Series A, A-1, B, B-1 and C preferred stock	—	—	21,038	21	174,310	—	174,331
Issuance of common stock from initial public offering, net	—	—	8,740	9	175,546	—	175,555
Issuance of common stock upon conversion of Junior Series A Preferred Stock	(3,000)	(3,000)	—	—	—	—	(3,000)
Reclassification of warrant liability	—	—	—	—	2,179	—	2,179
Reclassification of preferred stock issuance costs	—	—	—	—	(1,804)	—	(1,804)
Exercise of stock options/warrants	—	—	165	—	94	—	94
Share-based compensation	—	—	—	—	2,871	—	2,871
Preferred Stock dividends	—	—	—	—	(457)	(5,434)	(5,891)
Net loss	—	—	—	—	—	(51,145)	(51,145)
Balance at December 31, 2013	—	\$ —	31,413	\$ 31	\$ 352,739	\$ (183,050)	\$ 169,720

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

Ophthotech Corporation
(A Development Stage Company)

Statement of Cash Flows

(in thousands)

	Years ended December 31,			Period from January 5, 2007 (Inception) to December 31, 2013
	2013	2012	2011	
Operating Activities				
Net loss	\$ (51,145)	\$ (14,562)	\$ (18,633)	\$ (151,775)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation	20	31	32	174
Amortization of debt issuance costs	88	47	—	135
Accretion of debt discount	87	59	—	146
Non-cash change in fair value of warrant liability	1,181	366	7	1,563
Non-cash change in fair value of investor rights liability	—	—	—	(683)
Loss on extinguishment of debt	1,091	—	—	1,091
Share-based compensation	2,871	640	248	4,061
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	(6,761)	21	135	(6,804)
Other receivables	—	1,036	(738)	—
Security deposits	(96)	—	—	(255)
Accrued clinical drug supplies and trial costs	1,472	(485)	(822)	2,485
Accounts payable and accrued expenses	2,375	(235)	172	3,754
Deferred rent	42	(22)	(24)	42
Net cash used in operating activities	(48,775)	(13,104)	(19,123)	(136,564)
Investing Activities				
Purchase of marketable securities	—	—	—	(4,238)
Maturities of marketable securities	—	—	3,400	4,250
Purchase of property, equipment	(5)	—	(4)	(201)
Net cash used in investing activities	(5)	—	3,396	(189)
Financing Activities				
Payment of debt issuance costs	(43)	(377)	—	(421)
Proceeds from issuance of common stock	94	2	4	218
Proceeds from initial public offering, net	175,555	—	—	175,555
(Repayments on) Proceeds from issuance of notes payable, net	(11,900)	11,387	—	(302)
Proceeds from issuance of preferred stock, net	49,699	—	14,990	130,632
Proceeds from royalty purchase agreement	41,667	—	—	41,667
Net cash provided by financing activities	255,072	11,012	14,994	347,349
Net change in cash and cash equivalents	206,292	(2,092)	(733)	210,596
Cash and cash equivalents				
Beginning of period	4,304	6,396	7,129	—
End of period	\$ 210,596	\$ 4,304	\$ 6,396	\$ 210,596
Supplemental disclosure of cash paid				
Interest	\$ 1,523	\$ 437	\$ —	\$ 1,964
Income Taxes	\$ —	\$ —	\$ —	\$ —
Supplemental disclosures of cash flow information				
Conversion of preferred stock to common stock upon completion of IPO	\$ 174,310	\$ —	\$ —	\$ 174,310
Accrued dividends on Series A, Series A-1, Series of B, B-1 and Series C Preferred Stock	\$ 5,891	\$ 7,063	\$ 6,838	\$ 33,046
Notes payable and accrued interest converted to Series A Preferred Stock	\$ —	\$ —	\$ —	\$ 212

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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to 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 back 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 losses of \$51.1 million for the year ended December 31, 2013, \$14.6 million for the year ended December 31, 2012 and \$18.6 million for the year ended December 31, 2011. As of December 31, 2013, the Company had a deficit accumulated during the development stage of \$183.1 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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

1. Business (Continued)

pharmaceutical and biotechnology companies and is dependent upon the services of its employees and 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. 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.

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.

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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

2. Significant Accounting Policies (Continued)

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
- 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.

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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

2. Significant Accounting Policies (Continued)

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 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.

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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

2. Significant Accounting Policies (Continued)

options granted to employees and non-employees and has been reported in the Company's statements of operations as follows:

	Years ended December 31,		
	2013	2012	2011
	(in thousands)		
Research and development	\$ 2,062	\$ 412	\$ 159
General and administrative	809	228	89
Total	<u>\$ 2,871</u>	<u>\$ 640</u>	<u>\$ 248</u>

The Company had no shares of unvested restricted common stock granted to employees at December 31, 2013 or at December 31, 2012, respectively.

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. There are, however, no standards for which adoption has been delayed that would have a significant impact on the financial statements of the Company.

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 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 for public companies on a prospective basis for fiscal years beginning after

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

2. Significant Accounting Policies (Continued)

December 15, 2012. As an emerging growth company as defined by the JOBS Act, the Company has delayed adoption of this pronouncement. However, the Company has not incurred any components of comprehensive income for the periods presented and the ASU requires only additional presentation, as such, there will be no impact to the Company's results of operations or financial position upon adoption.

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 stockholders, the outstanding shares of preferred stock, 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.

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

4. Net Loss Per Common Share (Continued)

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:

	Years ended December 31,		
	2013	2012	2011
Basic and diluted net loss per common share calculation:			
Net loss	\$ (51,145)	\$ (14,562)	\$ (18,633)
Accretion of preferred stock dividends	(5,891)	(7,063)	(6,838)
Net loss attributable to common shareholders	<u>\$ (57,036)</u>	<u>\$ (21,625)</u>	<u>\$ (25,471)</u>
Weighted average common shares outstanding	<u>9,003</u>	<u>1,452</u>	<u>1,394</u>
Net loss per share of common stock—basic and diluted	<u>\$ (6.34)</u>	<u>\$ (14.89)</u>	<u>\$ (18.27)</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:

	Years ended December 31,		
	2013	2012	2011
Redeemable convertible preferred stock	—	16,663	16,064
Options outstanding	2,708	1,344	1,113
Warrants	88	94	39
Total	<u>2,796</u>	<u>18,101</u>	<u>17,216</u>

5. Financing Activities

On June 18, 2007, the Company issued convertible promissory notes (the "Convertible Notes") totaling \$0.2 million to certain investors. The Convertible Notes carried an interest rate of 8% per annum. The Convertible 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 7 remained in effect within 10 days of the date of the Series A Agreement (the "First Milestone Event Closing") and (c) 17,319,656 shares upon initiation of a Phase 1b study with respect to assets acquired or licensed under certain of the Product and Technology Agreements entered into by the Company in 2007 described in Note 7. As of December 31, 2007, the Company and the Series A Investors had completed

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

5. Financing Activities (Continued)

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 Company's agreement with its collaborative partners referred to in Note 7 remained 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").

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.

Prior to the Company's initial public offering, the Series A warrants were accounted for as a liability and were marked to market using a hybrid method of an option pricing model and a probability-weighted return methodology. During the periods prior to the initial public offering, the change in fair value of the Series A warrant liability was recorded within other loss. As of December 31, 2012, the value of the Series A warrant liability was \$0.5 million 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.

Under ASC 480, *Distinguishing Liabilities from Equity*, the Company 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 adjusted the carrying value of such rights to their estimated fair value at each reporting date prior to the completion of its initial public offering. Pursuant to ASC 480, increases or decreases in the fair value of such rights were 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.

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

5. Financing Activities (Continued)

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 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 certain of its Product and Technology Agreements entered into by the Company (see Note 7), 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 7), 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.

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.

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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

5. Financing Activities (Continued)

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. In conjunction with the secured promissory note issued on March 15, 2013, 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. 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 B Preferred Stock, including for subdivisions, combinations and stock dividends.

Prior to the completion of the Company's initial public offering, the Series B warrants were accounted for as a liability and were 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 was 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.

Upon completion of the Company's IPO on September 30, 2013, the underlying preferred stock of the Series A and Series B warrants were 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 \$1.2 million for the year ended December 31, 2013.

6. 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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

6. Royalty Agreement and Series C Agreement (Continued)

Purchase and Sale Agreement, none of which have occurred prior to the date of these financial statements.

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 December 31, 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.

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

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6. Royalty Agreement and Series C Agreement (Continued)

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 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.

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Notes to Financial Statements (Continued)

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7. 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 (Eyetechn), 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 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 12—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

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Notes to Financial Statements (Continued)

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7. Product and Technology Agreements (Continued)

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, formerly known as ARC1905 (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 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 collaborative 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 deemed to be fair

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Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

7. Product and Technology Agreements (Continued)

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.

8. Property, Plant and Equipment

Property and equipment at December 31, 2013 and 2012 were as follows:

	Useful Life (Years)	December 31, 2013	December 31, 2012
Computer and other equipment	5	\$ 85	\$ 80
Furniture and fixtures	7	117	117
		202	197
Accumulated depreciation and amortization		(175)	(155)
Property, plant and equipment, net		<u>\$ 27</u>	<u>\$ 42</u>

For the years ended December 31, 2013, 2012 and 2011, depreciation expense was \$20 thousand, \$31 thousand, \$32 thousand, respectively.

9. 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, 2013, the Company does not believe any material uncertain tax positions are

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Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

9. Income Taxes (Continued)

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:

	Years ended December 31,		
	2013	2012	2011
Percent of pre-tax income:			
U.S. federal statutory income tax rate	35.0%	35.0%	35.0%
State taxes, net of federal benefit	—	—	3.4%
Permanent items	(2.2)%	(1.0)%	(0.6)%
Research and development credit	2.7%	1.0%	0.7%
Change in valuation allowance	(35.5)%	(35.0)%	(33.3)%
Effective income tax rate	<u>—</u>	<u>—</u>	<u>5.2%</u>

Significant components of the Company's deferred tax assets/liabilities for 2013 and 2012 consist of the following:

	December 31,	
	2013	2012
Deferred tax assets/(liabilities)		
Federal net operating loss carryforwards	\$ 30,084	\$ 29,464
State and local net operating loss carryforwards	5,026	4,825
License and technology payments	6,407	5,566
Share-based compensation	1,396	476
Depreciation	(7)	(11)
Federal research and development credit carryforwards	2,966	1,562
State research and development credit carryforwards	1,483	781
Deferred income tax assets	<u>47,355</u>	<u>42,663</u>
Valuation allowance	(47,355)	(42,663)
Net deferred tax assets (liabilities)	<u>—</u>	<u>—</u>

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

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9. Income Taxes (Continued)

therefore, the deferred tax assets are fully offset by a valuation allowance at December 31, 2013 and 2012.

Deferred tax assets relating to employee share-based compensation deductions were reduced to reflect exercises of non-qualified stock option grants and vesting of restricted stock. Although certain of these deductions were reported on the corporate tax returns and increased net operating losses, these related tax benefits were not recognized for financial reporting purposes. The Company has unrealized excess tax benefits related to stock based compensation costs of \$0.8 million that it expects to credit to stockholder's equity in future periods.

The following table summarizes carryforwards of net operating losses and tax credits as of December 31, 2013:

	<u>Amount</u>	<u>Expiration</u>
Federal net operating losses	\$ 85,955	2033
Research and development credits	\$ 2,966	2033

The federal, state, and local net operating loss carryforwards will start to expire in 2027. 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 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.

10. 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 in January 2019, whereas the Company's New York, New York office space lease expires in February 2020.

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Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

10. Operating Leases (Continued)

Future minimum rental commitments under noncancelable operating leases in effect as of December 31, 2013, are as follows:

2014	\$ 777
2015	894
2016	875
2017	877
2018	884
Thereafter	740
Total	<u>\$ 5,047</u>

Rent expense is calculated on the straight-line basis and amounted to \$0.5 million, \$0.4 million and \$0.4 million for the years ended December 31, 2013, 2012 and 2011, respectively.

11. 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. Such amounts were approximately \$0.3 million and \$0.2 million as of December 31, 2013 and 2012, respectively.

12. Commitments and Contingencies

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

- Under the Company's acquisition agreement with OSI (Eyetechnology), Inc., which agreement is now held by OSI Pharmaceuticals, Inc., ("OSI Pharmaceuticals"), a subsidiary of Astellas US, LLC, for rights to particular anti-PDGF aptamers, including Fovista, the Company is 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. 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 the Company successfully commercializes.
- Under a license agreement with Archemix Corp., ("Archemix"), with respect to pharmaceutical products comprised of or derived from any anti-PDGF aptamer, the Company is obligated to make future payments to Archemix of up to an aggregate of \$14.0 million if the Company achieves specified clinical and regulatory milestones with respect to Fovista, up to an aggregate of \$3.0 million if the Company achieves specified commercial milestones with respect to Fovista and, for each other anti-PDGF aptamer product that the Company may develop under the agreement, up to an aggregate of approximately \$18.8 million if the Company achieves specified clinical and regulatory milestones and up to an aggregate of \$3.0 million if the Company achieves specified commercial milestones. No royalties are payable to Archemix under this license agreement. From inception through December 31, 2013, the Company has made

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Notes to Financial Statements (Continued)

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12. Commitments and Contingencies (Continued)

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 the Company's 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 the Company may develop under the agreement, including Zimura (formerly known as ARC1905), the Company is obligated to make future payments to Archemix of up to an aggregate of \$57.5 million if the Company 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 the Company achieves specified commercial milestones. The Company is also obligated to pay Archemix a double-digit percentage of specified non-royalty payments the Company may receive from any sublicensee of its rights under this license agreement. No royalties are payable to Archemix under this license agreement. From inception through December 31, 2013, the Company has made payments totaling \$2.0 million under this agreement.
- Under a license, manufacturing and supply agreement with Nektar Therapeutics ("Nektar"), for specified pegylation reagents used to manufacture Fovista, the Company is obligated to make future payments to Nektar of up to an aggregate of \$4.5 million if the Company achieves specified clinical and regulatory milestones, and an additional payment of \$3.0 million if the Company achieves a specified commercial milestone with respect to Fovista. The Company is obligated to pay Nektar tiered royalties at low to mid-single-digit percentages of net sales of any licensed product the Company successfully commercializes, with the royalty percentage determined by the Company's level of licensed product sales, the extent of patent coverage for the licensed product and whether the Company 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 the Company receives in connection with granting any third-party commercialization rights to a licensed product less certain milestone events the Company has previously paid, and a higher double-digit percentage of other specified amounts, such as milestone payments, the Company receives in connection with any such commercialization agreement, subject to agreed minimum and maximum amounts. From inception through December 31, 2013, the Company has 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 the Company's Phase 3 clinical program for Fovista in August 2013.
- Under the Company's royalty agreement with Novo A/S with respect to Fovista, the Company is 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.

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Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

12. Commitments and Contingencies (Continued)

The Company also has 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, the Company has agreements with contract service providers to assist in the performance of the Company's research and development and manufacturing activities. Expenditures to CROs represent a significant cost in clinical development. The Company can elect to discontinue the work under these agreements at any time. The Company 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.

13. 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 year ended December 31, 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 the Company's 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 December 31, 2013, the Company had approximately 2,708,000 stock options outstanding under the 2013 Plan and approximately 503,000 shares available for grant under the 2013 Plan. In

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Notes to Financial Statements (Continued)

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13. Stock Option and Compensation Plans (Continued)

connection with the evergreen provisions of the 2013 Plan, the number of shares available for issuance under the 2013 Plan was increased by approximately 1,257,000, effective as of January 1, 2014.

Cash proceeds from, and the aggregate intrinsic value of, stock options exercised during the years ended December 31, 2013, 2012 and 2011, respectively, were as follows:

	Year ended December 31		
	2013	2012	2011
Cash proceeds from options exercised	\$ 93	\$ 2	\$ 4
Aggregate intrinsic value of options exercised	\$ 4,545	\$ 28	\$ 36

A summary of the stock option activity, weighted average exercise prices, options outstanding and exercisable as of December 31, 2013 is as follows:

	For the Year ended December 31,					
	2013		2012		2011	
	Common Stock Options	Weighted Average Exercise Price	Common Stock Options	Weighted Average Exercise Price	Common Stock Options	Weighted Average Exercise Price
Outstanding at beginning of year:	1,344	\$ 1.65	1,113	\$ 1.30	953	\$ 1.20
Granted	1,583	\$ 14.82	250	\$ 3.12	184	\$ 1.65
Exercised	(151)	\$ 0.61	(19)	\$ 0.12	(24)	\$ 0.17
Expired or forfeited	(68)	\$ 1.53	—	—	—	—
Outstanding at end of year:	2,708	\$ 9.41	1,344	\$ 1.65	1,113	\$ 1.30

	Year ended December 31,		
	2013	2012	2011
Options exercisable at end of year	984	823	561
Weighted average grant date fair value (per share) of options granted during the period	\$ 10.48	\$ 1.65	\$ 1.18

	As of December 31, 2013				
	Total Options Outstanding	Options Outstanding		Options Exercisable	
		Weighted Average Remaining Life (Years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
<u>Range of Exercise Prices</u>					
\$0.12 - \$10.03	1,800	7.8	\$ 4.89	969	\$ 2.50
\$10.04 - \$20.00	604	9.5	\$ 13.37	10	\$ 13.22
\$20.01 - \$33.27	304	9.8	\$ 28.34	5	\$ 32.58
	2,708			984	
Aggregate Intrinsic Value	\$ 62,185			\$ 29,107	

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Notes to Financial Statements (Continued)

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13. Stock Option and Compensation Plans (Continued)

In connection with stock option awards granted to employees, the Company recognized share-based compensation expense approximately \$2.2 million, \$0.5 million, and \$0.2 million, for the years ended December 31, 2013, 2012, and 2011, respectively. As of December 31, 2013, there was approximately \$14.6 million of unrecognized compensation costs, net of estimated forfeitures, related to stock option awards to employees, which are expected to be recognized over a remaining weighted average period of 3.3 years.

In connection with stock options awards granted to consultants, the Company recognized approximately \$0.7 million, \$0.1 million and \$0.1 million in share-based compensation expense during the years ended December 31, 2013, 2012 and 2011, respectively. As of December 31, 2013, there were approximately \$1.9 million of unrecognized compensation costs, net of estimated forfeitures, related to stock option award granted to consultants which are expected to be recognized over a remaining weighted average period of 3.0 years.

14. Employee Benefit Plan

The Company maintains a defined contribution 401(k) plan available to employees. Employee contributions are voluntary and are determined on an individual basis, limited by the maximum amounts allowable under federal tax regulations. The Company does not match any of the employee contributions.

15. 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.

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(tabular dollars and shares in thousands, except per share data)

15. 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, 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)
Assets			
Investments in U.S. Treasury money market funds*	\$ 203,828	\$ —	\$ —
Liabilities			
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 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)
Assets			
Investments in money market funds*	\$ 524	\$ —	\$ —
Liabilities			
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.

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 Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

15. 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 years ended December 31, 2013 and 2012:

	Level 3	
	Series A Warrant Liability	Series B Warrant Liability
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	523	443
Warrants issued in connection with venture debt facility	—	32
Change in fair value of warrant liability	379	802
Conversion of warrant liability to equity	(902)	(1,277)
Balance at December 31, 2013	\$ —	\$ —

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 \$1.2 million as other loss in its results of operations for the year ended December 31, 2013.

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

16. 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.

The Company repaid in full the outstanding principal of the Notes, together with accrued and unpaid 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 year ended December 31, 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 year ended December 31, 2013.

17. Selected Quarterly Financial Information (unaudited)

The following is a summary of the quarterly results of operations for the years ended December 31, 2013 and 2012

	2013			
	March 31	June 30	September 30	December 31
Revenues	\$ —	\$ —	\$ —	\$ —
Research and development	2,390	4,345	11,101	15,379
General and administrative	1,738	3,241	4,166	5,065
Loss from operations	(4,128)	(7,586)	(15,267)	(20,444)
Net loss attributable to common shareholders	\$ (6,361)	\$ (11,863)	\$ (18,424)	\$ (20,388)
Basic and diluted earnings per common share	\$ (4.33)	\$ (8.07)	\$ (10.26)	\$ (0.65)

	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)	\$ (3.81)

18. Subsequent Events

On January 23, 2014, in connection with its royalty agreement with Novo A/S, the Company received cash proceeds of approximately \$41.7 million in royalty financing 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

OPHTHOTECH CORPORATION
(A Development Stage Company)

Notes to Financial Statements (Continued)

(tabular dollars and shares in thousands, except per share data)

18. Subsequent Events (Continued)

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.

On February 18, 2014, the Company closed a follow-on public offering of 2,628,571 shares of common stock at a public offering price of \$31.50 per share of common stock. The Company sold 1,900,000 shares and 728,571 shares were sold by selling stockholders, 342,857 of which were sold by the selling stockholders upon the full exercise by the underwriters of their option to purchase additional shares in the offering. Net proceeds to the Company were approximately \$55.5 million, after deducting underwriters' commissions and other offering expenses. The Company did not receive any proceeds from the sale of shares by the selling stockholders in the offering.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
3.1	Restated Certificate of Incorporation of the Registrant	S-1/A	333-190643	9/9/2013	3.3	
3.2	Amended and Restated Bylaws of the Registrant	S-1/A	333-190643	9/9/2013	3.4	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-190643	9/9/2013	4.1	
10.1	Amended and Restated 2007 Stock Incentive Plan, as amended	S-1	333-190643	8/15/2013	10.1	
10.2	Form of Incentive Stock Option Agreement under Amended and Restated 2007 Stock Incentive Plan	S-1	333-190643	8/15/2013	10.2	
10.3	Form of Nonstatutory Stock Option Agreement under 2007	S-1	333-190643	8/15/2013	10.3	
10.4	2013 Stock Incentive Plan	S-1/A	333-190643	9/9/2013	10.4	
10.5	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-190643	9/9/2013	10.5	
10.6	Form of Nonqualified Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-190643	9/9/2013	10.6	
10.7	Lease Agreement, dated as of September 30, 2007, between the Registrant and One Penn Plaza LLC, as the same has been supplemented by agreement dated March 12, 2013 and amended by the Amendment of Lease, dated as of August 30, 2013 and Second Amendment to Lease, entered into on January 7, 2014	S-1	333-193681	1/31/2014	10.7	
10.8	Lease Agreement with Carnegie 214 Associates Limited Partnership, dated as of October 25, 2013	S-1	333-193681	1/31/2014	10.8	
10.9†	Divestiture Agreement, dated as of July 27, 2007, by and between the Registrant and (OSI) Eyetech, Inc.	S-1	333-190643	8/15/2013	10.9†	
10.10†	License, Manufacturing and Supply Agreement, dated as of September 30, 2006, by and between Nektar Therapeutics AL, Corporation and (OSI) Eyetech, Inc., as the same was assigned to the Registrant on July 27, 2007 and amended by Amendment No. 1 thereto, dated as of April 5, 2012, and supplemented by a letter agreement, dated as of June 20, 2013	S-1	333-190643	8/15/2013	10.10†	

Exhibit Number	Description of Exhibit	Incorporated by Reference			Filed Herewith
		Form	File Number	Date of Filing	
10.11†	Amended and Restated Exclusive License Agreement, dated as of September 12, 2011, by and between the Registrant and Archemix Corp., as amended by Amendment No. 1 thereto dated December 20, 2011 and supplemented by a letter agreement, dated as of April 30, 2012	S-1	333-190643	8/15/2013	10.11†
10.12†	Amended and Restated Exclusive License Agreement, dated as of September 12, 2011, by and between the Registrant and Archemix Corp., as amended by Amendment No. 1 thereto, dated as of December 20, 2011	S-1	333-190643	8/15/2013	10.12†
10.13†	Purchase and Sale Agreement, dated as of May 23, 2013, by and between the Registrant and Novo A/S	S-1	333-190643	8/15/2013	10.13†
10.14+	Offer of Employment between the Registrant and David Guyer	S-1/A	333-190643	9/9/2013	10.14
10.15+	Second Amended and Restated Employment Agreement between the Registrant and Samir Patel	S-1/A	333-190643	9/9/2013	10.15
10.16+	Amended and Restated Offer of Employment between the Registrant and Bruce Peacock	S-1/A	333-190643	9/9/2013	10.16
10.17	Office Lease Agreement, dated as of August 22, 2013, by and between the Registrant and PSN Partners, L.P.	S-1/A	333-190643	9/9/2013	10.17
23.1	Consent of Ernst & Young LLP				Yes
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.				Yes
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.				Yes
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				Yes

Exhibit Number	Description of Exhibit	Incorporated by Reference			Filed Herewith
		Form	File Number	Date of Filing	
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				Yes
101.INS	XBRL Instance Document.				Yes
101.SCH	XBRL Taxonomy Extension Schema Document.				Yes
101.CAL	XBRL Taxonomy Calculation Linkbase Document.				Yes
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				Yes
101.LAB	XBRL Taxonomy Label Linkbase Document.				Yes
101.PRE	XBRL Taxonomy Presentation Linkbase Document.				Yes

† Confidential treatment has been requested as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

+ Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

- (1) Registration Statement (Form S-8 No. 333-193694) pertaining to the 2013 Stock Incentive Plan of Ophthotech Corporation effective January 31, 2014,
- (2) Registration Statement (Form S-8 No. 333-191767) pertaining to the 2013 Stock Incentive Plan and Amended and Restated 2007 Stock Incentive Plan of Ophthotech Corporation effective October 16, 2013,

of our report dated March 11, 2014, with respect to the financial statements of Ophthotech Corporation, included in this Annual Report (Form 10-K) for the year ended December 31, 2013.

/s/ ERNST & YOUNG LLP

MetroPark, New Jersey
March 11, 2014

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[Exhibit 23.1](#)

[CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM](#)

CERTIFICATIONS

I, David R. Guyer, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Ophthotech Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2014

By: /s/ DAVID R. GUYER, M.D.

David R. Guyer, M.D.
Chief Executive Officer
(Principal Executive Officer)

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[Exhibit 31.1](#)

[CERTIFICATIONS](#)

CERTIFICATIONS

I, Bruce A. Peacock, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ophthotech Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2014

By: /s/ BRUCE A. PEACOCK

Bruce A. Peacock
Chief Financial and Business Officer
(Principal Financial Officer)

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[Exhibit 31.2](#)

[CERTIFICATIONS](#)

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Ophthotech Corporation (the "Company") for the year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David R. Guyer, M.D., Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2014

By: /s/ DAVID R. GUYER M.D.

David R. Guyer M.D.
Chief Executive Officer
(Principal Executive Officer)

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[Exhibit 32.1](#)

[CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002](#)

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Ophthotech Corporation (the "Company") for the year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Bruce A. Peacock, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2014

By: /s/ BRUCE A. PEACOCK

Bruce A. Peacock
Chief Financial and Business Officer
(Principal Financial Officer)

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[Exhibit 32.2](#)

[CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002](#)