AERIE PHARMACEUTICALS INC
Form S-1/A
October 21, 2013
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As filed with the Securities and Exchange Commission on October 21, 2013

Registration No. 333-191219

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 3

to

FORM S-1

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

AERIE PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	2836	20-3109565
(State or other jurisdiction of incorporation or organization)	(Primary standard industrial classification code number)	(I.R.S. employer identification number)

135 US Highway 206, Suite 15

Bedminster, New Jersey 07921

(908) 470-4320

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Vicente Anido, Jr., PhD

Chief Executive Officer

Aerie Pharmaceuticals, Inc.

135 US Highway 206, Suite 15

Bedminster, New Jersey 07921

Tel. No.: (908) 470-4320

Fax No.: (908) 470-4329

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Andrew B. Barkan, Esq.	*Copies to:* **Richard J. Rubino**	**Glenn R. Pollner, Esq.**
Steven G. Scheinfeld, Esq.	**Chief Financial Officer**	**Gibson, Dunn & Crutcher LLP**
Fried, Frank, Harris, Shriver & Jacobson LLP	**Aerie Pharmaceuticals, Inc.**	**200 Park Avenue**
One New York Plaza	**135 US Highway 206, Suite 15**	**New York, New York 10166**
New York, New York 10004	**Bedminster, New Jersey 07921**	**Tel. No.: (212) 351-4000**
Tel. No.: (212) 859-8000	**Tel. No.: (908) 470-4320**	**Fax No.: (212) 351-4035**
Fax No.: (212) 859-4000	**Fax No.: (908) 470-4329**	

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ¨

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

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 12b2 of the Exchange Act. (Check one):

Large Accelerated Filer ¨	Accelerated filer ¨
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company ¨

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED[1]	PROPOSED MAXIMUM OFFERING PRICE PER SHARE	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE [2]	AMOUNT OF REGISTRATION FEE[3]
Common Stock, $0.001 par value per share	6,037,500	$14.00	$84,525,000	$11,323.82

(1) Includes shares of common stock that may be purchased by the underwriters upon the exercise of their option to purchase additional shares, if any.
(2) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(a) under the Securities Act of 1933.
(3) Previously paid.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information contained in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED OCTOBER 21, 2013

PRELIMINARY PROSPECTUS

5,250,000 Shares

Common Stock

We are offering 5,250,000 shares of our common stock. This is our initial public offering and no public market currently exists for our common stock. We expect the initial public offering price to be between $12.00 and $14.00 per share. We have applied to list our common stock on the NASDAQ Global Market under the symbol AERI.

Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page 13 of this prospectus.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, and will be subject to reduced public company reporting requirements.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public Offering Price	$	$
Underwriting Discounts and Commissions	$	$
Proceeds to Aerie Pharmaceuticals, Inc. before expenses [1]	$	$

[1] See Underwriting for additional information regarding underwriter compensation.

Our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of approximately $10 million of shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, any of these stockholders may determine to purchase more, less or no shares in this offering, or

the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders.

Delivery of the shares of common stock is expected to be made on or about , 2013. We have granted the underwriters an option for a period of 30 days to purchase an additional 787,500 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $, and the total proceeds to us, before expenses, will be $.

RBC Capital Markets **Stifel**

Canaccord Genuity **Needham & Company**

Prospectus dated , 2013

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You should rely only on the information contained in this prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We have not authorized anyone to provide you with information that is different. We are offering to sell shares of our common stock, and seeking offers to buy shares of our common stock, only in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

Until and including , 2013, 25 days after the date of this prospectus, all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer s obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.

For investors outside of the United States: neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. Before you decide to invest in our common stock, you should read the entire prospectus carefully, including the Risk Factors section and the financial statements and related notes appearing at the end of this prospectus. In this prospectus, unless otherwise stated or the context otherwise indicates, references to Aerie, we, us, our and similar references refer to Aerie Pharmaceuticals, Inc.

Overview

We are a clinical-stage pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with glaucoma and other diseases of the eye. Glaucoma is one of the largest segments in the global ophthalmic market. In 2012, branded and generic glaucoma product sales exceeded $4.5 billion in the United States, Europe and Japan in aggregate, according to IMS, and prescription volume is expected to grow, driven in large part by the aging population. Our strategy is to advance our product candidates, including dual-action AR-13324 and triple-action PG324, to regulatory approval and commercialize these products ourselves in the United States. We plan to build a commercial team of approximately 100 sales representatives to target approximately 10,000 high prescribing eye-care professionals throughout the United States. For certain key markets outside the United States, including Europe, Japan and emerging markets, we intend to explore partnership opportunities through collaboration and licensing arrangements. We plan to further maximize our commercial potential by identifying and advancing additional product candidates, both through our internal discovery efforts and through possible in-licensing or acquisitions of additional ophthalmic products or product candidates that would complement our current product portfolio. Our senior leadership team has extensive experience in the ophthalmology market and has overseen the development and commercialization at major pharmaceutical companies of several successful ophthalmic products, including *Acular*, *Alphagan P*, *Bepreve*, *Besivance*, *Bromday*, *Istalol*, *Ocuflox*, *Retisert*, *Vitrase*, *Xibrom* and *Zylet*. If our products are approved and we are commercially successful, we believe Aerie could become a market-leading ophthalmic company.

Our product candidates are once-daily eye drops that, if approved, will provide eye-care professionals with the first novel intraocular pressure-lowering mechanisms of action, or MOA, to treat glaucoma in nearly 20 years. Our lead product candidate, dual-action AR-13324, recently completed a Phase 2b clinical trial. We are currently planning two Phase 3 registration trials for this product candidate, which we expect to commence in mid-2014. Additionally, we are planning to commence a Phase 2b clinical trial by early 2014 for our triple-action PG324, a fixed-dose combination of AR-13324 and the prostaglandin analogue, or PGA, latanoprost, the most commonly prescribed drug for the treatment of patients with glaucoma.

Glaucoma is a progressive and highly individualized disease, in which elevated levels of intraocular pressure, or IOP, are associated with damage to the optic nerve, which results in irreversible vision loss and potentially blindness. Patients may suffer the adverse effects of glaucoma across a wide range of IOP levels. The level of IOP in healthy individuals is generally accepted to be 10 to 21 millimeters of mercury, or mmHg. The majority of glaucoma patients have IOP of 26 mmHg or below at the time of diagnosis, which we refer to as low to moderately elevated IOP. Glaucoma is treated by the reduction of IOP, which has been shown to slow the progression of vision loss. The U.S. Food and Drug Administration, or FDA, recognizes sustained lowering of IOP as the primary clinical endpoint for regulatory approval. Once glaucoma develops, it is a chronic condition that requires life-long treatment. The initial treatment for glaucoma patients is typically the use of a prescription eye drop. PGAs have become the most widely prescribed glaucoma drug class. The most frequently prescribed PGA is once-daily latanoprost. The most commonly prescribed non-PGA drugs belong to the beta blocker class. The most frequently prescribed beta blocker is twice-daily timolol. Other non-PGA drug classes include the alpha agonists and carbonic anhydrase inhibitors. When PGA monotherapy is insufficient to control IOP, non-

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PGA products are used either as add-on therapy to the PGA or as an alternative monotherapy. Due to the multiple daily dosings, side effects and contraindications of non-PGA products, we believe there is a significant unmet need in the non-PGA market segment, which represents approximately half of the U.S. and European glaucoma market based on prescription volumes.

Our primary product candidates, once-daily dual-action AR-13324 and once-daily triple-action PG324, lower IOP through novel MOAs. Our product candidates inhibit both Rho Kinase, or ROCK, and the norepinephrine transporter, or NET. Through ROCK inhibition, they reduce IOP by increasing fluid outflow through the trabecular meshwork, or the TM, the tissue responsible for elevated IOP in glaucoma and the eye s primary drain, which accounts for approximately 80% of fluid drainage. Through NET inhibition, AR-13324 also lowers IOP by reducing the production of eye fluid. PG324, a single-drop fixed-dose combination of AR-13324 with latanoprost, lowers IOP through the same MOAs as AR-13324, and also by increasing fluid outflow through the uveoscleral pathway, the eye s secondary drain.

We believe that dual-action AR-13324 has several significant differentiating characteristics that would make it a strong competitor in the non-PGA market segment, if approved, including:

Strong IOP-Lowering Effect In our Phase 2b clinical trial, once-daily AR-13324 demonstrated mean IOP reductions of 5.7 and 6.2 mmHg on days 28 and 14, respectively. Studies have shown that a sustained 5 mmHg reduction in IOP reduces risk of disease progression by approximately 50%. If confirmed in our planned Phase 3 registration trials, we believe this level of IOP reduction would equal or exceed that of all currently marketed non-PGA drugs.

Once-Daily Dosing Advantage The most commonly prescribed non-PGA drugs are dosed two to three times daily. AR-13324 is being developed as a once-daily dosed glaucoma therapy. This more convenient dosing regimen is expected to result in higher patient compliance, which may lead to improved outcomes.

Favorable Tolerability Profile Currently marketed non-PGA drugs have several tolerability issues indicated on their product labels, including blurred vision, unusual tastes, ocular allergic reaction and itching of the eye. In our Phase 2a and Phase 2b clinical trials for AR-13324, a total of 209 patients were exposed to AR-13324. The main tolerability finding for AR-13324 was transient, or temporary, hyperemia, which is a cosmetic asymptomatic redness of the eye. Most hyperemia was scored as mild. Hyperemia is a common tolerability finding associated with the most widely prescribed glaucoma drugs.

Lack of Systemic Side Effects AR-13324 has demonstrated a lack of systemic side effects in clinical trials to date. The currently marketed non-PGA drugs have systemic side effect issues indicated on their product labels, including among others, lethargy, reduced heart rate, Stevens Johnson syndrome and blood dyscrasias. Further, the most widely prescribed non-PGA drug, timolol, has contraindications, including bronchospasm, arrhythmia and heart failure.

Novel Dual-Action MOA If approved, we believe AR-13324 would be the only once-daily drug available that specifically targets the TM, the diseased tissue responsible for elevated IOP in glaucoma. We believe AR-13324 will also be the first glaucoma drug to inhibit NET, which reduces fluid production in the eye. In addition, we believe the AR-13324 dual-action MOA is highly complementary to the MOA of the market-leading PGAs, which increase fluid outflow through the uveoscleral pathway.

Consistent IOP-Lowering Effect Across Various Baseline IOPs In our Phase 2b clinical trial, AR-13324 demonstrated a distinct ability to reduce IOP at consistent levels across all baseline IOPs tested in the trial. Published studies have indicated that currently marketed PGA and non-PGA drugs do not lower IOP as effectively in patients with low to moderately elevated baseline IOPs relative to patients with higher IOPs. Patients with low to moderately elevated IOPs represent the significant majority of glaucoma patients.

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Despite various safety and tolerability issues and the need to dose two to three times daily, the most commonly prescribed non-PGA drugs each generated peak annual global revenues over $400 million prior to the introduction of their generic equivalents.

Based on our preclinical data to date, we believe that triple-action PG324 would be the only glaucoma product that covers the full spectrum of IOP-lowering mechanisms, giving it the potential to provide a greater IOP-lowering effect than any currently approved glaucoma product. Therefore, we believe that PG324 could compete with both PGA and non-PGA therapies.

We own the worldwide rights to all indications for our current product candidates. Our intellectual property portfolio contains patents and pending patent applications related to composition of matter, pharmaceutical compositions and methods of use for our product candidates. We have patent protection for our primary product candidates, AR-13324 and PG324, in the United States through at least 2030.

Our Product Pipeline

We discovered and developed our product candidates internally through a rational drug design approach that coupled medicinal chemistry with high content screening of compounds in proprietary cell-based assays. We selected and formulated our product candidates for preclinical *in vivo* testing following a detailed characterization of over 1,500 synthesized ROCK-selective and dual-action ROCK/NET inhibitors. We advanced one compound from each of these drug classes into Phase 2 clinical development to determine whether our single-action ROCK-selective drug, AR-12286, or our dual-action ROCK/NET drug, AR-13324, offered the better efficacy and tolerability profile in patients with glaucoma. We selected dual-action AR-13324 for advancement to Phase 3 clinical development based upon its superior clinical profile relative to AR-12286. We continue to discover and develop new compounds in our research laboratories and employ a scientific staff with expertise in medicinal chemistry, analytical chemistry, biochemistry, cell biology, pharmacology and pharmaceutical science.

Our decision to advance AR-13324 and discontinue development of AR-12286 was based upon a comparison of the outcomes of similarly designed 28-day Phase 2 clinical trials of the respective compounds. The trials showed that the IOP-lowering effect of AR-12286 declined by 1.4 mmHg from day 7 to day 28, while AR-13324 provided a stable IOP-lowering effect from day 7 to day 28. In addition, a subsequent three-month Phase 2 clinical trial for AR-12286 revealed that AR-12886 s loss of efficacy continued beyond day 28. Therefore, in June 2013, we discontinued development of AR-12286 and its fixed-dose combination product PG286, a combination of AR-12286 and the PGA travoprost.

Our lead product candidate AR-13324 has several important characteristics that distinguish it from AR-12286. AR-13324 lowers IOP through a dual mechanism of action by inhibiting both ROCK and NET, whereas AR-12286 has a single mechanism of action inhibiting only ROCK. In addition, AR-13324 has a distinct chemical composition that, when converted into its active form in the eye, results in a molecule that is ten times more potent at inhibiting ROCK than AR-12286. Furthermore, in addition to being a potent inhibitor of ROCK, AR-13324 also inhibits Protein Kinase C, or PKC, which we believe is an alternate pathway for smooth muscle contraction that can lead to contraction of the TM, even when ROCK is inhibited. AR-12286 does not inhibit PKC. Also, in a six-month toxicology study with exaggerated dosing of AR-12286, lens opacities, otherwise known as cataracts, were observed in rabbit eyes beginning at three months. In a similar six-month toxicology study with exaggerated dosing of AR-13324, no adverse lens effects were observed.

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The following table summarizes each of our existing product candidates, their MOAs and their development status, as well as our intellectual property rights for these product candidates.

	Product Candidate and Mechanism	Phase of Development	Intellectual Property Rights
AR-13324	Dual-action ROCK/NET inhibitor	Phase 3 registration trials expected to begin mid-2014	Wholly-Owned
PG324	Triple-action Combination of dual-action AR-13324 and latanoprost, a PGA	Phase 2b clinical trial expected to begin by early 2014	Wholly-Owned
AR-13533	Dual-action Second generation ROCK/NET inhibitor	Preclinical	Wholly-Owned

Overview of Dual-Action AR-13324

Our lead product candidate, AR-13324, is the first of a new dual-action class of glaucoma drugs that was discovered by our scientists. AR-13324 is a once-daily eye drop designed to reduce IOP in patients with glaucoma or ocular hypertension. It increases fluid outflow through the primary drain of the eye while also reducing eye fluid production. It acts through the inhibition of both ROCK and NET. In addition, AR-13324 has inhibitory activity against a secondary signaling pathway, PKC, which acts in parallel to the primary signaling pathway, ROCK, to promote cell contraction in the TM, contributing to the ability of AR-13324 to maintain its efficacy.

We completed an AR-13324 Phase 2b clinical trial in May 2013. This 28-day trial included 224 patients who were treated once daily with AR-13324 or latanoprost. Although AR-13324 is expected to compete primarily against other non-PGA drugs, latanoprost was used as the comparator because it is the most widely-prescribed drug of all currently marketed glaucoma products. In the Phase 2b trial, AR-13324 was highly effective with once-daily dosing at lowering IOP, with the highest dose resulting in mean IOP reductions of 5.7 and 6.2 mmHg on days 28 and 14, respectively. In the analysis of the full clinical trial cohort with a baseline IOP range of 22 to 36 mmHg, the mean IOP lowering for our once-daily AR-13324 was 1.2 mmHg less than that of latanoprost and in line with published historical data for twice-daily timolol, the most commonly prescribed non-PGA drug.

In a protocol specified analysis of patients with a moderately elevated baseline IOP range of 22 to 26 mmHg, the mean IOP lowering of latanoprost and AR-13324 were clinically and statistically equivalent. While latanoprost produced smaller IOP reductions in patients with moderately elevated IOPs than in patients with highly elevated IOPs, AR-13324 was shown to maintain essentially the same IOP-lowering effect irrespective of the baseline. Publications have reported a similarly declining efficacy trend, in line with that observed for latanoprost, for currently marketed non-PGA glaucoma drugs, including timolol. We believe this should place AR-13324 in a favorable competitive position because a significant majority of glaucoma patients have such moderately elevated baseline IOP.

We are planning two Phase 3 registration trials that will measure efficacy of AR-13324 over three months and safety over 12 months. The trials will include at least 1,200 patients in total. The primary efficacy endpoint of the trials will be to demonstrate non-inferiority of IOP lowering for AR-13324 (dosed once daily) compared to timolol (dosed twice daily), the most widely used comparator in registration trials for glaucoma. Assuming we commence the Phase 3 trials in mid-2014 as planned and fully enroll the trials within our anticipated timeframe, we would expect efficacy data from the two trials in mid-2015.

If approved, AR-13324 is expected to compete against non-PGA products, the significant majority of which have been in the market for at least 20 years. The non-PGA market segment represents approximately half of the total prescription volume of the glaucoma market, for which 2012 branded and generic product sales exceeded $4.5

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billion in the United States, Europe and Japan in aggregate according to IMS. Due to the multiple daily dosings, side effects and contraindications of the currently marketed non-PGA products, we believe there is a significant unmet need in this market segment. We believe that AR-13324 has several significant differentiating characteristics that would make it a strong competitor in the non-PGA market segment.

Overview of Triple-Action PG324

Our once-daily, triple-action product candidate PG324 is a combination of our dual-action compound AR-13324 formulated with latanoprost in a single eye drop. If approved, we believe that PG324 would be the first glaucoma product to lower IOP through all three MOAs:

- increasing fluid outflow through the TM, the eye s primary drain,
- increasing fluid outflow through the uveoscleral pathway, the eye s secondary drain, and
- reducing fluid production in the eye.

Triple-action PG324 has been tested in a preclinical primate model to assess its effectiveness at lowering IOP. The results of this three-day study show that at all time points measured, PG324 dosed once daily reduced IOP substantially more than latanoprost alone dosed once daily.

We plan to commence a randomized, controlled 28-day Phase 2b clinical trial in approximately 300 patients by early 2014. The trial will be designed to measure the efficacy of two concentrations of PG324 compared to latanoprost and to AR-13324, all dosed once daily. The efficacy endpoint will be superiority of PG324 to each of its components. Assuming we commence the Phase 2b trial by early 2014 and fully enroll the trial within our anticipated timeframe, we would expect results in mid-2014.

We believe PG324, if approved, would be the only glaucoma product that covers the full spectrum of IOP-lowering mechanisms, thereby giving it the potential to provide a greater IOP-lowering effect than any currently approved glaucoma product and could compete in both the PGA and non-PGA markets.

Overview of Second-Generation, Dual-Action AR-13533

In addition to our primary product candidates, AR-13324 and PG324, we are in the preclinical development stage with AR-13533, our second generation dual-action ROCK/NET inhibitor. AR-13533 does not require enzymatic conversion in the eye to deliver maximal ROCK inhibitor activity, and therefore AR-13533 may provide additional IOP-lowering effect in patients beyond that obtained with AR-13324. We have not submitted an investigational new drug application, or IND, for AR-13533 to the FDA and there can be no assurance that an IND will be submitted.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of innovative pharmaceutical products for the treatment of patients with glaucoma and other diseases of the eye. We believe our product candidates have the potential to address many of the unmet medical needs in the glaucoma market. Key elements of our strategy are to:

Advance the development of our product candidates to approval. Based on the results from our Phase 2b clinical trial for dual-action AR-13324, we plan to proceed into Phase 3 registration trials for this drug. Additionally, we plan to initiate a Phase 2b clinical trial for PG324, our triple-action combination of AR-13324 and latanoprost and, over the longer term, to evaluate opportunities associated with preclinical-stage AR-13533, our second generation dual-action ROCK/NET inhibitor.

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Establish internal sales capabilities to commercialize our product candidates in the United States. We own worldwide rights to all indications for our product candidates and we plan to retain U.S. commercialization rights. Ultimately, if our product candidates are approved, we plan to build a commercial team of approximately 100 sales representatives. We expect our sales organization to target approximately 10,000 high prescribing eye-care professionals throughout the United States.

Explore partnerships with leading pharmaceutical and biotechnology companies to maximize the value of our product candidates outside the United States. We currently plan to explore the licensing of commercialization rights or other forms of collaboration with qualified potential partners for the commercialization of our product candidates in certain key markets outside of the United States, including Europe, Japan and emerging markets.

Continue to leverage and strengthen our intellectual property portfolio. We believe we have a strong intellectual property position relating to our product candidates. Our intellectual property portfolio contains U.S. patents and pending U.S. and foreign patent applications related to composition of matter, pharmaceutical compositions and methods of use for our product candidates. We have patent protection for our primary product candidates in the United States through at least 2030.

Expand our product portfolio through internal discovery efforts and possible in-licensing or acquisitions of additional ophthalmic product candidates or products. We continually seek to discover and develop new compounds in our research laboratories and employ a scientific staff with expertise in medicinal chemistry, analytical chemistry, biochemistry, cell biology, pharmacology and pharmaceutical science. In addition, we also plan to evaluate the expansion of our product portfolio through in-licensing or acquisitions of additional ophthalmic product candidates or products.

Risk Factors Associated with Our Business

Our business is subject to numerous risks, as more fully described in the section entitled Risk Factors immediately following this prospectus summary. You should read these risks before you invest in our common stock. In particular, our risks include, but are not limited to, the following:

- we have not obtained and may never obtain regulatory approval for any of our product candidates;
- failure can occur at any stage of clinical development and, if the clinical trials for our product candidates are unsuccessful, we could be required to abandon development, as was the case recently with AR-12286 and PG286 when AR-12286 did not meet desired efficacy endpoints;
- regulatory approval could be substantially delayed for all or a subset of our product candidates if the FDA or European regulatory authorities require additional time or studies to assess the products;
- we currently have no source of revenue and we will need to obtain additional financing to fund our operations;
- we have incurred net losses since inception and, as of June 30, 2013, we had an accumulated deficit during the development stage of $74.0 million;
- we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability;
- we depend substantially on the success regarding safety, efficacy and tolerability of our product candidates;

we may be unable to successfully manufacture or commercialize our product candidates;

we face competition from established branded and generic pharmaceutical companies and if our competitors are able to develop and market products that are preferred over our products, our commercial opportunity will be reduced or eliminated;

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we depend upon our key personnel and our ability to attract and retain employees;

if we cannot successfully defend our intellectual property, additional competitors could enter the market and sales of affected products may decline materially; and

our independent registered public accounting firm issued an opinion on our financial statements as of and for the year ended December 31, 2012 that expresses doubt about our ability to continue as a going concern.

Corporate Information

We were incorporated under the laws of the State of Delaware in June 2005. Our principal executive offices are located at 135 US Highway 206, Suite 15, Bedminster, New Jersey 07921, and our telephone number is (908) 470-4320. Our website address is www.aeriepharma.com. The information contained on, or that can be accessed through, our website is not part of this prospectus. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Aerie is a registered trademark of Aerie Pharmaceuticals, Inc. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

Implications of Being an Emerging Growth Company

We qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from certain reporting requirements and other burdens that are otherwise applicable generally to public companies. These provisions include:

only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;

exemption from the auditor attestation requirement on the effectiveness of our internal controls over financial reporting;

reduced disclosure about our executive compensation arrangements; and

no requirements for non-binding advisory votes on executive compensation or golden parachute arrangements.

We may take advantage of these provisions for up to five years or such earlier time that we no longer qualify as an emerging growth company. We would cease to be an emerging growth company if we have more than $1.0 billion in annual revenue, have more than $700 million in market value of our capital stock held by non-affiliates or issue more than $1.0 billion of non-convertible debt over a three-year period. We may choose to take advantage of some but not all of these reduced burdens. For example, we have taken advantage of the reduced reporting requirements with respect to disclosure regarding our executive compensation arrangements, have presented only two years of audited financial statements, have presented reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure and have taken the exemption from auditor attestation on the effectiveness of our internal controls over financial reporting. To the extent that we take advantage of these reduced burdens, the information that we provide stockholders may be different than you might obtain from other public companies in which you hold equity interests.

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The Offering

Common stock to be offered by us	5,250,000 shares.
Common stock to be outstanding immediately after this offering	20,324,003 shares.
Option to purchase additional shares	We have granted the underwriters an option for 30 days from the date of this prospectus to purchase up to 787,500 additional shares of common stock.
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $60.0 million, assuming the shares are offered at $13.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus. We anticipate that the net proceeds from this offering will be used as follows: approximately $24.0 million and $10.0 million for direct clinical and non-clinical costs, respectively, associated with the completion of Phase 3 registration trials for our product candidate AR-13324; approximately $4.0 million and $1.5 million for direct clinical and non-clinical costs, respectively, associated with the completion of the Phase 2b clinical trial for our product candidate PG324; and the remainder for working capital and general corporate purposes. In the ordinary course of our business, we expect to evaluate from time to time acquiring, investing in or in-licensing complementary products, technologies or businesses. We currently do not have any agreements or commitments with respect to any potential acquisition, investment or license. See Use of Proceeds.
Proposed NASDAQ Global Market symbol	AERI
Risk factors	You should read the Risk Factors section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

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Our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of approximately $10 million in shares of our common stock in this offering at the initial public offering price. Assuming an initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, these stockholders would purchase an aggregate of 769,231 of the 5,250,000 shares offered in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may determine to purchase fewer shares than they have indicated an interest in purchasing or not to purchase any shares in this offering. It is also possible that these stockholders could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these stockholders than the stockholders have indicated an interest in purchasing or not to sell any shares to these stockholders.

In addition, at our request, certain of the underwriters have reserved up to 5% of the common stock being offered by this prospectus (excluding the underwriters option to purchase any additional shares) for sale at the initial public offering price to our directors, officers, employees, consultants and other individuals associated with us and members of their families. The number of shares available for sale to the general public will be reduced to the extent such persons purchase these reserved shares. See Underwriting.

The number of shares of common stock to be outstanding immediately after this offering is based on 1,021,209 shares of common stock outstanding as of September 30, 2013, and excludes:

- 3,189,660 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2013 under our 2005 Stock Option Plan, or the 2005 Plan, having a weighted average exercise price of $2.1634 per share;
- 3,229,068 shares of common stock reserved for future issuance under our 2013 Omnibus Incentive Plan (including 68,492 shares of common stock that were previously reserved for issuance under the 2005 Plan, under which no further awards may be granted following this offering), as well as any future increases in the number of shares of common stock reserved for issuance under this plan;
- 645,814 shares of common stock reserved for issuance under our 2013 Employee Stock Purchase Plan;
- 317,900 shares of restricted stock that are subject to vesting restrictions; and
- 717,801 shares of common stock issuable upon the exercise of warrants that are expected to remain outstanding following the closing of this offering. See Description of Capital Stock Warrants.

Unless otherwise indicated, all information in this prospectus assumes or gives effect to:

- a 1-for-5 reverse stock split of our common stock effected on October 8, 2013;
- the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,120,531 shares of common stock immediately prior to the closing of this offering;
- the conversion of the principal and accrued interest outstanding under our $18.0 million in aggregate principal amount of our 8% convertible notes due December 31, 2013, or the outstanding notes, into 1,431,048 shares of common stock immediately prior to the closing of this offering at a conversion price equal to the initial public offering price, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and, for illustrative purposes, assuming the conversion occurs on October 31, 2013;

the net exercise immediately prior to the closing of this offering of warrants to purchase 2,506,075 shares of convertible preferred stock that will subsequently be automatically converted into 501,215 shares of common stock immediately prior to the closing of this offering;

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the filing of our amended and restated certificate of incorporation, which will occur prior to the closing of this offering; and

no exercise of the underwriters option to purchase additional shares.

A $1.00 increase in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease the number of shares of our common stock issuable upon conversion of the outstanding notes and accrued interest thereon by 102,218 shares. A $1.00 decrease in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase the number of shares of our common stock issuable upon conversion of the outstanding notes and accrued interest thereon by 119,254 shares.

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Summary Financial Data

The following table summarizes our financial data. We have derived the following statement of operations and comprehensive loss data for the years ended December 31, 2012 and 2011 from our audited financial statements, included elsewhere in this prospectus. We have derived the following statement of operations and comprehensive loss data for the six months ended June 30, 2013 and 2012 and the period from inception (June 22, 2005) to June 30, 2013 and balance sheet data as of June 30, 2013 from our unaudited financial statements appearing elsewhere in this prospectus. The unaudited financial statements have been prepared on the same basis as the audited financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to fairly present our financial position as of June 30, 2013 and results of operations for the six months ended June 30, 2013 and 2012 and the period from inception (June 22, 2005) to June 30, 2013. Our historical results are not necessarily indicative of the results that may be expected in the future. The following summary financial data should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and related notes included elsewhere in this prospectus.

	SIX MONTHS ENDED JUNE 30,		YEAR ENDED DECEMBER 31,		PERIOD FROM INCEPTION (JUNE 22, 2005) TO JUNE 30, 2013
	2013	2012	2012	2011	
	(unaudited)	(in thousands, except share and per share data)			(unaudited)
Statement of Operations and Comprehensive Loss Data:					
Expenses:					
General and administrative	$ (3,406)	$ (2,285)	$ (5,020)	$ (3,521)	$ (23,303)
Research and development	(6,328)	(5,932)	(9,273)	(10,695)	(49,477)
Loss from operations	$ (9,734)	$ (8,217)	$ (14,293)	$ (14,216)	$ (72,780)
Other income (expense), net	(384)	376	(685)	1,249	(1,126)
Net loss	$ (10,118)	$ (7,841)	$ (14,978)	$ (12,967)	$ (73,906)
Net loss attributable to common stockholders basic and diluted [1]	$ (10,392)	$ (8,115)	$ (15,643)	$ (13,419)	
Net loss per share attributable to common stockholders basic and diluted[1]	$ (10.68)	$ (8.51)	$ (16.39)	$ (14.50)	
Weighted-average number of shares outstanding basic and diluted [1]	973,460	953,114	954,695	925,625	
Pro forma net loss per share attributable to common stockholders basic and diluted (unaudited)[2]	$ (0.55)		$ (0.93)		
Weighted-average number of pro forma shares outstanding basic and diluted (unaudited)[2]	15,434,550		15,415,785		

	AS OF JUNE 30, 2013		
	ACTUAL	PRO FORMA [3]	PRO FORMA AS ADJUSTED [4][5]
	(unaudited)	(unaudited)	(unaudited)
		(in thousands)	

Balance Sheet Data:			
Cash and cash equivalents [6]	$ 2,377	$ 9,877	$ 69,877
Total assets	3,685	11,185	71,185
Notes payable, net of discount, and accrued interest thereon	9,353		
Warrants liability related parties	4,603		
Convertible preferred stock	61,172		
Total stockholders (deficit) equity	(73,909)	8,719	68,719

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(1) Net loss attributable to common stockholders reflects the accretion on convertible preferred stock and, where applicable, preferred stock dividends. See Note 2 to our financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the basic and diluted net loss per share attributable to common stockholders.

(2) See Note 2 and Note 15 to our financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the pro forma basic and diluted net loss per share attributable to common stockholders and the number of shares used in the computation of the per share amounts.

(3) Pro forma amounts reflect the automatic conversion of all our outstanding shares of convertible preferred stock as of June 30, 2013 into an aggregate of 12,120,531 shares of our common stock, the conversion of the outstanding notes and accrued interest thereon into an aggregate of 1,431,048 shares of our common stock, the net exercise immediately prior to the closing of this offering of warrants to purchase 2,506,075 shares of convertible preferred stock that will subsequently be automatically converted into 501,215 shares of common stock, and the reclassification of the warrant liability to additional paid-in capital for warrants to purchase 3,589,005 shares of convertible preferred stock that are expected to remain outstanding following the closing of this offering and will be exercisable for 717,801 shares of common stock, at a weighted average exercise price of $3.23 per share. With respect to the outstanding notes, pro forma amounts reflect the notes issued in August 2013 and September 2013. A $1.00 increase in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease the number of shares of our common stock issuable upon conversion of the outstanding notes and accrued interest thereon by 102,218 shares. A $1.00 decrease in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase the number of shares of our common stock issuable upon conversion of the outstanding notes and accrued interest thereon by 119,254 shares.

(4) Pro forma as adjusted amounts further reflect the sale of 5,250,000 shares of our common stock in this offering at an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

(5) Each $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) each of cash and cash equivalents, total assets and total stockholders equity (deficit) by approximately $4.9 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) each of cash and cash equivalents, total assets and total stockholders equity (deficit) by approximately $12.1 million, if the assumed initial public offering price remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial public offering price and other terms of this offering determined at pricing.

(6) Cash and cash equivalents on a pro forma basis as of June 30, 2013 reflects $7.5 million in aggregate principal proceeds from the outstanding notes issued in August 2013 and September 2013 and does not otherwise reflect any changes in account balances subsequent to June 30, 2013. See Note 16 to our financial statements appearing elsewhere in this prospectus for further information. Cash and cash equivalents on a pro forma as adjusted basis includes the foregoing pro forma amounts and net proceeds from this offering at an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. We operate in an industry that involves numerous risks and uncertainties. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our common stock to decline, and you may lose all or part of your investment.

Risks Related to Development, Regulatory Approval and Commercialization

We depend substantially on the success of our product candidates, particularly AR-13324 and PG324, which are still in development. If we are unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

Our business and the ability to generate revenue related to product sales, if ever, will depend on the successful development, regulatory approval and commercialization of our product candidates for the treatment of patients with glaucoma, particularly AR-13324 and PG324, which are still in development, and other potential products we may develop or license. We have invested a significant portion of our efforts and financial resources in the development of our existing product candidates. The success of our product candidates will depend on several factors, including:

- successful completion of clinical trials;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property;
- launching commercial sales of our product candidates, if and when approved;
- obtaining reimbursement from third-party payors for product candidates, if and when approved;
- competition with other products; and
- continued acceptable safety profile for our product candidates following regulatory approval, if and when received.

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 our product candidates, which would materially harm our business and we may not be able to earn sufficient revenues and cash flows to continue our operations.

We have not obtained regulatory approval for any of our product candidates in the United States or any other country.

We currently do not have any product candidates that have gained regulatory approval for sale in the United States or any other country, and we cannot guarantee that we will ever have marketable products. Our business is substantially dependent on our ability to complete the development of, obtain regulatory approval for and successfully commercialize product candidates in a timely manner. We cannot commercialize product candidates in the United States without first obtaining regulatory approval to market each product from the FDA; similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. AR-13324 and PG324 are planned to be advanced into Phase 3 and Phase 2b clinical trials, respectively. We cannot predict whether these trials and future trials will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date.

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Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate in preclinical studies and well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA, that the product candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. In the United States, we have not submitted a new drug application, or NDA, for any of our product candidates. An NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate s safety and effectiveness for each desired indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and approval may not be obtained. If we submit an NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA.

Regulatory authorities outside of the United States, such as in Europe and Japan and in emerging markets, also have requirements for approval of drugs for commercial sale with which we must comply prior to marketing in those areas. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and obtaining regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could require additional non-clinical studies or clinical trials, which could be costly and time consuming. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain foreign regulatory approvals on a timely basis, if at all.

The process to develop, obtain regulatory approval for and commercialize product candidates is long, complex and costly both inside and outside of the United States, and approval is never guaranteed. Even if our product candidates were to successfully obtain approval from the regulatory authorities, any approval might significantly limit the approved indications for use, or require that precautions, contraindications, or warnings be included on the product labeling, or require expensive and time-consuming post-approval clinical studies or surveillance as conditions of approval. Following any approval for commercial sale of our product candidates, certain changes to the product, such as changes in manufacturing processes and additional labeling claims, will be subject to additional FDA review and approval. Also, regulatory approval for any of our product candidates may be withdrawn. If we are unable to obtain regulatory approval for our product candidates in one or more jurisdictions, or any approval contains significant limitations, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed. Furthermore, we may not be able to obtain sufficient funding or generate sufficient revenue and cash flows to continue the development of any other product candidate in the future.

Regulatory approval may be substantially delayed or may not be obtained for one or all of our product candidates if regulatory authorities require additional time or studies to assess the safety and efficacy of our product candidates.

We may be unable to initiate or complete development of our product candidates on schedule, if at all. The timing for the completion of the studies for our product candidates will require funding beyond the proceeds of this offering. In addition, if regulatory authorities require additional time or studies to assess the safety or efficacy of our product candidates, we may not have or be able to obtain adequate funding to complete the necessary steps for approval for any or all of our product candidates. Preclinical studies and clinical trials required to demonstrate the safety and efficacy of our product candidates are time consuming and expensive and together take several years or more to complete. Delays in regulatory approvals or rejections of applications for regulatory approval in the United States, Europe, Japan or other markets may result from many factors, including:

- our inability to obtain sufficient funds required for a clinical trial;
- regulatory requests for additional analyses, reports, data, non-clinical and preclinical studies and clinical trials;

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- regulatory questions regarding interpretations of data and results and the emergence of new information regarding our product candidates or other products;
- clinical holds, other regulatory objections to commencing or continuing a clinical trial or the inability to obtain regulatory approval to commence a clinical trial in countries that require such approvals;
- failure to reach agreement with the FDA or non-U.S. regulators regarding the scope or design of our clinical trials;
- our inability to enroll a sufficient number of patients who meet the inclusion and exclusion criteria in our clinical trials;
- our inability to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- unfavorable or inconclusive results of clinical trials and supportive non-clinical studies, including unfavorable results regarding effectiveness of product candidates during clinical trials;
- any determination that a clinical trial presents unacceptable health risks;
- lack of adequate funding to continue the clinical trial due to unforeseen costs or other business decisions;
- our inability to reach agreements on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- our inability to identify and maintain a sufficient number of sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indications targeted by our product candidates;
- our inability to obtain approval from institutional review boards to conduct clinical trials at their respective sites;
- our inability to timely manufacture or obtain from third parties sufficient quantities or quality of the product candidate or other materials required for a clinical trial; and
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data.

Changes in regulatory requirements and guidance may also occur and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to institutional review boards for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

If we are required to conduct additional clinical trials or other studies with respect to any of our product candidates beyond those that we initially contemplated, if we are unable to successfully complete our clinical trials or other studies or if the results of these studies are not positive or are only modestly positive, we may be delayed in obtaining regulatory approval for that product candidate, we may not be able to obtain regulatory approval at all or we may obtain approval for indications that are not as broad as intended. Our product development costs will also increase if we experience delays in testing or approvals and we may not have sufficient funding to complete the testing and approval process. Significant clinical trial delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products if

and when approved. If any of this occurs, our business will be materially harmed.

If we are unable to establish a direct sales force in the United States, our business may be harmed.

We currently do not have an established sales organization and do not have a marketing or distribution infrastructure. To achieve commercial success for any approved product, we must either develop a sales and

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marketing organization or outsource these functions to third parties. If our product candidates are approved by the FDA for commercial sale, we intend to market directly to eye-care professionals in the United States through our own sales force, targeting approximately 10,000 high-prescribing eye-care professionals in the United States. We will need to incur significant additional expenses and commit significant additional time and management resources to establish and train a sales force to market and sell our products. We may not be able to successfully establish these capabilities despite these additional expenditures.

Factors that may inhibit our efforts to successfully establish a sales force include:

- our inability to compete with other pharmaceutical companies to recruit, hire, train and retain adequate numbers of effective sales and marketing personnel with requisite knowledge of our target market;
- the inability of sales personnel to obtain access to adequate numbers of eye-care professionals to prescribe any future approved products;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- a delay in bringing products to market after efforts to hire and train our sales force have already commenced.

In the event we are unable to successfully market and promote our products, our business may be harmed.

We currently intend to explore the licensing of commercialization rights or other forms of collaboration outside of the United States, which will expose us to additional risks of conducting business in international markets.

The non-U.S. markets are an important component of our growth strategy. If we fail to obtain licenses or enter into collaboration arrangements with selling parties, or if these parties are not successful, our revenue-generating growth potential will be adversely affected. Moreover, international business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- efforts to enter into collaboration or licensing arrangements with third parties in connection with our international sales, marketing and distribution efforts may increase our expenses or divert our management s attention from the acquisition or development of product candidates;
- changes in a specific country s or region s political and cultural climate or economic condition;
- differing regulatory requirements for drug approvals and marketing internationally;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- potentially reduced protection for intellectual property rights;
- potential third-party patent rights in countries outside of the United States;

unexpected changes in tariffs, trade barriers and regulatory requirements;

economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including several countries in Europe;

compliance with tax, employment, immigration and labor laws for employees traveling abroad;

the effects of applicable foreign tax structures and potentially adverse tax consequences;

foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incidental to doing business in another country;

workforce uncertainty in countries where labor unrest is more common than in the United States;

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- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;

- failure of our employees and contracted third parties to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

Failure can occur at any stage of clinical development. If the clinical trials for our product candidates are unsuccessful, we could be required to abandon development.

A failure of one or more clinical trials can occur at any stage of testing for a variety of reasons. The outcome of preclinical testing and early clinical trials may not be predictive of the outcome of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In addition, adverse events may occur or other risks may be discovered in Phase 2 or Phase 3 clinical trials that will cause us to suspend or terminate our clinical trials. In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in or adherence to trial protocols, differences in size and type of the patient populations and the rates of dropout among clinical trial participants. Our future clinical trial results therefore may not demonstrate safety and efficacy sufficient to obtain regulatory approval for our product candidates.

Flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. In addition, clinical trials often reveal that it is not practical or feasible to continue development efforts. Further, we have never submitted an NDA for any potential products.

We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants. Further, regulatory agencies, institutional review boards or data safety monitoring boards may at any time order the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. Since our inception, we have not voluntarily or involuntarily suspended or terminated a clinical trial due to unacceptable safety risks to participants.

If the results of our clinical trials for our current product candidates or clinical trials for any future product candidates do not achieve the primary efficacy endpoints or demonstrate unexpected safety issues, the prospects for approval of our product candidates will be materially adversely affected. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have failed to achieve similar results in later clinical trials, including longer term trials, or have failed to obtain regulatory approval of their product candidates. Many compounds that initially showed promise in clinical trials or earlier stage testing have later been found to cause undesirable or unexpected adverse effects that have prevented further development of the compound. Our upcoming trials for our primary product candidates, AR-13324 and PG324, may not produce the results that we expect. In addition, if based on clinical results of AR-13324 we discontinue the advancement of this product candidate, in certain circumstances we may similarly determine not to advance PG324, which combines AR-13324 with latanoprost. Our clinical trials are also designed to test the use of AR-13324 and

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PG324 as a monotherapy, rather than as an add-on therapy. Accordingly, the efficacy of our primary product candidates may not be similar or correspond directly to their efficacy when used as an add-on therapy.

Several companies have previously pursued ROCK inhibitors for ophthalmic use but to date no ROCK inhibitors have been approved and most of those companies have chosen to discontinue clinical development of their ROCK inhibitors. One of our ROCK inhibitors, AR-12286, was discontinued in the clinical stage of development due to an inability to maintain its effectiveness over time. In a 28-day Phase 2b clinical trial, AR-12286 lowered IOP by 6.7 mmHg on day seven, but lowered IOP by only 5.3 mmHg on day 28. This trend continued in a follow-up three-month study. As a result, in June 2013 we discontinued any further clinical development of AR-12286 and its fixed-dose combination product PG286. AR-13324 showed a 0.1 mmHg change in IOP from day seven to day 28 in our Phase 2b trial, and published clinical data for other ROCK inhibitors similarly have not shown a loss of efficacy over time. However, we have not previously conducted a three-month Phase 2b clinical trial for AR-13324, and therefore there can be no assurance as to the efficacy of AR-13324 beyond 28 days. In addition, our current product candidates remain subject to the risks associated with clinical drug development as indicated above.

In addition to the circumstances noted above, we may experience numerous unforeseen events that could cause our clinical trials to be delayed, suspended or terminated, or which could delay or prevent our ability to receive regulatory 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 implement a clinical hold;
- 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 have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may elect or be required to suspend or terminate clinical trials of our product candidates based on a finding that the participants are being exposed to health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable adverse effects or other unexpected characteristics.

If we elect or are required to suspend or terminate a clinical trial of any of our product candidates, our commercial prospects will be adversely impacted and our ability to generate product revenues may be delayed or eliminated.

Our product candidates may have undesirable adverse effects, which may delay or prevent regulatory approval or, if approval is received, require our products to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Unforeseen adverse effects from any of our product candidates could arise either during clinical development or, if approved, after the approved product has been marketed. To date, the main tolerability finding of AR-13324 has been transient hyperemia, or eye-redness. PG324 combines AR-13324 with latanoprost. The main adverse effects of latanoprost include hyperemia, irreversible change in iris color, discoloration of the skin around the eyes and droopiness of eyelids.

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Any undesirable adverse effects that may be caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale. In addition, if any of our product candidates receives regulatory approval and we or others later identify undesirable adverse effects caused by the product, we could face one or more of the following consequences:

- regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication, or other labeling changes;
- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may seize the product;
- we may be required to change the way that the product is administered, conduct additional clinical trials or recall the product;
- we may be subject to litigation or product liability claims fines, injunctions, or criminal penalties; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing such product, which in turn could delay or prevent us from generating significant revenues from its sale.

We face competition from established branded and generic pharmaceutical companies and if our competitors are able to develop and market products that are preferred over our products, our commercial opportunity will be reduced or eliminated.

The development and commercialization of new drug products is highly competitive. We face competition from established branded and generic pharmaceutical companies, as well as from academic institutions, government agencies and private and public research institutions, which may in the future develop products to treat patients with glaucoma. 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. Sucampo Pharmaceuticals, Inc. recently commercially relaunched Rescula, a twice-daily dosed PGA, with the claim that it reduces elevated IOP by increasing the outflow of aqueous humor through the TM. In addition, early-stage companies that are also developing glaucoma treatments may prove to be significant competitors, such as Inotek Pharmaceuticals, which is developing an adenosine receptor agonist. We expect that our competitors will continue to develop new glaucoma treatments, which may include eye drops, oral treatments, surgical procedures, implantable devices or laser treatments. Alternative treatments beyond eye drops continue to develop. For example, although surgical procedures are currently used in severe cases, less invasive procedures are currently under development and we expect that we will compete with other companies that develop implantable devices or other products or procedures for use in the treatment of glaucoma. Other early-stage companies may also compete through collaborative arrangements with large and established companies. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer adverse effects, are more convenient or are less expensive than our potential products. We expect that our ability to compete effectively will depend upon, among other things, our ability to:

- successfully complete clinical trials and obtain all requisite regulatory approvals in a timely and cost-effective manner;

obtain and maintain patent protection and non-patent exclusivity for our products and otherwise prevent the introduction of generics of our products;

attract and retain key personnel;

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build an effective selling and marketing infrastructure;

demonstrate the advantages of our product candidates compared to alternative therapies;

compete against other products with fewer contraindications; and

obtain and sustain adequate reimbursement from third-party payors.

If our competitors market products that are more effective, safer, have fewer side effects or are less expensive than our potential products or that reach the market sooner than our future products, if any, we may not achieve commercial success.

The commercial success of our potential products will depend on the degree of market acceptance among eye-care professionals, patients, patient advocacy groups, healthcare payors and the medical community.

Our potential products may not gain market acceptance among eye-care professionals, patients, patient advocacy groups, healthcare payors and the medical community. There are a number of available therapies marketed for the treatment of glaucoma. Some of these drugs are branded and subject to patent protection, but most others, including latanoprost and many beta blockers, are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by eye-care professionals, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. The degree of market acceptance of our potential products will depend on a number of factors, including:

the market price, affordability and patient out-of-pocket costs of our potential products relative to other available products, which are predominantly generics;

the effectiveness of our potential products as compared with currently available products;

patient willingness to adopt our potential products in place of current therapies;

varying patient characteristics including demographic factors such as age, health, race and economic status;

changes in the standard of care for the targeted indications for any of our product candidates;

the prevalence and severity of any adverse effects;

limitations or warnings contained in a product candidate s FDA-approved labeling;

limitations in the approved clinical indications for our product candidates;

relative convenience and ease of administration;

the strength of our selling, marketing and distribution capabilities;

the quality of our relationship with patient advocacy groups;

sufficient third-party coverage or reimbursement; and

potential product liability claims.

In addition, the potential market opportunity for our potential products is difficult to precisely estimate. Our estimates of the potential market opportunity for our potential products 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, independent sources have not verified all of our assumptions. If any of these assumptions proves to be inaccurate, then the actual market for our potential products could be smaller than our estimates of our potential market opportunity. If the actual market for our potential products is smaller than we expect, our product revenue may be limited, and it may be more difficult for us to achieve or maintain profitability. If we fail to achieve market acceptance of our potential products in the United States and abroad, our revenue will be more limited and it will be more difficult to achieve profitability.

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If we fail to obtain and sustain an adequate level of reimbursement for our potential products by third-party payors, potential future sales would be materially adversely affected.

The course of treatment for glaucoma patients includes primarily older drugs, and the leading products for the treatment of glaucoma currently in the market, including latanoprost and timolol, are available as generic brands. There will be no commercially viable market for our potential products without reimbursement from third-party payors, and any reimbursement policy may be affected by future healthcare reform measures. We cannot be certain that reimbursement will be available for our potential products or any other product candidate we develop. Additionally, even if there is a commercially viable market, if the level of reimbursement is below our expectations, our anticipated revenue and gross margins will be adversely affected.

Third-party payors, such as government or private healthcare insurers, carefully review and increasingly question and challenge the coverage of and the prices charged for drugs. Reimbursement rates from private health insurance companies vary depending on the company, the insurance plan and other factors. Reimbursement rates may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. A current trend in the United States healthcare industry is toward cost containment. Large public and private payors, managed care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, may question the coverage of, and challenge the prices charged for, medical products and services, and many third-party payors limit coverage of or reimbursement for newly approved healthcare products. In particular, third-party payors may limit the covered indications. Cost-control initiatives could decrease the price we might establish for products, which could result in product revenues being lower than anticipated. We believe our drugs will be priced significantly higher than existing generic drugs and consistently with current branded drugs. If we are unable to show a significant benefit relative to existing generic drugs, Medicare, Medicaid and private payors may not be willing to reimburse for our drugs, which would significantly reduce the likelihood of them gaining market acceptance. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted.

We expect that private insurers will consider the efficacy, cost effectiveness, safety and tolerability of our potential products in determining whether to approve reimbursement for such products and at what level. Obtaining these approvals can be a time consuming and expensive process. Our business would be materially adversely affected if we do not receive approval for reimbursement of our potential products from private insurers on a timely or satisfactory basis. Limitations on coverage could also be imposed at the local Medicare carrier level or by fiscal intermediaries. Medicare Part D, which provides a pharmacy benefit to Medicare patients as discussed below, does not require participating prescription drug plans to cover all drugs within a class of products. Our business could be materially adversely affected if Part D prescription drug plans were to limit access to, or deny or limit reimbursement of, our product candidates or other potential products.

Reimbursement in the European Union must be negotiated on a country-by-country basis and in many countries the product cannot be commercially launched until reimbursement is approved. The negotiation process in some countries can exceed 12 months. 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 products to other available therapies.

If the prices for our potential products decrease or if governmental and other third-party payors do not provide adequate coverage and reimbursement levels, our revenue, potential for future cash flows and prospects for profitability will suffer.

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If we are found in violation of federal or state fraud and abuse laws or other healthcare laws and regulations, we may be required to pay a penalty and/or be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition and results of operation.

In the United States, we are subject to various federal and state healthcare fraud and abuse laws, including anti-kickback laws, false claims laws and other laws intended, among other things, to reduce fraud and abuse in federal and state healthcare programs. The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce the referral of business, including the purchase, order or prescription of a particular drug for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under the Federal Anti-Kickback Statute. The Federal False Claims Act prohibits anyone from, among other things, knowingly presenting or causing to be presented for payment to the government, including the federal healthcare programs, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services that were not provided as claimed, or claims for medically unnecessary items or services. Many states have similar false claims laws. Cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products or the provision of kickbacks have resulted in the submission of false claims to governmental healthcare programs. Under the Health Insurance Portability and Accountability Act of 1996, we are prohibited from knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services to obtain money or property of any healthcare benefit program. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the government under the Federal False Claims Act as well as under the false claims laws of several states.

Many states have adopted laws similar to the Federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare services reimbursed by any source, not just governmental payors. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America s Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties.

Neither the government nor the courts have provided definitive guidance on the application of fraud and abuse laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. While we believe we have structured our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, we could be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from governmental funded federal or state healthcare programs and the curtailment or restructuring of our operations. Were this to occur, our business, financial condition and results of operations and cash flows may be materially adversely affected.

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Recently enacted and future legislation may increase the difficulty and cost of commercializing our potential products and may 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 regulatory approval of our potential products, restrict or regulate post-marketing activities and affect our ability to profitably sell our potential products for which we obtain regulatory approval.

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. The legislation expanded Medicare coverage for drug purchases by the elderly by establishing Medicare Part D and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs under Medicare Part B. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class under the new Part D program. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement rate that we receive for any of our approved products. While the MMA only applies 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 Reconciliation Act of 2010, collectively PPACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. PPACA increased manufacturers rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate amount for both branded and generic drugs and revised the definition of average manufacturer price, or AMP, which may also increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also expanded Medicaid drug rebates, which previously had been payable only on fee-for-service utilization, to Medicaid managed care utilization, and created an alternative rebate formula for certain new formulations of certain existing products that is intended to increase the rebates due on those drugs. The Centers for Medicare & Medicaid Services, which administers the Medicaid Drug Rebate Program, also has proposed to expand Medicaid rebates to the utilization that occurs in the territories of the United States, such as Puerto Rico and the Virgin Islands. Further, beginning in 2011, PPACA imposed a significant annual fee on companies that manufacture or import branded prescription drug products and requires manufacturers to provide a 50% discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the donut hole. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. For example, pharmaceutical companies are required to track certain payments made to physicians, with the first reports due in March 2014 and the reported information to be made publicly available on a searchable website beginning in September 2014. We will not know the full effects of PPACA until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the full effect of PPACA, the new law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been introduced at both the state and federal level to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing approval testing and other requirements.

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If we face allegations of noncompliance with the law and encounter sanctions, our reputation, revenues and liquidity may suffer, and our products could be subject to restrictions or withdrawal from the market.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenues from our product sales, our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

If our product candidates receive regulatory approval, we will be subject to ongoing regulatory requirements and we may face future development, manufacturing and regulatory difficulties.

Our product candidates, if approved, will also be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping, submission of safety and other post-market approval information, importation and exportation. In addition, approved products, manufacturers and manufacturers facilities are required to comply with extensive FDA and European Medicines Agency, or EMA, requirements and the requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practice, or cGMP, requirements. As such, we and our potential future contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work will be required to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and EMA and other similar agencies and to comply with certain requirements concerning advertising and promotion for our potential products. Promotional communications with respect to prescription drugs also are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product s approved labeling. Accordingly, once approved, we may not promote our products, if any, for indications or uses for which they are not approved.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our potential products fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- require product recalls;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us or our potential future collaborators to enter into a consent decree or permanent injunction, which can include shutdown of manufacturing facilities, imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other administrative or judicial civil or criminal penalties or pursue criminal prosecution;
- withdraw regulatory approval;
- refuse to approve pending applications or supplements to approved applications filed by us or by our potential future collaborators;

impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products.

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We may not be able to identify additional therapeutic opportunities for our potential product candidates or to expand our portfolio of products.

We may explore other therapeutic opportunities with ROCK inhibition in ophthalmology and seek to commercialize a portfolio of new ophthalmic drugs in addition to our product candidates that we are currently developing.

Research programs to pursue the development of our product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not we ultimately are successful. Our research programs may initially show promise in identifying potential indications and/or product candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs than we will possess, thereby limiting our ability to diversify and expand our product portfolio.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects.

Our product candidates are all designed to treat patients with glaucoma, and the success or failure of any one of our product candidates could impact sales of our other potential products in the future.

Our product candidates are designed to be once-daily dosed ROCK inhibitor eye drops to be applied topically to lower IOP for the treatment of glaucoma through various mechanisms of action. Accordingly, increased sales for one of our potential products may negatively impact sales for our other potential products. Our commercialization strategy is unique for each of our product candidates. However, we cannot guarantee that cannibalization of sales among our potential product lines will not occur in the future. Because each of our product candidates are ROCK inhibitor eye drops designed to treat patients with glaucoma, any challenges or failures with respect to any of these potential products could negatively impact sales or the public perception of our other potential products.

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Risks Related to Our Financial Position and Need for Additional Capital

We currently have no source of revenue and may never become profitable.

We are a development-stage pharmaceutical company with a limited operating history. Our ability to generate revenue and become profitable depends upon our ability to successfully complete the development of our product candidates for the management of glaucoma and obtain the necessary regulatory approvals for our product candidates. We have never been profitable, have no products approved for commercial sale and to date have not generated any revenue from product sales. Even if we receive regulatory approval for our products for commercial sale, we do not know when such potential products will generate revenue, if at all. Our ability to generate product revenue depends on a number of factors, including our ability to:

- successfully complete clinical development, and receive regulatory approval, for our product candidates;
- set an acceptable price for our potential products and obtain adequate reimbursement from third-party payors;
- obtain commercial quantities of our potential products at acceptable cost levels; and
- successfully market and sell our potential products in the United States and abroad.

In addition, because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we are required by the FDA or other regulatory authorities to perform studies in addition to those that we currently anticipate. Even if our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of these products.

Our ability to become and remain profitable depends on our ability to generate revenue. Even if we are able to generate revenues from the sale of our potential products, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations. 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 or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have incurred net losses since inception and anticipate that we will continue to incur net losses for the foreseeable future.

We have incurred losses in each year since our inception in June 2005. Our net losses were $10.1 million, $7.8 million, $15.0 million and $13.0 million for the six months ended June 30, 2013 and 2012 and years ended December 31, 2012 and 2011, respectively. As of June 30, 2013, we had a deficit accumulated during the development stage of $74.0 million.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or become commercially viable. We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of convertible preferred stock and convertible debt. Our product candidates will require the completion of regulatory review, significant marketing efforts and substantial investment before they can provide us with any revenue.

We expect our research and development expenses to continue to be significant in connection with our ongoing and planned Phase 2 and Phase 3 clinical trials. In addition, if we obtain regulatory approval for our product

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candidates, we expect to incur increased sales and marketing expenses. As a result, we expect to continue to incur significant and increasing operating losses and negative cash flows for the foreseeable future. These losses have had and will continue to have a material adverse effect on our stockholders deficit, financial position, cash flows and working capital.

Our recurring operating losses have raised substantial doubt regarding our ability to continue as a going concern.

Our recurring operating losses raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements as of and for the year ended December 31, 2012 included elsewhere in this prospectus. We have no current source of revenue to sustain our present activities, and we do not expect to generate revenue until and unless we receive regulatory approval of and successfully commercialize our product candidates. The perception of our ability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees.

We will need to obtain additional financing to fund our operations and, if we are unable to obtain such financing, we may be unable to complete the development and commercialization of our primary product candidates.

Our operations have consumed substantial amounts of cash since inception. From the period from inception (June 22, 2005) to June 30, 2013, we have cumulative net cash flows used by operating activities of $66.4 million. We will need to obtain additional financing to fund our future operations, including completing the development and commercialization of our primary product candidates. We will need to obtain additional financing to conduct additional trials for the approval of our drug candidates if requested by regulatory bodies, and completing the development of any additional product candidates we might acquire. Moreover, our fixed expenses such as rent, interest expense and other contractual commitments are substantial and are expected to increase in the future.

Our future funding requirements will depend on many factors, including, but not limited to:

- the progress, timing, scope and costs of our clinical trials, including the ability to timely enroll patients in our planned and potential future clinical trials;
- the time and cost necessary to obtain regulatory approvals that may be required by regulatory authorities;
- our ability to successfully commercialize our product candidates;
- the amount of sales and other revenues from product candidates that we may commercialize, if any, including the selling prices for such potential products and the availability of adequate third-party reimbursement;
- selling and marketing costs associated with our potential products, including the cost and timing of expanding our marketing and sales capabilities;
- the terms and timing of any potential future collaborations, licensing or other arrangements that we may establish;
- cash requirements of any future acquisitions and/or the development of other product candidates;
- the costs of operating as a public company;

the time and cost necessary to respond to technological and market developments; and

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

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Until we can generate a sufficient amount of revenue, we may finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances and marketing or distribution arrangements. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available, we may be required to delay or reduce the scope of or eliminate one or more of our research or development programs or our commercialization efforts. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. In addition, 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 to grant licenses on terms that may not be favorable to us.

We believe that the net proceeds from this offering, together with existing cash and cash equivalents, will be sufficient to fund our projected operating requirements for at least 12 months following the completion of this offering. We expect that these funds will not be sufficient to enable us to complete all necessary development or commercially launch our current product candidates. Accordingly, we will be required to obtain further funding through other public or private offerings, debt financing, collaboration and licensing arrangements or other sources. Adequate additional funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. Our forecast of the period of time through which our financial resources will be adequate to support our operating requirements is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this Risk Factors section. We have based this estimate on a number of assumptions that may prove to be wrong, and changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. Our inability to obtain additional funding when we need it could seriously harm our business.

We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional funds to support our operations, we may sell additional equity or debt securities, which would result in dilution to all of our stockholders or impose restrictive covenants that adversely impact our business. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected.

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

We are a development stage company. We were incorporated and commenced active operations in the second quarter of 2005. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital and developing our product candidates. We have not yet demonstrated our ability to successfully complete a Phase 3 registration trial, obtain regulatory approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing 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.

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Risks Related to Our Reliance on Third Parties

We have no manufacturing capacity and anticipate continued reliance on third-party manufacturers for the development and commercialization of our product candidates in accordance with manufacturing regulations.

We do not currently operate manufacturing facilities for clinical or commercial production of our product candidates. We have no experience in drug formulation, and we lack the resources and the capabilities to manufacture our product candidates and potential products on a clinical or commercial scale. We do not intend to develop facilities for the manufacture of product candidates and potential products for clinical trials or commercial purposes in the foreseeable future. We currently rely on third-party manufacturers to produce the active pharmaceutical ingredient and final drug product for our clinical trials. We manage such production with all our vendors on a purchase order basis in accordance with applicable master service and supply agreements. We do not have long-term agreements with any of these or any other third-party suppliers. To the extent we terminate our existing supplier arrangements in the future and seek to enter into arrangements with alternative suppliers, we might experience a delay in our ability to obtain our commercial supplies. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates if and when they are approved. With respect to commercial production of our potential products in the future, we plan on outsourcing production of the active pharmaceutical ingredients and final product manufacturing if and when approved for marketing by the applicable regulatory authorities. This process is difficult and time consuming and we can give no assurance that we will enter commercial supply agreements with any contract manufacturers on favorable terms or at all.

Reliance on third-party manufacturers entails risks, including:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of their agreements with us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- product loss due to contamination, equipment failure or improper installation or operation of equipment or operator error;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Our manufacturers may not perform as agreed or may not remain in the contract manufacturing business. In the event of a natural disaster, business failure, strike or other difficulty, we may be unable to replace a third-party manufacturer in a timely manner and the production of our product candidates and potential products could be interrupted, resulting in delays and additional costs. We may also have to incur other charges and expenses for products that fail to meet specifications and undertake remediation efforts.

If third-party manufacturers fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.

Before a third party can begin commercial manufacture of our product candidates and potential products, contract manufacturers must obtain regulatory approval of their manufacturing facilities, processes and quality systems. Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, any potential third-party manufacturer may be unable to initially pass federal, state or international regulatory inspections in a cost effective manner. If contract manufacturers are not approved by the FDA, our commercial supply of drug substance will be significantly delayed and may result in significant additional costs.

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In addition, pharmaceutical manufacturing facilities are continuously subject to inspection by the FDA and foreign regulatory authorities, before and after product approval, and must comply with cGMP. Our contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. In addition, contract manufacturers failure to achieve and maintain high manufacturing standards in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, could result in patient injury, product liability claims, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business. If a third-party manufacturer with whom we contract is unable to comply with manufacturing regulations, we may also be subject to fines, unanticipated compliance expenses, recall or seizure of our products, product liability claims, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions could materially adversely affect our financial results and financial condition.

Furthermore, changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, will require prior FDA review and/or approval of the manufacturing process and procedures in accordance with the FDA s regulations, or comparable foreign requirements. This review may be costly and time consuming and could delay or prevent the launch of a product. The new facility will also be subject to pre-approval inspection. In addition, we have to demonstrate that the product made at the new facility is equivalent to the product made at the former facility by physical and chemical methods, which are costly and time consuming. It is also possible that the FDA may require clinical testing as a way to prove equivalency, which would result in additional costs and delay.

Any collaboration arrangement that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our current and potential future product candidates.

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our current and potential future product candidates outside of the United States. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we choose to enter into such arrangements, and the terms of the arrangements may not be favorable to us. If and when we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations.

Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

We currently depend on third parties to conduct some of the operations of our clinical trials and other portions of our operations, and we may not be able to control their work as effectively as if we performed these functions ourselves.

We rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to oversee and conduct our clinical trials, and to perform data collection and analysis of our product candidates. We expect to rely on these third parties to conduct clinical trials of any other potential

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products that we develop. These parties are not our employees and we cannot control the amount or timing of resources that they devote to our program. In addition, any CRO that we retain will be subject to the FDA s regulatory requirements or similar foreign standards and we do not have control over compliance with these regulations by these providers. Our agreements with third-party service providers are on a trial-by-trial and project-by-project bases. Typically, we may terminate the agreements with notice and are responsible for the third party s incurred costs. If any of our relationships with our third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. 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 regulatory approval of our product candidates or commercialization of our potential products, producing additional losses and depriving us of potential product revenue.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities, and we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan, the protocols for the trial and the FDA s regulations and international standards, referred to as Good Clinical Practice requirements, 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. Preclinical studies must also be conducted in compliance with the Animal Welfare Act requirements. Managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers.

Furthermore, these third parties may produce or manufacture competing drugs or may have relationships with other entities, some of which may be our competitors. The use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

If these third parties do not successfully carry out their contractual duties or obligations and meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols according to regulatory requirements or for other reasons, our financial results and the commercial prospects for our current product candidates or our other potential product candidates could be harmed, our costs could increase and our ability to obtain regulatory approval and commence product sales could be delayed.

If we fail to establish an effective distribution process our business may be adversely affected.

We do not currently have the infrastructure necessary for distributing pharmaceutical products to patients. We intend to contract with third-party logistics wholesalers to warehouse these products and distribute them to pharmacies. This distribution network will require significant coordination with our sales and marketing and finance organizations. Failure to secure contracts with wholesalers could negatively impact the distribution of our products, and failure to coordinate financial systems could negatively impact our ability to accurately report product revenue. If we are unable to effectively establish and manage the distribution process, the commercial launch and sales of our products will be delayed or severely compromised and our results of operations may be harmed.

Risks Related to Intellectual Property

We may not be able to protect our proprietary technology in the marketplace.

We depend on our ability to protect our proprietary technology. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing and other agreements with employees and third parties, all of which offer only limited protection. Our success depends in large part on our ability and any future licensee s ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We believe we will be able to obtain, through prosecution of our current pending patent

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applications, adequate patent protection for our proprietary drug technology. If we are compelled to spend significant time and money protecting or enforcing our patents, designing around patents held by others or licensing or acquiring, potentially for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed. If we are unable to effectively protect the intellectual property that we own, other companies may be able to offer the same or similar products for sale, which could materially adversely affect our competitive business position and harm our business prospects. Our patents may be challenged, narrowed, invalidated, or circumvented, which could limit our ability to stop competitors from marketing the same or similar products or limit the length of term of patent protection that we may have for our products.

The patent positions of pharmaceutical products are often complex and uncertain. The breadth of claims allowed in pharmaceutical patents in the United States and many jurisdictions outside of the United States is not consistent. For example, in many jurisdictions the support standards for pharmaceutical patents are becoming increasingly strict. Some countries prohibit method of treatment claims in patents. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or create uncertainty. In addition, publication of information related to our current product candidates and potential products may prevent us from obtaining or enforcing patents relating to these product candidates and potential products, including without limitation composition-of-matter patents, which are generally believed to offer the strongest patent protection.

Our intellectual property includes issued patents and pending patent applications for compositions of matter and methods of use. As of June 30, 2013, we own two patents in the United States and have 13 patent applications in the United States and certain foreign jurisdictions for our primary product candidates AR-13324 and PG324 (patent protection for PG324 arises from the U.S. patents that cover AR-13324). The two patents individually cover composition of matter and method of use. We own 14 patents and have 20 pending patent applications in the United States and certain foreign jurisdictions relating to our previously discontinued product candidates and other proprietary technology. With respect to our current product candidates, our patents are exclusively in the United States, although we have patent applications pending in the United States and certain foreign jurisdictions. See Business Intellectual Property included elsewhere in this prospectus for further information about our issued patents and patent applications.

Patents that we own or may license in the future do not necessarily ensure the protection of our intellectual property for a number of reasons, including without limitation the following:

- our patents may not be broad or strong enough to prevent competition from other products that are identical or similar to our product candidates;
- there can be no assurance that the term of a patent can be extended under the provisions of patent term extension afforded by U.S. law or similar provisions in foreign countries, where available;
- our issued patents and patents that we may obtain in the future may not prevent generic entry into the U.S. market for our AR-13324 and PG324 product candidates;
- we do not at this time own or control a granted European patent or national phase patents in any European jurisdictions that would prevent generic entry into the European market for our AR-13324 product candidate;
- we do not at this time own or control issued foreign patents outside of Europe that would prevent generic entry into those markets for our product candidates;
- we may be required to disclaim part of the term of one or more patents;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim;

there may be prior art of which we are aware, which we do not believe affects the validity or enforceability of a patent claim, but which, nonetheless, ultimately may be found to affect the validity or enforceability of a patent claim;

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there may be other patents issued to others that will affect our freedom to operate;

if our patents are challenged, a court could determine that they are invalid or unenforceable;

there might be a significant change in the law that governs patentability, validity and infringement of our patents that adversely affects the scope of our patent rights;

a court could determine that a competitor s technology or product does not infringe our patents; and

our patents could irretrievably lapse due to failure to pay fees or otherwise comply with regulations or could be subject to compulsory licensing.

If we encounter delays in our development or clinical trials, the period of time during which we could market our potential products under patent protection would be reduced.

Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications to the FDA in which our competitors claim that our patents are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, ownership, priority, validity or enforceability. In that regard, third parties may challenge our patents in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and potential products. In addition, 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.

A significant portion of our intellectual property portfolio currently comprises pending patent applications that have not yet been issued as granted patents. If our pending patent applications fail to issue our business will be adversely affected.

Our commercial success will depend significantly on maintaining and expanding patent protection for our product candidates, as well as successfully defending our current and future patents against third-party challenges. As of June 30, 2013, we own 16 patents and have 33 pending patent applications in the United States and certain foreign jurisdictions relating to our current and previously discontinued product candidates and proprietary technology. See Business Intellectual Property included elsewhere in this prospectus for further information about our issued patents and patent applications. Our issued patents include two U.S. patents for composition of matter and method of use covering our lead product candidate, AR-13324 (these patents also cover our other primary product candidate PG324 to the extent that AR-13324 forms a part of PG324). The remainder of our portfolio is made up of patents covering previously discontinued product candidates and pending patent applications that have not yet been issued by the U.S. Patent and Trademark Office, or USPTO, or any other jurisdiction that cover our current and previously discontinued product candidates or other proprietary technology.

There can be no assurance that our pending patent applications will result in issued patents in the United States or foreign jurisdictions in which such applications are pending. Even if patents do issue on any of these applications, there can be no assurance that a third party will not challenge their validity or that we will obtain sufficient claim scope in those patents to prevent a third party from competing successfully with our products.

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. We do not currently have any issued patents in any foreign jurisdictions that cover our most advanced product candidates. To the extent we are able to obtain patents or other intellectual property rights in any foreign jurisdictions, it may be difficult for us to stop the infringement of our patents or the misappropriation of these intellectual property rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our products.

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. For example, there could be issued patents of which we are not aware that our product candidates or potential products infringe. There also could be patents that we believe we do not infringe, but that we may ultimately be found to infringe.

Moreover, patent applications are in some cases maintained in secrecy until patents are issued. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our product candidates or potential products infringe. For example, pending applications may exist that claim or can be amended to claim subject matter that our product candidates or potential products infringe. Competitors may file continuing patent applications claiming priority to already issued patents in the form of continuation, divisional, or continuation-in-part applications, in order to maintain the pendency of a patent family and attempt to cover our product candidates.

Third parties may assert that we are employing their proprietary technology without authorization and may sue us for patent or other intellectual property infringement. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and scientific personnel. If we are sued for patent infringement, we would need to demonstrate that our product candidates, potential products or methods either do not infringe the claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion. If a court holds that any third-party patents are valid, enforceable and cover our products or their use, the holders of any of these patents may be able to block our ability to commercialize our products unless we acquire or obtain a license under the applicable patents or until the patents expire. We may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost or on reasonable terms. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition

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of the manufacture or sale of products by us. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, in any such proceeding or litigation, we could be found liable for monetary damages, including treble damages and attorneys fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including trade secrets, of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities, biotechnology companies or other pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the intellectual property and other proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property, including trade secrets or other proprietary information. Litigation may be necessary to defend against these claims. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but litigation may be necessary in the future to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such 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. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. However, any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets. Accordingly, these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. In addition, others may independently discover our trade secrets and proprietary information. Further, the FDA, as part of its Transparency Initiative, a proposal by the FDA to increase disclosure and make data more accessible to the public, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA s disclosure policies may change in the future, if at all. Failure to obtain or maintain trade secret protection could enable

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competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position and financial results.

Any lawsuits relating to infringement of intellectual property rights brought by or against us will be costly and time consuming and may adversely impact the price of our common stock.

We may be required to initiate litigation to enforce or defend our intellectual property. These lawsuits can be very time consuming and costly. There is a substantial amount of litigation involving patent and other intellectual property rights in the pharmaceutical industry generally. Such litigation or proceedings could substantially increase our operating expenses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

In any infringement litigation, any award of monetary damages 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 litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are resolved. Further, any claims we assert against a perceived infringer could provoke these parties to assert counterclaims against us alleging that we have infringed their patents. 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.

In addition, our patents and patent applications could face other challenges, such as interference proceedings, opposition proceedings, re-examination proceedings, and other forms of post-grant review. In the United States, for example, post-grant review has recently been expanded. Any of these challenges, if successful, could result in the invalidation of, or in a narrowing of the scope of, any of our patents and patent applications subject to challenge. Any of these challenges, regardless of their success, would likely be time consuming and expensive to defend and resolve and would divert our management and scientific personnel s time and attention.

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 material adverse effect on the market price of our common stock.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of our existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

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If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation extending the terms of our patents and obtaining data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA regulatory approval for our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Patent term restorations, however, cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the FDA.

The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain earlier approval of competing products, and our ability to generate revenues could be materially adversely affected.

Risks Related to Our Business Operations and Industry

We depend upon our key personnel and our ability to attract and retain employees.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. We are highly dependent on our senior management team and our scientific founders, as well as the other principal members of our management and scientific teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. The loss of the services of any member of our senior management or scientific team or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. In particular, the loss of Vicente Anido, Jr., our Chairman of the Board of Directors and Chief Executive Officer, Thomas A. Mitro, our President and Chief Operating Officer, Richard J. Rubino, our Chief Financial Officer, Brian Levy, our Chief Medical Officer or Casey C. Kopczynski, our Chief Scientific Officer, could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We do not currently carry key person insurance on the lives of members of executive management. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. 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.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon completion of this offering, we will become subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission, or SEC. We

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believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

We are currently a small company with 23 employees as of September 30, 2013. In order to commercialize our potential products, we will need to substantially increase our operations. We plan to continue to build our compliance, financial and operating infrastructure to ensure the maintenance of a well-managed company. We expect to expand our employment base to approximately 300 when we are in the full commercial stages of our current potential products life cycle.

Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our future financial performance and our ability to commercialize our potential products and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

- manage our clinical trials and the regulatory process effectively;
- manage the manufacturing of product candidates and potential products for clinical and commercial use;
- integrate current and additional management, administrative, financial and sales and marketing personnel;
- develop a marketing and sales infrastructure;
- hire new personnel necessary to effectively commercialize our product candidates;
- develop our administrative, accounting and management information systems and controls; and
- hire and train additional qualified personnel.

Product candidates that we may acquire or develop in the future may be intended for patient populations that are large. In order to continue development and marketing of these product candidates, if approved, we would need to significantly expand our operations. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties.

If we engage in acquisitions in the future, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.

We may attempt to acquire businesses, technologies, services, products or product candidates in the future that we believe are a strategic fit with our business. We have no present agreement regarding any material acquisitions. However, if we do undertake any acquisitions, the process of integrating an acquired business, technology, service, products or product candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management s attention from our core

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business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, actual or contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

Our business is affected by macroeconomic conditions.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and foreign currency exchange rates and overall economic conditions and uncertainties, including those resulting from the current and future conditions in the global financial markets. For instance, if inflation or other factors were to significantly increase our business costs, it may not be feasible to pass through price increases to patients. Interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the value of our investments and our ability to liquidate our investments in order to fund our operations.

Interest rates and the ability to access credit markets could also adversely affect the ability of patients, payors and distributors to purchase, pay for and effectively distribute our products. Similarly, these macroeconomic factors could affect the ability of our potential future contract manufacturers, sole-source or single-source suppliers or licensees to remain in business or otherwise manufacture or supply product. Failure by any of them to remain in business could affect our ability to manufacture products.

If product liability lawsuits are successfully brought against us, our insurance may be inadequate and we may incur substantial liability.

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates. We will face an even greater risk if we commercially sell our potential products or any other product candidate that we develop. We maintain primary product liability insurance and excess product liability insurance that cover our clinical trials, and we plan to maintain insurance against product liability lawsuits for commercial sale of our potential products. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with our clinical trials and, in the future, commercial use of our potential products, for which our insurance coverage may not be adequate, and the cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial.

For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;

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termination of clinical trial sites or entire trial programs;

initiation of investigations by regulators;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

significant costs to defend resulting litigation;

diversion of management and scientific resources from our business operations;

substantial monetary awards to trial participants or patients;

loss of revenue; and

the inability to commercialize any products that we may develop.

We will need to increase our insurance coverage if and when we begin selling our product candidates if and when they receive marketing approval. However, the product liability insurance we will need to obtain in connection with the commercial sales of our product candidates if and when they receive regulatory approval may be unavailable in meaningful amounts or at a reasonable cost. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates if and when they obtain regulatory approval, which could materially adversely affect our business, financial condition, results of operations, cash flows and prospects.

Additionally, we do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers compensation, products liability and directors and officers insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would materially adversely affect our financial position, cash flows and results of operations.

Business interruptions could delay us in the process of developing our products and could disrupt our sales.

Our headquarters is located in Bedminster, New Jersey, our research and development facility is located in Research Triangle Park, North Carolina and we have an office in Newport Beach, California. We are vulnerable to natural disasters, such as severe storms and other events that could disrupt our operations. We do not carry insurance for natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

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Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We intend to adopt a code of conduct prior to completion of this offering, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Risks Related to this Offering and Ownership of Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has not been a public market for our common stock. Although we expect that our common stock will be approved for listing on the NASDAQ Global Market, or NASDAQ, if an active trading market for our common stock does not develop following this offering, you may not be able to sell your shares quickly or above the initial public offering price. The initial public offering price for the shares will be determined by negotiations between us and representatives of the underwriters and may not be indicative of prices that will prevail in the trading market, and the value of our common stock may decrease from the initial public offering price.

The trading price of our common stock is likely to be volatile, and you can lose all or part of your investment. The following factors, in addition to other factors described in this Risk Factors section and elsewhere in this prospectus, may have a significant impact on the market price of our common stock:

- announcements of regulatory approval or a complete response letter, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- any adverse changes to our relationship with manufacturers or suppliers;
- the results of our testing and clinical trials;
- the results of our efforts to acquire or license additional product candidates;

variations in the level of expenses related to our existing product candidates or preclinical and clinical development programs;

any intellectual property infringement actions in which we may become involved;

announcements concerning our competitors or the pharmaceutical industry in general;

achievement of expected product sales and profitability;

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manufacture, supply or distribution shortages;

actual or anticipated fluctuations in our quarterly or annual operating results;

changes in financial estimates or recommendations by securities analysts;

trading volume of our common stock;

sales of our common stock by us, our executive officers and directors or our stockholders in the future;

general economic and market conditions and overall fluctuations in the U.S. equity markets;

changes in accounting principles; and

the loss of any of our key scientific or management personnel.

In addition, the stock market, in general, and small pharmaceutical and biotechnology companies have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Further, the current decline in the financial markets and related factors beyond our control may cause our stock price to decline rapidly and unexpectedly.

We may be subject to securities litigation, which is expensive and could divert management attention.

Our share price may be volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Litigation of this type could result in substantial costs and diversion of management s attention and resources, which could adversely impact our business. Any adverse determination in litigation could also subject us to significant liabilities.

Our existing principal stockholders, executive officers and directors own a significant percentage of our common stock and will be able to exert a significant control over matters submitted to our stockholders for approval.

After this offering, our officers and directors, and stockholders who own more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own approximately 69.6% of our common stock (after giving effect to the conversion of all outstanding shares of our convertible preferred stock, the conversion of all of our outstanding notes and accrued interest thereon, and the net exercise immediately prior to the closing of this offering of warrants to purchase 2,506,075 shares of convertible preferred stock that will subsequently be automatically converted into 501,215 shares of common stock, but assuming no exercise of the underwriters option to purchase additional shares, no exercise of outstanding options, no exercise of warrants expected to remain outstanding following the closing of this offering, no purchases by our existing principal stockholders, including their affiliated entities, who have indicated an interest in purchasing an aggregate of approximately $10 million of shares of our common stock in this offering at the initial public offering price, and no purchases by our directors or officers in our directed share program).

This significant concentration of share ownership may adversely affect the trading price for our common stock because investors often perceive disadvantages in owning stock in companies with controlling stockholders. As a result, these stockholders, if they acted together, could significantly influence all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. These stockholders may be able to determine all matters requiring stockholder approval. The interests of these stockholders may not always coincide with our interests or the interests of other stockholders. This may also prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for

their common stock, and might affect the prevailing market price for our common stock.

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Additionally, our amended and restated certificate of incorporation that will become effective prior to the closing of this offering will renounce any interest or expectancy that we have in, or in being offered an opportunity to participate in, corporate opportunities that are presented to our existing principal investors, their affiliates and their partners, members, directors, stockholders, employees or agents (whether or not any such person is our director), other than someone who is our employee, except that we do not renounce our interest in any corporate opportunity offered to any such person if such opportunity is offered to such person expressly and solely in his or her capacity as our director. These provisions will apply even if the opportunity is one that we might reasonably have pursued or had the ability or desire to pursue if granted the opportunity to do so. See Description of Capital Stock Corporate Opportunities.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The assumed initial public offering price is substantially higher than the net tangible book value per share of our common stock. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the net tangible book value of our common stock. As a result, investors purchasing common stock in this offering will incur immediate dilution of $9.67 per share, based on the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover of this prospectus, and our pro forma net tangible book value as of June 30, 2013. In addition, as of September 30, 2013, options under the 2005 Plan to purchase 3,189,660 shares of our common stock at a weighted average exercise price of $2.1634 per share were outstanding, as well as warrants to purchase 3,589,005 shares of our convertible preferred stock that are expected to remain outstanding following the closing of this offering and, upon the closing of this offering, in accordance with their terms, will instead become exercisable for an aggregate of 717,801 shares of our common stock. See Description of Capital Stock Warrants. The exercise of these options or warrants would result in additional dilution. This dilution is due to our investors who purchased shares prior to this offering having paid substantially less than the price offered to the public in this offering when they purchased their shares. Further, because we will need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. These future issuances of equity or equity-linked securities, together with the exercise of outstanding options and warrants and any additional shares issued in connection with acquisitions, if any, may result in further dilution to investors.

As a result of this dilution, investors purchasing stock in this offering may receive significantly less than the purchase price paid in this offering in the event of liquidation. For more information, see Dilution included elsewhere in this prospectus.

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

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Substantially all of our existing stockholders are subject to lock-up agreements with the underwriters of this offering that restrict the stockholders ability to transfer shares of our common stock for at least 180 days from the date of this prospectus. The lock-up agreements limit the number of shares of common stock that may be sold immediately following the public offering. After this offering, we will have 20,324,003 outstanding shares of common stock based on the number of shares outstanding as of September 30, 2013, assuming we sell 5,250,000 shares in this offering. Subject to limitations, approximately 15,074,003 shares will become eligible for sale upon expiration of the lock-up period, as calculated and described in more detail in the section entitled Shares Eligible for Future Sale. In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

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Moreover, after this offering, holders of an aggregate of 14,006,166 shares of our common stock will have rights, subject to certain 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. Registration of these shares under the Securities Act of 1933, as amended, or the Securities Act, would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Our management will have broad discretion in the use of the net proceeds from this offering and may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the use of the net proceeds, including for any of the purposes described in the section entitled Use of Proceeds, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing instruments and U.S. government securities. These investments may not yield a favorable return to our stockholders.

If securities or industry analysts do not publish or cease publishing research or reports about us, our business or our market, or if they adversely change their recommendations or publish negative reports regarding our business or our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts may publish about us, our business, our market or our competitors. We do not have any control over these analysts and we cannot provide any assurance that analysts will cover us or provide favorable coverage. If any of the analysts who may cover us adversely change their recommendation regarding our stock, or provide more favorable relative recommendations about our competitors, our stock price could decline. If any analyst who may cover us were to cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Because we do not intend to declare cash dividends on our shares of common stock in the foreseeable future, stockholders must rely on appreciation of the value of our common stock for any return on their investment.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, we expect that only appreciation of the price of our common stock, if any, will provide a return to investors in this offering for the foreseeable future.

Our ability to use our net operating loss carry-forwards may be limited.

As of December 31, 2012, we had net operating losses of approximately $60.8 million, which may be utilized against future federal and state income taxes. These net operating losses will begin to expire at various dates beginning in 2024, if not utilized. If we experience an ownership change for purposes of Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, we may be subject to annual limits on our ability to utilize net operating loss carry-forwards. An ownership change is, as a general matter, triggered by sales or acquisitions of our stock in excess of 50% on a cumulative basis during a three-year period by persons owning 5% or more of our total equity value. We are not currently subject to any annual limits on our ability to utilize net operating loss carry-forwards. Our deferred tax assets have been fully offset by a valuation allowance as of December 31, 2012.

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The requirements associated with being a public company will require significant company resources and management attention.

Following this offering, we will become subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, the listing requirements of the securities exchange on which our common stock is traded, and other applicable securities rules and regulations. The Exchange Act requires that we file annual, quarterly and current reports with respect to our business and financial condition and maintain effective disclosure controls and procedures and internal control over financial reporting. In addition, subsequent rules implemented by the SEC and NASDAQ may also impose various additional requirements on public companies. As a result, we will incur additional legal, accounting and other expenses that we did not incur as a nonpublic company, particularly after we are no longer an emerging growth company as defined in the JOBS Act. Further, the need to establish the corporate infrastructure demanded of a public company may divert management s attention from implementing our growth strategy. We have made, and will continue to make, changes to our corporate governance standards, disclosure controls and financial reporting and accounting systems to meet our reporting obligations. However, the measures we take may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives. Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we will operate in an increasingly challenging regulatory environment. Once we no longer qualify as an emerging growth company under the JOBS Act, we will be required to comply with the Sarbanes-Oxley Act and the related rules and regulations of the SEC, expanded disclosures, accelerated reporting requirements and more complex accounting rules. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We estimate that we will annually incur approximately $1.5 million to $2.5 million in expenses to ensure compliance with these requirements.

Section 404(a) of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting, starting with the second annual report that we would expect to file with the SEC and we will be required to disclose material changes made in our internal controls and procedures on a quarterly basis. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. However, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act until the later of the year following our first annual report required to be filed with the SEC or the date we are no longer an emerging growth company as defined in the JOBS Act, because we are taking advantage of the exemptions contained in the JOBS Act.

To build the infrastructure to allow us to assess the effectiveness of our internal control over financial reporting, we will need to hire additional accounting personnel and improve our accounting systems, disclosure policies, procedures and controls. We are currently in the process of:

- hiring additional accounting and financial staff with appropriate public company experience;
- initiating plans to establish an outsourced internal audit function;

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initiating plans to upgrade our computer systems, including hardware and software;

establishing more robust policies and procedures; and

enhancing internal controls and our financial statement review process.

If we are unsuccessful in building an appropriate accounting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures, or comply with existing or new reporting requirements.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

The recently enacted JOBS Act will allow us to postpone the date by which we must comply with some of the laws and regulations intended to protect investors and to reduce the amount of information we provide in our reports filed with the SEC, which could undermine investor confidence in our company and adversely affect the market price of our common stock.

For so long as we remain an emerging growth company as defined in the JOBS Act, we may take advantage of certain exemptions from various requirements that are applicable to public companies that are not emerging growth companies including:

the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;

the say on pay provisions (requiring a non-binding stockholder vote to approve compensation of certain executive officers) and the say on golden parachute provisions (requiring a non-binding stockholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations) of the Dodd-Frank Act and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of its chief executive officer;

the requirement to provide detailed compensation discussion and analysis in proxy statements and reports filed under the Exchange Act, and instead provide a reduced level of disclosure concerning executive compensation; and

any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation or a supplement to the auditor s report on the financial statements.

We may take advantage of these exemptions until we are no longer an emerging growth company. We would cease to be an emerging growth company upon the earliest of: (i) the last day of the first fiscal year following the fifth anniversary of the completion of this offering; (ii) the last day of the first fiscal year in which our annual gross revenues are $1 billion or more; (iii) the date on which we have, during the previous three-year period, issued more than $1 billion in non-convertible debt securities; or (iv) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded $700 million as of the end of the second quarter of that fiscal year.

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Although we are still evaluating the JOBS Act, we currently intend to take advantage of some, but not all, of the reduced regulatory and reporting requirements that will be available to us so long as we qualify as an emerging growth company. For example, we have irrevocably elected under Section 107 of the JOBS Act not to take advantage of the extension of time to comply with new or revised financial accounting standards available under Section 102(b) of the JOBS Act. Our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an emerging growth company, which may increase the risk that weaknesses or deficiencies in our internal control over financial reporting go undetected. Likewise, so long as we qualify as an emerging growth company, we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our bylaws that will become effective prior to the closing of this offering, as well as provisions of the Delaware General Corporation Law, or DGCL, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions include:

- establishing a classified board of directors such that not all members of the board are elected at one time;
- allowing the authorized number of our directors to be changed only by resolution of our board of directors;
- limiting the removal of directors by the stockholders;
- authorizing the issuance of blank check preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; and
- requiring 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 our bylaws.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or

preventing a change of control, whether or not it is desired by or beneficial to our stockholders.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND OTHER DATA

This prospectus includes forward-looking statements. We may, in some cases, use terms such as predicts, believes, potential, continue, estima anticipates, expects, plans, intends, may, could, might, will, should or other words that convey uncertainty of future events or ou identify these forward-looking statements.

Forward-looking statements appear in a number of places throughout this prospectus and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things:

- the success, timing and cost of our ongoing clinical trials and anticipated Phase 3 and Phase 2b clinical trials for our current product candidates, including statements regarding the timing of initiation and completion of the trials;
- the timing of and our ability to obtain and maintain FDA or other regulatory authority approval of, or other action with respect, to our product candidates;
- the commercial launch and potential future sales of our current or any other future product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- third-party payor reimbursement for our product candidates;
- our estimates regarding anticipated capital requirements and our needs for additional financing;
- our expectations regarding the clinical effectiveness of our product candidates and results of our clinical trials;
- the glaucoma patient market size and the rate and degree of market adoption of our product candidates by eye-care professionals and patients;
- the timing, cost or other aspects of the commercial launch of our product candidates;
- our plans to pursue development of our product candidates for additional indications and other therapeutic opportunities;
- the potential advantages of our product candidates;
- our ability to protect our proprietary technology and enforce our intellectual property rights;
- our expectations related to the use of proceeds from this offering; and

our expectations regarding licensing, acquisitions and strategic operations.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on regulatory approvals and economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. We discuss many of these risks in this prospectus in greater detail under the heading Risk Factors and elsewhere in this prospectus. You should not rely upon forward-looking statements as predictions of future events.

Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this prospectus. In addition, even if our results of operations, financial condition and liquidity, and events in the industry in which we operate are consistent with the forward-looking statements contained in this prospectus, they may not be predictive of results or developments in future periods.

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Any forward-looking statements that we make in this prospectus speak only as of the date of such statement. Except as required by law, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this prospectus.

We obtained the industry and market data in this prospectus from our own internal estimates and research as well as from publicly available industry and general publications and research, surveys, studies and trials conducted by third parties. Industry publications, trials, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Some data is also based on our good faith estimates, which are derived from management s knowledge of the industry and independent sources. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Similarly, we believe our internal research is reliable, even though such research has not been verified by any independent sources. While we believe the market opportunity and market size information included in this prospectus is generally reliable, such information is inherently imprecise. In addition, information relating to projections, assumptions and estimates of our future performance and the future performance of the industry in which we operate is necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in Risk Factors and elsewhere in this prospectus. These and other factors could cause our results to differ materially from those expressed in the estimates made by third parties and by us.

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USE OF PROCEEDS

We estimate that the net proceeds we will receive from the sale of 5,250,000 shares of common stock in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $60.0 million ($69.5 million if the underwriters option to purchase additional shares is exercised in full). This estimate assumes an initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus.

We anticipate that the net proceeds from this offering will be used as follows:

- approximately $24.0 million and $10.0 million for direct clinical and non-clinical costs, respectively, associated with the completion of Phase 3 registration trials for our product candidate AR-13324;
- approximately $4.0 million and $1.5 million for direct clinical and non-clinical costs, respectively, associated with the completion of the Phase 2b clinical trial for our product candidate PG324; and
- the remainder for working capital and general corporate purposes.

In the ordinary course of our business, we expect to evaluate from time to time acquiring, investing in or in-licensing complementary products, technologies or businesses. We currently do not have any agreements or commitments with respect to any potential acquisition, investment or license.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our clinical trials and development efforts, as well as any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

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

Each $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by approximately $4.9 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $12.1 million, assuming that the assumed initial public offering price remains the same, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

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DIVIDEND POLICY

In October 2012, we formed a wholly-owned entity, Novaer Holding, Inc., or Novaer, and contributed certain non-core, non-competitive intellectual property relating to certain ophthalmic implant technology, as well as an exclusive license for all of our intellectual property for non-ophthalmic indications, and $0.1 million in cash for initial funding. Our board of directors declared a dividend and distributed 100% of this entity s equity interests to our stockholders and warrant holders of record as of September 6, 2012. The $0.1 million of cash included in the transaction was recorded as a cash dividend, as further explained in Note 13 to our financial statements appearing elsewhere in this prospectus. On September 6, 2013, we terminated our agreement to exclusively license to Novaer our intellectual property for non-ophthalmic indications. No consideration, or future obligation thereof, was exchanged in connection with this termination. As of September 6, 2013, we own all of the worldwide rights to our current product candidates for all indications, both ophthalmic and non-ophthalmic.

We have not declared or paid any other cash dividends on our capital stock since our inception. We currently anticipate that we will retain future earnings, if any, for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, we anticipate that only appreciation of the price of our common stock, if any, will provide a return to investors in this offering for at least the foreseeable future.

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CAPITALIZATION

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

- on an actual basis;
- on a pro forma basis to give effect to (i) the automatic conversion of all outstanding shares of our convertible preferred stock and the conversion of all of our outstanding notes and accrued interest thereon, in each case immediately prior to the closing of this offering, into an aggregate of 13,551,579 shares of our common stock assuming an initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover of this prospectus, (ii) the net exercise immediately prior to the closing of this offering of warrants to purchase 2,506,075 shares of convertible preferred stock that will subsequently be automatically converted into 501,215 shares of common stock, and (iii) the reclassification of the warrant liability to additional paid-in capital for warrants to purchase 3,589,005 shares of convertible preferred stock that are expected to remain outstanding following the closing of this offering and will instead become exercisable for 717,801 shares of common stock, at a weighted average exercise price of $3.23 per share; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 5,250,000 shares of our common stock in this offering at an assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with Selected Financial Data, our financial statements and the related notes appearing elsewhere in this prospectus and the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this prospectus.

	AS OF JUNE 30, 2013		
	ACTUAL (unaudited)	PRO FORMA [1] (unaudited)	PRO FORMA AS ADJUSTED [1][2] (unaudited)
	(in thousands, except share and per share data)		
Cash and cash equivalents [3]	$ 2,377	$ 9,877	$ 69,877
Notes payable, net of discount related parties [4]	$ 9,115	$	$
Interest payable related parties	238		
Warrants liability related parties [5]	4,603		
Convertible preferred stock, $0.001 par value, 82,672,909 shares authorized:			
Series A-1 2,000,000 shares authorized; 2,000,000 shares issued and outstanding	1,000		
Series A-2 10,010,029 shares authorized; 10,000,000 shares issued and outstanding	10,000		
Series A-3 22,479,476 shares authorized; 20,979,476 shares issued and outstanding	20,979		
Series A-4 5,683,404 shares authorized; 4,895,904 shares issued and outstanding	4,752		
Series B 42,500,000 shares authorized; 22,727,273 shares issued and outstanding [6]	24,441		
Stockholders (deficit) equity:			
Common stock, $0.001 par value: 20,000,000 shares authorized; 995,881 shares issued and outstanding, actual; 15,074,003 shares	5	15	20

issued and outstanding, pro forma; and 150,000,000 shares authorized; 20,324,003 shares issued and outstanding, pro forma as adjusted			
Additional paid-in capital	128	87,900	147,895
Deficit accumulated during the development stage	(74,042)	(79,196)	(79,196)
Total stockholders (deficit) equity	(73,909)	8,719	68,719
Total capitalization	$ 1,219	$ 8,719	$ 68,719

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(1) A $1.00 increase in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease the number of shares of our common stock issuable upon conversion of the outstanding notes and accrued interest thereon by 102,218 shares. A $1.00 decrease in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase the number of shares of our common stock issuable upon expected conversion of the outstanding notes and accrued interest thereon by 119,254 shares.

(2) A $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase (decrease) each of cash and cash equivalents, additional paid-in capital, total stockholders equity and total capitalization on a pro forma as adjusted basis by approximately $4.9 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) Cash and cash equivalents on a pro forma basis as of June 30, 2013 reflects $7.5 million in aggregate principal proceeds from the outstanding notes issued in August 2013 and September 2013 and does not otherwise reflect any changes in account balances subsequent to June 30, 2013. See Note 16 to our financial statements appearing elsewhere in this prospectus for further information. Cash and cash equivalents on a pro forma as adjusted basis includes the foregoing pro forma amounts and net proceeds from this offering at an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

(4) In August 2013 and September 2013, we issued an additional $4.5 million and $3.0 million, respectively, in aggregate principal amount of notes to related parties. Refer to Note 16 to our financial statements appearing elsewhere in this prospectus.

(5) In connection with our issuance of an additional $4.5 million and $3.0 million in aggregate principal amount of notes in August 2013 and September 2013, respectively, we concurrently issued warrants to purchase 1,022,727 and 681,816 shares, respectively, of our Series B convertible preferred stock.

(6) On August 9, 2013, we amended our certificate of incorporation to increase the number of shares of our Series B convertible preferred stock authorized for issuance to 50,000,000. On September 16, 2013, we amended the certificate of incorporation to reflect the re-designation of 2,300,000 unissued shares of our Series B convertible preferred stock as common stock. On October 8, 2013, we amended our certificate of incorporation to effect a 1-for-5 reverse stock split of our common stock.

In the table above, the number of shares of common stock outstanding as of June 30, 2013 does not include:

1,509,430 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2013 under the 2005 Plan, having a weighted average exercise price of $1.0170 per share;

343,228 shares of restricted stock outstanding as of June 30, 2013 that are subject to vesting restrictions and are not considered outstanding for accounting purposes; and

warrants outstanding as of June 30, 2013 to purchase 2,738,390 shares of convertible preferred stock that are expected to remain outstanding following the closing of this offering and that will be automatically converted into warrants to purchase 547,678 shares of common stock immediately prior to the closing of this offering. See Description of Capital Stock Warrants.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock upon closing of this offering. Net tangible book value per share of our common stock is determined at any date by subtracting our total liabilities from the amount of our total tangible assets (total assets less intangible assets) and dividing the difference by the number of shares of our common stock deemed to be outstanding at that date.

Our historical net tangible book value (deficit) as of June 30, 2013 was approximately $(74.9) million, or $(75.24) per share, based on 995,881 shares of common stock outstanding as of June 30, 2013.

On a pro forma basis, before giving effect to this offering and after giving effect to (i) the automatic conversion of all outstanding shares of our convertible preferred stock into 12,120,531 shares of our common stock, (ii) the conversion of all of our outstanding notes and accrued interest thereon into 1,431,048 shares of common stock, (iii) the net exercise immediately prior to the closing of this offering of warrants to purchase 2,506,075 shares of convertible preferred stock that will subsequently be automatically converted into 501,215 shares of common stock, (iv) the receipt of $7.5 million in aggregate principal proceeds from the outstanding notes issued in August 2013 and September 2013 (see Note 16 to our financial statements appearing elsewhere in this prospectus), and (v) the vesting of 25,328 shares of restricted stock, our net tangible book value as of June 30, 2013 would have been approximately $7.7 million, or approximately $0.51 per share of our pro forma outstanding common stock.

Investors participating in this offering will incur immediate and substantial dilution. After giving effect to our receipt of approximately $60.0 million of estimated net proceeds (after deducting underwriting discounts and commissions and estimated offering expenses payable by us) from our sale of common stock in this offering at an assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, our pro forma as adjusted net tangible book value as of June 30, 2013 would have been $67.7 million, or $3.33 per share. This amount represents an immediate increase in net tangible book value of $2.82 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of $9.67 per share of our common stock to new investors purchasing shares of common stock in this offering.

The following tables illustrate this dilution on a per share basis:

Assumed initial public offering price per share		$ 13.00
Historical net tangible book value per share	$ (75.24)	
Increase attributable to the pro forma transactions described above, before giving effect to this offering	75.75	
Pro forma net tangible book value per share before this offering	0.51	
Increase per share attributable to new investors	2.82	
Pro forma as adjusted net tangible book value per share after this offering		3.33
Dilution per share to new investors		$ 9.67

If the underwriters option to purchase additional shares is exercised in full, the pro forma as adjusted net tangible book value per share after giving effect to this offering would be $3.66 per share, which amount represents an immediate increase in pro forma net tangible book value of $3.15 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of $9.34 per share of our common stock to new investors purchasing shares of common stock in this offering.

Each $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value by $4.9 million, the pro forma as adjusted net tangible book value per share after this offering by $0.26 per share and the dilution in pro forma as adjusted net tangible book value to new investors in this offering by $0.74 per share, assuming the number of shares offered by us, as set forth on the

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cover page of this prospectus, remains the same and after deducting the underwriting discounts and commissions. We may also increase or decrease the number of shares we are offering. An increase of 1.0 million shares in the number of shares offered by us, together with a concurrent $1.00 increase in the assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, (a) would increase our pro forma as adjusted net tangible book value as of June 30, 2013 by approximately $17.9 million and (b) would also increase the pro forma as adjusted net tangible book value per share after this offering and the dilution in net tangible book value per share to new investors by $0.70 and $0.30, respectively, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions. Conversely, a decrease of 1.0 million shares in the number of shares offered by us together with a concurrent $1.00 decrease in the assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, (a) would decrease our pro forma as adjusted net tangible book value as of June 30, 2013 by approximately $16.0 million and (b) would also decrease the pro forma as adjusted net tangible book value per share after this offering and the dilution in net tangible book value per share to new investors by $0.67 and $0.33, respectively, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions.

The following table summarizes, as of June 30, 2013, giving effect to the pro forma adjustments noted above, the differences between the number of shares purchased from us, the total consideration paid to us, and the average price per share paid to us by existing stockholders and by new investors purchasing shares in this offering, before deducting underwriting discounts and commissions and estimated offering expenses payable by us, at an assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus.

	SHARES PURCHASED		TOTAL CONSIDERATION (in thousands, except share and per share data)		AVERAGE PRICE PER SHARE
	NUMBER	PERCENT	AMOUNT	PERCENT	
Existing stockholders	15,074,003	74.2%	$ 79,262	53.7%	$ 5.26
New investors	5,250,000	25.8%	68,250	46.3%	$ 13.00
Total	20,324,003	100%	$ 147,512	100%	

As of June 30, 2013, the number of shares of our common stock to be outstanding immediately following this offering set forth above excludes:

- 1,509,430 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2013 under the 2005 Plan, having a weighted average exercise price of $1.0170 per share;
- 343,228 shares of restricted stock outstanding as of June 30, 2013 that are subject to vesting restrictions and are not considered outstanding for accounting purposes; and
- warrants outstanding as of June 30, 2013 to purchase 2,738,390 shares of convertible preferred stock that are expected to remain outstanding following the closing of this offering and that will be automatically converted into warrants to purchase 547,678 shares of common stock immediately prior to the closing of this offering. See Description of Capital Stock Warrants.

Our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of approximately $10 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may determine to purchase fewer shares than they have indicated an interest in purchasing or not to purchase any shares in this offering. It is also possible that these stockholders could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these stockholders than the stockholders have indicated an interest in purchasing or not to sell any shares to these stockholders. The foregoing discussion and tables do not reflect any potential purchases of any shares in this offering by these stockholders or their affiliated entities.

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SELECTED FINANCIAL DATA

The following table sets forth our selected financial data for the periods and as of the dates indicated. You should read the following selected financial data in conjunction with our annual (audited) and interim (unaudited) financial statements and the related notes thereto included elsewhere in this prospectus and the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this prospectus. We have derived the following statement of operations and comprehensive loss data for the years ended December 31, 2012 and 2011 from our audited financial statements, included elsewhere in this prospectus. We have derived the following statement of operations and comprehensive loss data for the six months ended June 30, 2013 and 2012 and the period from inception (June 22, 2005) to June 30, 2013 and balance sheet data as of June 30, 2013 from our unaudited financial statements appearing elsewhere in this prospectus. The unaudited financial statements have been prepared on the same basis as the audited financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to fairly present our financial position as of June 30, 2013 and results of operations and comprehensive loss for the six months ended June 30, 2013 and 2012 and the period from inception (June 22, 2005) to June 30, 2013. Our historical results are not necessarily indicative of the results that may be expected in the future.

	SIX MONTHS ENDED JUNE 30,		YEAR ENDED DECEMBER 31,		PERIOD FROM INCEPTION (JUNE 22, 2005) TO JUNE 30, 2013
	2013	2012	2012	2011	
	(unaudited)	(in thousands, except share and per share data)			(unaudited)
Statement of Operations and Comprehensive Loss Data:					
Expenses:					
General and administrative	$ (3,406)	$ (2,285)	$ (5,020)	$ (3,521)	$ (23,303)
Research and development	(6,328)	(5,932)	(9,273)	(10,695)	(49,477)
Loss from operations	$ (9,734)	$ (8,217)	$ (14,293)	$ (14,216)	$ (72,780)
Other income (expense), net	(384)	376	(685)	1,249	(1,126)
Net loss	$ (10,118)	$ (7,841)	$ (14,978)	$ (12,967)	$ (73,906)
Comprehensive loss	$ (10,118)	$ (7,841)	$ (14,978)	$ (12,967)	$ (73,906)
Net loss attributable to common stockholders basic and diluted [1]	$ (10,392)	$ (8,115)	$ (15,643)	$ (13,419)	
Net loss per share attributable to common stockholders basic and diluted[1]	$ (10.68)	$ (8.51)	$ (16.39)	$ (14.50)	
Weighted-average number of shares outstanding basic and diluted[1]	973,460	953,114	954,695	925,625	
Pro forma net loss per share attributable to common stockholders basic and diluted (unaudited) [2]	$ (0.55)		$ (0.93)		
Weighted-average number of pro forma shares outstanding basic and diluted (unaudited)[2]	15,434,550		15,415,785		

	DECEMBER 31,

	JUNE 30, 2013 (unaudited)	2012	2011
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 2,377	$ 2,925	$ 15,068
Total assets	3,685	3,219	15,458
Notes payable, net of discount, and accrued interest thereon	9,353	2,347	
Warrants liability related parties	4,603	2,456	1,098
Convertible preferred stock	61,172	60,898	60,348
Total stockholders deficit	(73,909)	(63,919)	(48,697)

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(1) Net loss attributable to common stockholders reflects the accretion on convertible preferred stock and, where applicable, preferred stock dividends. See Note 2 to our financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the basic and diluted net loss per share attributable to common stockholders.

(2) See Note 2 and Note 15 to our financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the pro forma basic and diluted net loss per share attributable to common stockholders and the number of shares used in the computation of the per share amounts.

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MANAGEMENT S DISCUSSION AND ANALYSIS

OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of the prospectus contain forward-looking statements based upon current expectations that involve risks and uncertainties. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under Risk Factors and elsewhere in this prospectus.

Overview

We are a clinical-stage pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with glaucoma and other diseases of the eye. Our lead product candidate, once-daily, dual-action AR-13324, recently completed a Phase 2b clinical trial in patients with open-angle glaucoma and ocular hypertension. We are also developing a second product candidate, once-daily, triple-action PG324, which is a fixed-dose combination of AR-13324 and latanoprost, the most commonly prescribed drug for the treatment of patients with glaucoma. We are focused on glaucoma because we believe our product candidates provide important new opportunities to improve the treatment of the disease.

We are developing AR-13324 as the first of a new class of compounds that is designed to lower IOP in patients through a novel dual mechanism of action, or MOA. PG324 is designed to lower IOP through all three MOAs: increasing fluid outflow through the TM, the eye s primary drain, increasing fluid outflow through the uveoscleral pathway, the eye s secondary drain, and reducing fluid production in the eye.

We are a development stage company and have incurred net losses since our inception in June 2005. Our operations to date have been limited to research and development and raising capital. Through June 30, 2013, we have raised net cash proceeds of $71.0 million from the sale of $43.8 million of convertible preferred stock and $27.2 million of convertible notes. Subsequent to their issuance, $16.2 million of convertible notes converted into shares of convertible preferred stock and $0.5 million in cash payments were made. To date, we have not generated any revenue and have primarily financed our operations through the private placement of our equity securities and issuance of convertible promissory notes. As of June 30, 2013, we had a deficit accumulated during the development stage of $74.0 million. We recorded a net loss of $10.1 million and $7.8 million for the six months ended June 30, 2013 and 2012, respectively. We recorded annual net losses of $15.0 million in 2012 and $13.0 million in 2011. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the development and obtaining regulatory approval and preparing for potential commercialization of our product candidates.

We expect our research and development expenses to increase if and when we initiate Phase 3 and Phase 2b clinical trials for our AR-13324 and PG324 product candidates, respectively, and pursue regulatory approval. As we prepare for commercialization, we will likely incur significant commercial, sales, marketing and outsourced manufacturing expenses. Upon completion of this offering, we also expect to incur additional expenses associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses at least for the next several years. We do not expect to generate product revenue unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates.

We anticipate that we will use approximately $34.0 million of the net proceeds from this offering for direct clinical and non-clinical costs associated with the completion of Phase 3 registration trials for our AR-13324 product candidate and approximately $5.5 million for direct clinical and non-clinical costs associated with the completion of the Phase 2b clinical trial for our PG324 product candidate. We intend to use the remainder of the proceeds of this offering for working capital and general corporate purposes. We expect that these funds will not be sufficient to enable us to complete all necessary development or commercially launch these product candidates. Accordingly, we

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will be required to obtain further funding through other public or private offerings, debt financing, collaboration and licensing arrangements or other sources. Adequate additional funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Financial Overview

Revenue

We have not generated any revenue from the sale of any products, and we do not expect to generate any revenue unless or until we obtain regulatory approval of and commercialize our products.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and stock-based compensation for all officers and employees in general management, finance and administration. Other significant expenses include facilities expenses and professional fees for accounting and legal services. We expect that our general and administrative expenses will increase with the continued advancement of our product candidates and with the increased management, legal, compliance, accounting and investor relations expenses we will have as we begin to operate as a public company after the completion of this offering. We expect these increases will likely include increased expenses for insurance, expenses related to the hiring of additional personnel and payments to outside consultants, lawyers and accountants.

Research and Development Expenses

Since our inception, we have focused on our development programs. Research and development expenses consist primarily of costs incurred for the research and development of our preclinical and clinical candidates, which include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense for research and development personnel;
- expenses incurred under agreements with CROs, contract manufacturing organizations and consultants that conduct clinical trials and preclinical studies;
- costs associated with preclinical activities and development activities;
- costs associated with regulatory operations; and
- depreciation expense for assets used in research and development activities.

We expense research and development costs to operations as incurred. The costs for certain development activities, such as clinical trials, are recognized based on the terms of underlying agreements as well as an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations along with additional information provided to us by our vendors.

Expenses relating to activities, such as manufacturing and stability and toxicology studies, that are supportive of the product candidate itself, are classified as direct non-clinical. Expenses relating to clinical trials and similar activities, including costs associated with CROs, are classified as direct clinical. Expenses relating to activities that support more than one development program or activity such as salaries, stock-based compensation and depreciation are not allocated to direct clinical or non-clinical expenses and are separately classified as unallocated.

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The following table shows our research and development expenses by type of activity for the six months ended June 30, 2013 and 2012 and years ended December 31, 2012 and 2011.

	SIX MONTHS ENDED JUNE 30,		YEAR ENDED DECEMBER 31,	
	2013	2012	2012	2011
	(in thousands)			
AR-13324:				
Direct non-clinical	$ 901	$ 1,562	$ 2,318	$ 2,809
Direct clinical	1,301	530	993	
Total	$ 2,202	$ 2,092	$ 3,311	$ 2,809
Discontinued product candidates:				
Direct non-clinical	$ 465	$ 1,419	$ 2,312	$ 4,675
Direct clinical	2,575	1,095	1,475	1,023
Total	$ 3,040	$ 2,514	$ 3,787	$ 5,698
Unallocated	1,086	1,326	2,175	2,188
Total research and development expense	$ 6,328	$ 5,932	$ 9,273	$ 10,695

From inception through June 30, 2013, we did not incur any direct non-clinical or direct clinical costs for PG324 or AR-13533. Costs for these product candidates were primarily comprised of internal employee salaries and were included in unallocated costs. Discontinued product candidates relate to previously developed AR-12286 and related compounds, as they did not meet their primary endpoints in clinical trials. We incurred direct non-clinical and direct clinical expenses for these discontinued product candidates in all periods presented.

From inception through June 30, 2013, we have incurred approximately $49.5 million in research and development expenses. Prior to January 1, 2011, we recorded and managed research and development expenses in the aggregate due to the similarities of product candidates during that period. From the period June 22, 2005 (date of inception) to December 31, 2010, we incurred $23.2 million in aggregate research and development expenses.

Research and development activities associated with the discovery and development of new drugs and products for the treatment of diseases of the eye are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect our research and development expenses to increase as we initiate Phase 3 and Phase 2b clinical trials for our product candidates, or if the FDA requires us to conduct additional trials for approval.

Our research and development expenditures are subject to numerous uncertainties in timing and cost to completion. Development timelines, the probability of success and development expenses can differ materially from expectations. The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others, the following:

- number of trials required for approval;
- number of sites included in the trials;
- length of time required to enroll suitable patients;

number of patients that participate in the trials;

drop-out or discontinuation rates of patients;

duration of patient follow-up;

costs related to compliance with regulatory requirements;

number and complexity of analyses and tests performed during the trial;

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phase of development of the product candidate; and

efficacy and safety profile of the product candidate.

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with research institutions, consultants and CROs that conduct and manage clinical trials on our behalf. We generally accrue expenses related to clinical trials based on contracted amounts applied to the level of patient enrollment and activity according to the protocol. If future timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis. Historically, such modifications have not been material.

As a result of the uncertainties discussed above, we are unable to determine with certainty the duration and completion costs of our development programs or precisely when and to what extent we will receive revenue from the commercialization and sale of our products. We may never succeed in achieving regulatory approval for one or more of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future preclinical studies and clinical trials, uncertainties in the clinical trial enrollment rate and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including efficacy and tolerability profiles, competition, manufacturing capability and commercial viability.

Other Income (Expense), Net

Other income consists of interest earned on our cash and cash equivalents as well as the net proceeds from the sale of our net operating loss state tax benefits as described in Note 7 to our financial statements appearing elsewhere in this prospectus. Interest income is not considered significant to our financial statements but we expect our interest income to increase following this offering as we invest the net proceeds from this offering pending their use in operations.

Other expense consists of interest accrued under existing convertible notes, amortization of debt discounts and non-cash expense related to changes in the fair value of our warrants liability arising from the stock purchase warrants described in Note 10 to our financial statements appearing elsewhere in this prospectus.

Accretion of Convertible Preferred Stock

Shares of our convertible preferred stock were initially recorded on our balance sheet at their cost, less associated issuance costs. Series A-1, A-2 and A-3 of our convertible preferred stock are fully accreted as of December 31, 2012.

Our Series A-4 Convertible Preferred Stock issued on February 23, 2011, resulting from the conversion of the notes issued in 2010, was recorded at fair value. The difference between redemption and initial carrying value of $1.3 million is being ratably accreted over the period from February 23, 2011 until the earliest redemption date, which is August 17, 2015. Accretion amounted to $0.1 million, $0.1 million, $0.3 million, $0.2 million and $0.7 million for the six months ended June 30, 2013 and 2012, the year ended December 31, 2012 and 2011 and the period from February 23, 2011 to June 30, 2013, respectively.

Series B Convertible Preferred Stock issued on February 23, 2011 was recorded at fair value net of $1.2 million of issuance costs, which is being ratably accreted over the period from February 23, 2011 until the earliest redemption date, which is August 17, 2015. Accretion amounted to $0.1 million, $0.1 million, $0.3 million, $0.2 million and $0.6 million for the six months ended June 30, 2013 and 2012, the year ended December 31, 2012 and 2011 and the period from February 23, 2011 to June 30, 2013, respectively.

The composition of our convertible preferred stock is further described in Note 8 to our financial statements appearing elsewhere in this prospectus.

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Debt Discounts

Our notes payable were issued with warrant coverage. We recorded notes payable on our balance sheet net of a discount equal to the estimated fair value of the associated warrant instrument. The discount is amortized ratably through interest expense over the term of the associated notes. Refer to Note 2 to our financial statements appearing elsewhere in this prospectus.

Critical Accounting Policies and Use of Estimates

Our management s discussion and analysis of financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. The preparation of financial statements also requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, costs and expenses and related disclosures. We evaluate our estimates and judgments on an ongoing basis. Significant estimates include assumptions used in the determination of the fair value measurement of stock purchase warrants, stock-based compensation and certain research and development expenses. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are more fully described in Note 2 to our financial statements included elsewhere in this prospectus. The following accounting policies are the most critical in fully understanding and evaluating our reported financial results and affect significant judgments and estimates that we use in the preparation of our financial statements.

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable vendor personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. 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. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued expenses include:

- fees paid to CROs in connection with clinical trials; and
- fees paid to investigative sites in connection with clinical trials.

We accrue our expenses related to clinical trials based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct research activities and/or manage clinical trials 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. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. 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 level of effort varies from our estimate, we will adjust the accrual accordingly. If we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. Although we do not currently anticipate the future settlement of existing accruals to differ materially from our estimates, 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 for any period. There have been no material changes in estimates for the periods presented.

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Fair Value Measurements

We record certain financial assets and liabilities at fair value in accordance with the provisions of ASC Topic 820 on fair value measurements. As defined in the guidance, fair value, defined as an exit price, represents the amount that would be received to sell an asset or pay to transfer a liability in an orderly transaction between market participants. As a result, fair value is a market-based approach that should be determined based on assumptions that market participants would use in pricing an asset or a liability. As a basis for considering these assumptions, the guidance defines a three-tier value hierarchy that prioritizes the inputs used in the valuation methodologies in measuring fair value.

Level 1 Unadjusted quoted prices in active, accessible markets for identical assets or liabilities.

Level 2 Other inputs that are directly or indirectly observable in the marketplace.

Level 3 Unobservable inputs that are supported by little or no market activity.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

Our material financial instruments at June 30, 2013 and 2012 and December 31, 2012 and 2011 consisted primarily of cash and cash equivalents, other current assets, accounts payable, accrued expenses, long-term debt and stock purchase warrant liabilities. The fair value of cash and cash equivalents, other current assets, accounts payable, accrued expenses and notes approximate their respective carrying values due to the short-term nature of these instruments. We have determined the stock purchase warrants liability to be Level 3 fair value. See Note 10 to our financial statements appearing elsewhere in this prospectus.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees ratably over the requisite service period, which in most cases is the vesting period of the award for employees, based on the estimated fair value of the awards on the date of grant. Compensation expense for options granted to non-employees is determined as the fair value of consideration received or the fair value of the equity instruments issued, whichever is more reliably measured. The fair value of the awards granted to non-employees is re-measured each period until the related service is complete. Compensation expense related to restricted stock awards is based on the market value of our common stock on the grant date and is expensed ratably over the vesting period.

Stock-based compensation expense was $0.4 million and $0.2 million for the six months ended June 30, 2013 and 2012, and $0.4 million and $0.3 million for the years ended December 31, 2012 and 2011, respectively.

Significant Factors, Assumptions and Methodologies Used in Determining Fair Value

Determining the appropriate fair value measurement of stock-based awards requires the use of subjective assumptions. In the absence of a public trading market for our common stock, we conducted periodic assessments of the valuation of our common stock. These assessments were completed on an annual basis for all periods prior to December 31, 2012 and on a quarterly basis beginning in 2013. In connection with our December 31, 2012 valuation of our common stock and in preparation of this initial public offering, we completed a retrospective valuation for the first three quarters in 2012, as described below in Common Stock Valuation. The determination of the fair value measurement of options using the Black-Scholes option pricing model is affected by our estimated common stock fair values as well as assumptions regarding the number of other subjective variables. These other variables include the expected term of the options, our expected stock price volatility over the expected term of the options, stock option exercise and cancellation behaviors, risk-free interest rates and expected dividends.

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We estimated the fair value of stock options at the grant date using the following assumptions:

Fair Value of our Common Stock. Since no public market exists for our stock, we must estimate its fair value, as discussed in Common Stock Valuations below.

Volatility. As we do not have a trading history for our common stock, we utilize the most recent 36 months of data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the pharmaceutical industry with similar characteristics to us, including stage of product development and therapeutic focus.

Expected Term. We used the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, as we do not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.

Risk-free Rate. The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected time to liquidity.

Forfeiture. Forfeitures are estimated such that we only recognize expense for the shares expected to vest, and adjustments are made if actual forfeitures differ from those estimates. We estimated our annual forfeiture rates to be zero for 2013, 2012 and 2011.

Dividend Yield. Except for a one-time cash dividend related to the spin-off of certain non-core intellectual property (further described in Note 13 to our financial statements appearing elsewhere in this prospectus), we have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future.

The table below lists the assumptions utilized in the Black-Scholes option pricing model for the six months ended June 30, 2013 and years December 31, 2012 and 2011. The volatility of comparable companies was more stable in 2012 than in 2011, resulting in a lower volatility assumption in 2012 when compared to that in 2011.

	SIX MONTHS ENDED JUNE 30, 2013	DECEMBER 31, 2012	DECEMBER 31, 2011
Expected term (years)	6.25	6.25	6.25
Expected stock price volatility	60.00%	60.00%	126.90%
Risk-free interest rate	1.71%	1.05%	1.15%
Dividend yield	0.00%	0.00%	0.00%

The estimation of the number of stock awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from our current estimates, such amounts will be recorded as a cumulative adjustment in the period in which estimates are revised.

Common Stock Valuations

Our common stock valuations are determined by our board of directors in its sole discretion based on recommendations from management and taking into account advice and assistance provided by third-party valuation consultants engaged to assist us in connection with such valuations. All options granted are intended to be exercisable at a price per share not less than the per share fair value of our common stock underlying those options on the date of grant. All stock awards previously granted or to be granted in the future were or are expected to be exercisable at the grant date value. The valuations of our common stock were determined utilizing guidelines outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, referred to as the AICPA Practice

Aid. The methodologies used to determine fair value of our common stock included estimating the fair value of the enterprise and then allocating this value to all classes of equity securities using the option pricing method.

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The assumptions used in the valuation models that ultimately determine the fair value of our common stock as of the valuation date are based on numerous objective and subjective factors combined with management judgment, including the following:

- progress of research and development activities, including milestones achieved;
- sale of our convertible preferred stock in arm s length transactions, and the rights, preferences and privileges of that preferred stock relative to our common stock;
- our operating and financial performance;
- our business strategy, including material risks related to our business;
- likelihood of achieving a liquidity event for our stockholders; and
- external market conditions affecting the life sciences and pharmaceutical industry sectors.

The following table presents the grant dates and related exercise or purchase prices of stock options that we granted from January 1, 2012 through the date of this prospectus, along with the corresponding exercise price for each option grant and the fair value per share utilized to calculate stock-based compensation expense.

DATE OF GRANT	EQUITY TYPE	NUMBER OF SHARES UNDERLYING AWARDS GRANTED	EXERCISE PRICE PER OPTION	COMMON STOCK FAIR VALUE PER SHARE ON GRANT DATE
1/1/2012 [1]	Common Stock Option	154,000	$ 1.44	$ 1.47
2/1/2012	Common Stock Option	8,800	1.47	1.47
3/29/2012	Common Stock Option	56,000	1.47	1.47
6/1/2012	Common Stock Option	800	1.47	1.47
6/26/2012	Common Stock Option	800	1.47	1.47
9/6/2012	Common Stock Option	9,000	1.47	1.47
10/15/2012 [1]	Common Stock Option	345,000	1.47	2.90
3/21/2013 [2]	Common Stock Option	304,800	2.90	2.90
3/21/2013 [2]	Restricted Common Stock	371,034	N/A	2.90
8/26/2013	Common Stock Option	330,453	3.15	12.00 [4]
9/12/2013 [3]	Common Stock Option	1,374,299	3.15	12.00 [4]

(1) Refer to Retrospective 2012 Valuations section below for additional information. In addition, in March 2013 this grant was amended. Please see Executive Compensation Outstanding Equity Awards at Fiscal Year-End for additional information.

(2) Refer to Retrospective 2012 Valuations section below for additional information. Please see Executive Compensation Outstanding Equity Awards at Fiscal Year-End for additional information.

(3) On September 12, 2013, our board of directors authorized an aggregate of 1,374,299 common stock option grants, consisting of 1,142,299 to executive officers and employees, 208,000 to members of the board of directors and 24,000 to third-party consultants.

(4) We assessed the fair value of our common stock subsequent to the grant date of these awards.

Based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, the intrinsic value of all stock options outstanding as of June 30, 2013 was $29.6 million, of which $11.5 million and $18.1 million related to stock options that were vested and unvested, respectively, at that date. The intrinsic value of all stock options outstanding as of September 30, 2013 was $46.7 million, of which $12.1 million and $34.6 million related to stock options that were vested and unvested, respectively, at that date.

The estimated fair value per share of common stock in the table above represents the determination by our board of directors of the fair value of our common stock as of the date of grant, taking into consideration various objective and subjective factors, based on recommendations of our management and taking into account advice and assistance provided around the date of such grant by third-party valuation consultants engaged to assist us in connection with such valuations, as discussed below. For grants of stock awards made on dates for which there

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was no valuation performed by an independent valuation specialist, our board of directors determined the fair value of our common stock on the date of grant based upon the immediately preceding valuation recommendations of our management and other pertinent information available to it at the time of grant. The estimated fair value of our common stock and the related assumptions are set forth below for each of the valuations performed as of June 30, 2013 and December 31, 2012 and 2011, respectively.

Valuation of Common Stock as of June 30, 2013 and December 31, 2012

The market research conducted at our direction during the third quarter of 2012 expressed the view that our current product candidates should be well-positioned to compete effectively with existing drug therapies. Based on this research, we developed projections of our future revenues and operating expenses to determine projected free cash flows from our current product candidates AR-13324 and PG324 through patent expiration with respect to our June 30, 2013 valuation, and with respect to our December 31, 2012 valuation, these product candidates as well as our AR-12286 franchise. The enterprise value was determined by utilizing a risk adjusted discounted cash flow model, which is an income approach. The allocation of the determined equity value was based on the option pricing method. Key assumptions underlying the discounted cash flow model are described below.

Earnings before Interest, Taxes, Depreciation and Amortization, or EBITDA. EBITDA as a percentage of revenue was limited to less than or equal to 45% throughout the projection period for each product candidate as of June 30, 2013. EBITDA as a percentage of revenue was limited to less than or equal to 50% throughout the projection period for each product candidate as of December 31, 2012. These limits are in line with observable public specialty pharmaceutical companies.

Probability of Success. Our unlevered, after-tax free cash flows were adjusted by benchmarking stage of development for each of our product candidates to the drug development success rates as published by the Tufts Center for the Study of Drug Development, Tufts University, Boston, Massachusetts, United States, as adjusted for our circumstances. The probability of success rates utilized ranged between 15% and 40% as of December 31, 2012 and between 27% and 85% as of June 30, 2013. The increase in the probability of success relates to the continued positive progression through Phase 2b clinical trial for our lead product candidate, AR-13324.

Development Delay Sensitivity. To address the probability of unexpected changes to the development timeline of our product candidates, a delay sensitivity, or delay to expected launch date, of 0 to 2 year was applied.

Discount and Income Tax Rates. We assumed rates of 19% and 40%, respectively, and applied them to all probability-adjusted cash flows.

The allocation of the determined equity value was based on the option pricing method, which analyzes the rights of the common stock relative to those of the preferred stock by assessing the break points, or the points at which it is economically viable for the holders of preferred stock to convert their preferred stock into common stock. Our convertible preferred stock has a participation cap distribution equal to three times the original investments, which includes the liquidation preference. At the June 30, 2013 and December 31, 2012 valuation dates, the models incorporated a time to a liquidity event of one year. The liquidity events utilized in the allocation model were a private transaction and an initial public offering, whereby the gross proceeds exceeded the economic criteria as previously described, and were weighted 15% and 85% and 25% and 75% as of June 30, 2013 and December 31, 2012, respectively. The option model respected the contractually provided break points, and resulting values were determined according to the assumptions used in regards to enterprise value and time to exit.

Due to the inability of the determined enterprise value to satisfy the aforementioned preferred claims of the preferred stock and the uncertainty surrounding our product strategy resulting from the discontinuation of the AR-12286 product franchise, we determined that the receipt from the holders of preferred stock of the requisite consents for conversion was less than probable. As a result, we assigned no probability to this conversion scenario.

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The enterprise and per share value of common stock on a fully marketable basis on June 30, 2013 as determined by us was $114.8 million and $3.60, respectively. After the application of a 13% discount for lack of marketability, the fair value per share of common stock on a non-marketable interest basis was $3.15 as of June 30, 2013. The enterprise and per share value of common stock on a fully marketable basis on December 31, 2012, was $106.8 million and $3.55, respectively. After the application of an 18% discount for lack of marketability, the fair value per share of common stock on a non-marketable interest basis was $2.90 as of December 31, 2012. The Finnerty and Chaffe models were utilized to estimate the discount for lack of marketability in the aforementioned common stock valuations and 2012 retrospective common stock valuations described below. These models are commonly used for estimating illiquidity discounts for securities of medium volatility and have decreased over time as we progressed towards this offering. The financial statement impact to stock-based compensation expense and change in fair value measurements as of June 30, 2013 and December 31, 2012 was based on the initial public offering liquidation event.

In the third quarter of 2012, we received and evaluated results from our clinical trials conducted earlier in the year. Based on these results, we determined that our common stock value increased from $1.47 per share as of June 30, 2012 to $2.90 per share as of September 30, 2012. Due to the timing of our clinical trials, we did not have clinical and or regulatory milestones that would significantly alter the key assumptions utilized in our common stock valuations as of March, 31, 2013, December 31, 2012 and September 30, 2012 (See Retrospective 2012 Valuations below). This resulted in a consistent common stock value on a non-marketable interest basis for each of these valuation dates. During the second quarter of 2013, we evaluated the results of our Phase 2b clinical trials for AR-13324 and our discontinued product candidates. Based on these results, we determined that our common stock value increased from $2.90 per share as of March 31, 2013 to $3.15 per share as of June 30, 2013, the key drivers for which are discussed above.

Retrospective 2012 Valuations

A third-party valuation consultant was engaged to advise and assist our company in connection with the valuations of our common stock as of September 30, 2012, June 30, 2012 and March 31, 2012. For the purpose of such valuations, our projections as of December 31, 2012 were adjusted to reflect the development stage of our products as of such retrospective valuation dates. Due to the timing of the first Phase 2 clinical trial, we determined that AR-13324 was a viable product candidate in the late third quarter of 2012 and, therefore, included it in our financial and operation projections as of September 30, 2012. Enterprise values as of these retrospective valuation dates were determined by utilizing a risk-adjusted discounted cash flow model, which is an income approach, and the allocation of the determined equity value was based on the option pricing method. Key assumptions underlying the risk-adjusted discounted cash flow model are described below.

EBITDA. EBITDA as a percentage of revenue was limited to less than or equal to 50% throughout the projection period for each product candidate, in line with observable selected public specialty pharmaceutical companies. This was consistent for all retrospective 2012 valuations.

Probability of Success. Our unlevered, after-tax free cash flows were adjusted by benchmarking stage of development for each of our product candidates to the drug development success rates as published by the Tufts Center for the Study of Drug Development, Tufts University, Boston, Massachusetts, United States, as adjusted for our circumstances. The probability of success rates utilized ranged between 15% and 40%, 18% and 35% and 18% and 35% for the September 30, June 30 and March 31, 2012 retrospective valuations, respectively.

Development Delay Sensitivity. To address the probability of unexpected changes to the development timeline of our product candidates, a delay sensitivity, or delay to expected launch date, of 0 to 1 year was applied. This was consistent for all retrospective 2012 valuations.

Discount and Income Tax Rates. We assumed rates of 19% and 40%, respectively, and applied them to all probability adjusted cash flows for all retrospective 2012 valuations.

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The timing and weighting of the liquidation events described above remained consistent for all retrospective 2012 valuations. The fair value of our common stock on a non-marketable interest basis as determined by us was $2.90, $1.10 and $1.20 as of September 30, June 30 and March 31, 2012, respectively, and, after application of a discount for lack of marketability, was 20%, 22% and 24% as of September 30, June 30 and March 31, 2012, respectively.

We believe that the application of the income approach corroborates the utilization of the December 31, 2011 valuation of $1.47, which was based on a market approach, in pricing all stock options grants prior to September 30, 2012. Stock-based compensation related to options granted subsequent to September 30, 2012 reflected the retrospective valuation as of September 30, 2012. The exercise price on the options granted on January 1, 2012 reflects the most recent common stock value that was available to the board of directors. The exercise price of $1.44 was less than the fair value as of December 31, 2011 by an immaterial amount.

Valuation of Common Stock as of December 31, 2011

In conducting this valuation, a market approach was utilized to back-solve from prospective transactions involving convertible preferred stock equity securities. Specifically, based on our capital plan at the valuation date, we estimated that we would need additional funding of $27.5 million to continue the advancement of our single product candidate at that time. At the valuation date, we expected that such a new investment, Series C, would be issued as a flat round with the same price and preference amount as Series B, issued in February 2011, but would rank ahead of it in terms of liquidation. The allocation of the determined equity value was based on the option pricing method, which analyzes the rights of the common stock to those of preferred. Our convertible preferred stock has a participation cap distribution equal to three times original investment, which includes the liquidation preference. At the valuation date, we expected that the additional financing would occur in 2012 with a three year estimate for a liquidity event. The enterprise and per share value of common stock on a fully marketable basis as of December 31, 2011 as determined by us was $75.5 million and $2.15, respectively. After the application of a 30% discount for lack of marketability and incremental risk adjustment of 2.25%, the fair value per share of common stock on a non-marketable interest basis was $1.47. This fair value determination was utilized as the exercise price per share for all 2012 stock option grants, except for the January 1, 2012 grant. The issuance of Series C convertible preferred stock did not occur subsequent to the valuation date.

Initial Public Offering Price

In October 2013, we determined the estimated price range for this offering, as set forth on the cover page of this prospectus. As is typical in initial public offerings, the estimated price range for this offering was not derived using a formal determination of fair value of our common stock, but was determined by us in consultation with the underwriters. Among the factors that were considered in determining the price range were: our future prospects and those of our industry in general; an analysis of the typical valuation ranges seen in recent initial public offerings for companies in our industry; the general condition of the securities markets and the recent market prices of, and the demand for, publicly traded common stock of generally comparable companies; and interest in investing in a company with our profile and at our stage of development.

The midpoint of the estimated price range for this offering of $13.00 per share reflects a significant increase over the valuation of our common stock compared to our valuation conducted as of June 30, 2013, which was $3.15 per share after giving effect to the 1:5.0 reverse stock split effected on October 8, 2013. We believe this difference is primarily the result of the following factors:

- The estimated price range necessarily assumes that this offering has occurred and a public market for our common stock has been created, and therefore excludes any discount for lack of marketability of our common stock. In addition, our discussions with the underwriters in preparation of this offering considered the increased optimism with respect to market conditions and the initial public offering market, which contributed to an increase in the value of our common stock indicated in the estimated price range.

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The holders of our preferred stock currently have substantial economic rights and preferences over the holders of common stock, including preferential liquidation and dividend rights. Immediately prior to the closing of this offering, all outstanding shares of preferred stock will convert into common stock pursuant to an automatic conversion feature. This conversion will eliminate the superior rights and preferences of the preferred stock and accordingly increase the value of the common stock. The option model that we used respected the contractually provided break points, and resulting values were determined according to the assumptions used in regards to the enterprise value and time to exit.

We believe that in the public capital markets there are investors who may apply more qualitative and subjective valuation criteria to certain of our clinical assets than the valuation methods applied in our valuations. As a result, the price that investors are willing to pay in the proposed offering may take into account other factors that have not been expressly considered in our prior valuations, are not objectively determinable and that valuation models are not able to quantify. For example, members of our senior management team, including our Chief Executive Officer who was appointed on July 25, 2013, have relevant experience operating a publicly-traded company. Investors might conclude that this experience could justify, in part, a higher valuation than the June 30, 2013 valuation that was based on more objective factors and by its nature would not have factored in this prior experience. Investors are cautioned that the midpoint of the price range set forth on the cover page of this prospectus does not necessarily represent the fair value of our common stock, but rather reflects an estimate of the proposed offering price range determined by us in consultation with the underwriters.

Equity Issuances Subsequent to June 30, 2013

In the context of the proposed offering, we have assessed certain assumptions utilized in determining the fair value of our common stock for all equity issuances subsequent to June 30, 2013. Given the anticipated proximity of the offering, for financial reporting purposes, we plan to recognize a stock-based compensation charge for the quarter ended September 30, 2013 using the low end of the estimated price range, $12.00, as the deemed fair value of our common stock for the measurement of all August 2013 and September 2013 equity transactions and all transactions that require fair value measurement as of September 30, 2013. Accordingly, for the quarter ended September 30, 2013, we plan to recognize a stock-based compensation charge of $0.3 million related to stock options granted on August 26, 2013 and September 12, 2013 and $0.8 million related to the re-measurement of grants to non-employees. The total unrecognized stock-based compensation expense related to the August and September 2013 option grants was $16.4 million and is expected to be recognized over the vesting period of the options. In addition, we measured the stock purchase warrants issued on August 9, 2013 and September 30, 2013 using the low end of the price range as the deemed fair value of our common stock, resulting in an initial measurement of the warrant liability of $2.4 million and $1.6 million, respectively.

Results of Valuation Models May Vary

Valuation models require the input of highly subjective assumptions. Because our common stock has characteristics significantly different from that of publicly traded common stock and because changes in the subjective input assumptions can materially affect the fair value estimate, in management s opinion, the existing models do not necessarily provide a reliable, single measure of the fair value of our common stock. The foregoing valuation methodologies are not the only valuation methodologies available and will not be used to value our common stock once this offering is complete. We cannot make complete assurances as to any particular valuation for our stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

Stock Purchase Warrants

We account for our stock purchase warrants as liabilities based upon the characteristics and provisions of the underlying instruments. These liabilities were recorded at their fair value on the date of issuance and are

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remeasured on each subsequent balance sheet date, with fair value changes recognized as income (decreases in fair value) or expense (increases in fair value) in Other income (expense), net in the statements of operations. The fair value of these liabilities is estimated using the Black-Scholes method, which, under our facts and circumstances, approximates, in all material respects, the values determined when using a Monte Carlo simulation. The composition of our stock purchase warrants and assumptions utilized in estimating fair value are described in Note 10 to our financial statements appearing elsewhere in this prospectus.

The Black-Scholes method and the Monte Carlo simulation require the use of subjective assumptions, including but not limited to stock price volatility, the expected life of the warrants, the risk free interest rate and the fair value of the underlying equity securities. The fair value of the underlying common stock is determined as discussed above under Stock-Based Compensation. We will continue to adjust the fair values of the warrants at each period end for any changes in fair value until the earlier of the exercise or expiration of the applicable warrants or until such time that the warrants are no longer determined to be derivative instruments. Our warrant liability is expected to fluctuate based on the assumptions used in our valuation model.

Tax Valuation Allowance

A valuation allowance is recorded if it is more likely than not that a deferred tax asset will not be realized. We provided a full valuation allowance on our deferred tax assets that primarily consist of cumulative net operating losses of $60.8 million for the period from inception (June 22, 2005) to December 31, 2012. We incurred net losses of $10.1 million for the six months ended June 30, 2013. Due to our three year cumulative loss position, history of operating losses and losses expected to be incurred in the foreseeable future, a full valuation allowance against our net deferred tax assets was considered necessary.

Results of Operations

Comparison of the six months ended June 30, 2013 and 2012

The following table summarizes the results of our operations for the six months ended June 30, 2013 and 2012:

	SIX MONTHS ENDED JUNE 30,		INCREASE (DECREASE)	% INCREASE (DECREASE)
	2013	2012		
	(unaudited)			
	(in thousands)			
Expenses				
General and administrative	$ (3,406)	$ (2,285)	$ 1,121	49%
Research and development	(6,328)	(5,932)	396	7%
Other financial income (expense), net	(384)	376	760	202%
Net loss	$ (10,118)	$ (7,841)		

General and administrative expenses

General and administrative expenses increased by $1.1 million for the six months ended June 30, 2013 as compared to the six months ended June 30, 2012. This increase was primarily attributable to an increase of $0.5 million in personnel costs, including new salaried employees, related employee stock-based compensation expense, and an increase of $0.6 million in accounting and legal fees and other operating costs.

Research and development expenses

Research and development expenses increased by $0.4 million for the six months ended June 30, 2013 as compared to the six months ended June 30, 2012. The net increase was primarily due to higher direct clinical costs of $2.3 million offset by a decrease in direct non-clinical costs of $1.6 million. The remaining difference is due to the

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change in unallocated expenses including employee salary and related expenses. The direct clinical costs for AR-13324 increased by $0.8 million due to activity related to its Phase 2b clinical trial. The remaining portion of the increase is attributable to the Phase 2b clinical trials for product candidates where further advancement for the treatment of glaucoma was discontinued during the second quarter of 2013. These products did not meet desired efficacy requirements for further advancement. The direct non-clinical costs for AR-13324 decreased $0.7 million due to the timing of testing activity, partially offset by increased manufacturing costs. The remaining portion of the decrease is attributable to a decline in manufacturing and testing for discontinued product candidates, as previously described. Research for PG324 was primarily comprised of internal employee salaries.

Other income (expense), net

Other income (expense), net decreased by $0.8 million for the six months ended June 30, 2013 as compared to the six months ended June 30, 2012. The decrease was mainly due to a $1.4 million increase in non-cash interest expense relating to the amortization of the debt discounts and accrued interest and $0.6 million unfavorable non-cash change (expense) in fair value of warrant liabilities. These increased expenses were partially offset by $1.3 million of income generated as a result of our participation in the New Jersey Economic Development Authority s sponsored Technology Business Tax Certificate Transfer Program.

Comparison of the Years Ended December 31, 2012 and 2011

The following table summarizes the results of our operations for the years ended December 31, 2012 and 2011:

	YEARS ENDED DECEMBER 31,		INCREASE (DECREASE)	% INCREASE (DECREASE)
	2012	2011		
	(in thousands)			
General and administrative expenses	$ (5,020)	$ (3,521)	$ 1,499	43%
Research and development expenses	(9,273)	(10,695)	(1,422)	(13)%
Other income (expense), net	(685)	1,249	1,934	155%
Net loss	$ (14,978)	$ (12,967)		

General and administrative expenses

General and administrative expenses increased by $1.5 million for the year ended December 31, 2012 as compared to the year ended December 31, 2011. This increase was primarily attributable to an increase of $0.9 million in personnel costs, including new salaried employees and related employee stock-based compensation expense resulting in part from the hiring in 2012 of a Chief Medical Officer and Chief Financial Officer, an increase of $0.3 million in legal and consulting fees for supporting intellectual property, patent and business related initiatives and $0.3 million in other operating costs.

Research and development expenses

Research and development expenses decreased by $1.4 million for the year ended December 31, 2012 as compared to the year ended December 31, 2011. This decrease was primarily due to lower direct non-clinical costs of $2.8 million, offset by an increase of direct clinical costs of $1.4 million. Direct non-clinical costs for AR-13324 decreased by $0.5 million due to the timing of testing and manufacturing requirements. The remaining portion of the decrease in direct non-clinical costs primarily related to the timing of manufacturing requirements for product candidates where further advancement for the treatment of glaucoma was discontinued during the second quarter of 2013. These product candidates did not demonstrate the efficacy endpoint required for further advancement. The direct clinical costs for AR-13324 increased by $1.0 million due to the timing of Phase 2a and Phase 2b clinical trials. The remaining portion of the increase relates to the timing of clinical trials of discontinued product candidates, as previously described. Unallocated expenses, including internal employee salary and related expenses, remained consistent across the periods.

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Other income (expense), net

Other income (expense), net primarily consisted of the fair value adjustments to warrants liability arising from stock purchase warrants issued in connection with various debt financings. The decrease in Other income (expense), net by $1.9 million for the year ended December 31, 2012 as compared to the year ended December 31, 2011 was due primarily to a one-time, non-cash gain of $0.8 million resulting from the conversion of notes and a $0.3 million favorable non-cash change in fair value of the warrant liability in 2011, with a $0.6 million unfavorable non-cash change in fair value of the warrant liability in 2012. The composition of Other income (expense), net is further described in Note 3 to our financial statements appearing elsewhere in this prospectus.

Liquidity and Capital Resources

We have incurred losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will increase over historical levels and, as a result, we will need additional capital to fund our operations, which we may obtain from additional public offerings, debt financing, collaboration and licensing arrangements or other sources.

For the period from inception (June 22, 2005) to June 30, 2013, we have cumulative net cash flows used by operating activities of $66.4 million and cumulative net losses of $73.9 million. We have incurred losses and experienced negative operating cash flows since inception, and have cumulative net cash flows used by operating activities of $58.8 million and cumulative net losses of $63.8 million for the period from inception (June 22, 2005) to December 31, 2012. The total future need for operating capital and research and development funding significantly exceeds the cash and cash equivalents that we have on our balance sheet at June 30, 2013. As a result, we will require additional funding in the future and may not be able to raise such additional funds. In the absence of product or other revenues, the amount, timing, nature or source of which cannot be predicted, our losses will continue as we conduct our research and development activities. If adequate funds are not available, we plan to delay, reduce or eliminate research and development programs or reduce administrative expenses. If we are unable to raise sufficient funding in 2013, we may be unable to continue to operate. There is no assurance that we will be successful in obtaining sufficient financing on acceptable terms and conditions to fund continuing operations, if at all. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition.

Since our inception, we have funded operations primarily through the sale of preferred stock and issuance of convertible notes payable. Through December 31, 2012, we have raised net cash proceeds of $63.5 million through the sales of $43.8 million of convertible preferred stock and $19.7 million from the issuance of convertible notes. Subsequent to their issuance, $16.2 million of convertible notes converted into shares of convertible preferred stock. As of June 30, 2013 and December 31, 2012, we had cash and cash equivalents on hand of approximately $2.4 million and $2.9 million, respectively. We invest cash in excess of immediate requirements in accordance with our investment policy primarily with a view to liquidity and capital preservation. As of December 31, 2012, our funds were held in cash and money market funds.

On December 7, 2012, we authorized the sale of convertible notes, or the outstanding notes, to related parties in the aggregate principal amount of $15.0 million. In December 2012, we issued $3.0 million aggregate principal amount of notes; in March 2013, we issued $3.0 million aggregate principal amount of notes; in May 2013, we issued $4.5 million aggregate principal amount of notes; and in August 2013, we issued $4.5 million aggregate principal amount of notes. In August 2013, we amended the agreements relating to the outstanding notes, authorizing the sale of an additional $3.0 million aggregate principal amount of notes and extending the maturity date from September 30, 2013 to December 31, 2013. In September 2013, we issued the additional $3.0 million

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aggregate principal amount of notes to related parties. Refer to Note 16 to our financial statements appearing elsewhere in this prospectus. The outstanding notes accrue interest at a rate of 8% with principal plus interest due upon maturity. We have obtained a written consent from the holders of our outstanding notes in which the holders agreed to convert all principal and interest accrued thereon to common stock upon the completion of this offering at the conversion price equal to the per share offering price. This conversion feature was accounted for as a bifurcated embedded derivative that had an immaterial impact to our financial statements as further described in Note 6 to our financial statements appearing elsewhere in this prospectus. No beneficial conversion feature will be recorded in connection with this offering. In addition, no other conversion option features or beneficial conversion features will be triggered in connection with this offering.

The following table summarizes our sources and uses of cash:

	SIX MONTHS ENDED JUNE 30,		YEARS ENDED DECEMBER 31,	
	2013	2012	2012	2011
			(in thousands)	
Net cash (used by) provided by:				
Net cash used by operating activities	$ (7,577)	$ (9,320)	$ (14,968)	$ (11,998)
Net cash used by investing activities	(17)	(51)	(51)	(49)
Net cash provided by financing activities	7,046	6	2,876	23,846
Net change in cash and cash equivalents	$ (548)	$ (9,365)	$ (12,143)	$ 11,799

During the six months ended June 30, 2013 and 2012, our operating activities used net cash of $7.6 million and $9.3 million, respectively. The use of net cash in all periods primarily resulted from our net losses. The decrease in net loss from operations for the six months ended June 30, 2013 as compared to June 30, 2012 was primarily attributable to $1.3 million of cash proceeds from the sale of deferred state tax benefits to an unrelated third party, as further described in Note 7 to our financial statements appearing elsewhere in this prospectus. Other changes from operating activities were caused by changes in accrued research and development expenses, stock-based compensation and the mark-to-market adjustment for the warrants liability. During the six months ended June 30, 2013 and 2012, our investing activities primarily related to purchases of office furnishings and equipment to facilitate our increased research and development activities and headcount. The net cash provided by financing activities during the six months ended June 30, 2013 was related to $7.5 million from the aforementioned sale of the convertible notes, offset by $0.5 million in payments made in preparation for this initial public offering.

During the years ended December 31, 2012 and 2011, our operating activities used net cash of $15.0 million and $12.0 million, respectively. The use of net cash in all periods primarily resulted from our net losses. The increase in net loss from operations for the year ended December 31, 2012 as compared to the year ended December 31, 2011 was due primarily to the aforementioned increase in general and administrative expenses. Other changes from operating activities were caused by changes in accrued research and development expenses, stock-based compensation and the mark-to-market adjustment for the warrants liability. In connection with a financing that took place in 2011 involving the conversion of notes issued in 2010, we recognized a non-cash gain of $0.8 million arising from the impact of the notes conversion, which decreased net cash from operating activities. During the years ended December 31, 2012 and 2011, our investing activities included primarily purchases of office furnishings and equipment to facilitate our increased research and development activities and headcount.

During the years ended December 31, 2012 and 2011, our financing activities provided net cash of $2.9 million and $23.8 million, respectively. The net cash provided by financing activities during the year ended December 31, 2012 was related to $3.0 million from the aforementioned sale of the convertible notes. The net cash provided by financing activities during the year ended December 31, 2011 was related to $25.0 million of proceeds from the sales of Series B convertible preferred stock, offset by $1.2 million in related issuance costs.

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Operating Capital Requirements

We expect to incur increasing operating losses for at least the next several years as we commence Phase 3 and Phase 2b clinical trials of our AR-13324 and PG324 product candidates. We believe that the net proceeds from this offering, together with existing cash and cash equivalents, will be sufficient to fund our projected operating requirements for at least the next 12 months following the completion of this offering.

Due to the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. We based our projections on assumptions that may prove to be incorrect or unreliable or may change due to circumstances beyond our control, and as a result we may consume our available capital resources earlier than we originally projected. Our future funding requirements will depend on many factors, including, but not limited to the following:

- timing and costs of any Phase 3 and Phase 2b clinical trials of our product candidates;
- costs of any follow-on development or products;
- timing and cost of the ongoing supportive non-clinical studies and activities for our product candidates;
- outcome, timing and costs of seeking regulatory approval;
- costs of commercialization activities for our product candidates, if we receive regulatory approval, including the costs and timing of establishing product sales, marketing, manufacturing and distribution capabilities;
- costs of operating as a public company, including legal, compliance, accounting and investor relations expenses;
- terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish; and
- filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims.

We expect that we will need to obtain substantial additional funding in order to obtain regulatory approvals on any product candidates and support commercialization and ongoing business activities. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interests of our existing stockholders may be materially diluted and the terms of these securities could include liquidation or other preferences that could adversely affect the rights of our existing stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to significantly delay, scale back or discontinue the development or commercialization of our product candidates, seek collaborators at an earlier stage than otherwise would be desirable or on terms that may be less favorable than might otherwise be available.

We will also incur costs as a public company that we have not previously incurred or previously incurred at lower rates, including but not limited to, increased costs and expenses for directors fees, increased personnel costs, increased directors and officers insurance premiums, audit and legal fees, investor relations fees, expenses for compliance with reporting requirements under the Exchange Act and rules implemented by the SEC and NASDAQ and various other costs. We estimate that we will annually incur approximately $1.5 million to $2.5 million in expenses to ensure compliance with these requirements.

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Contractual Obligations and Commitments

The following table summarizes our contractual obligations at June 30, 2013:

	TOTAL	LESS THAN 1 YEAR	1 TO 3 YEARS	3 TO 5 YEARS	MORE THAN 5 YEARS
			(in thousands)		
Operating lease obligations [1]	$ 1,014	$ 266	$ 422	$ 315	$ 11
Convertible notes payable [2]	10,500	10,500			
Accrued interest [2]	238	238			

(1) Our operating lease obligations are related to our corporate headquarters in New Jersey and research facility in North Carolina.

(2) Under the amended terms of the note agreement (further described in Note 16 to our financial statements appearing elsewhere in this prospectus), we may issue an aggregate amount of $18.0 million of convertible notes. On each of December 7, 2012 and March 28, 2013, we issued $3.0 million of our outstanding convertible notes. On May 23, 2013, we issued $4.5 million of our outstanding convertible notes. The table above does not reflect $4.5 million of outstanding notes issued in August 2013 and $3.0 million of outstanding notes issued in September 2013. All outstanding notes including accrued interest, will convert into common stock in connection with this offering.

We have no other contractual obligations or commitments that are not subject to our existing financial statement accrual processes.

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 SEC rules.

Net Operating Loss Carry-Forwards

We have incurred significant net operating losses since our inception in June 2005. We expect to continue to incur net operating losses for the foreseeable future as we continue to develop our product portfolio, seek regulatory approval, and, if such approval is obtained, prepare to commercialize our products.

As of December 31, 2012, we had approximately $60.8 million of net operating loss carry-forwards, which may be utilized against future federal and state income taxes. These net operating losses will begin to expire at various dates beginning in 2024, if not utilized. We also have federal research and development tax credit carry-forwards of $0.4 million to offset future federal income taxes, which expire at various dates beginning in 2024, if not utilized.

Net operating loss and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Code, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of our company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

As of December 31, 2012, we recorded a full valuation allowance against our net deferred tax assets and development tax credit carry-forwards, as we believe, based on our history of operating losses, it is more likely than not that the tax benefits will not be realized. In the future, if we determine that a portion or all of the tax benefits associated with our tax carry-forwards will be realized, net income would increase in the period of such

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determination. In January 2013, we participated in the New Jersey Economic Development Authority s Sponsored Technology Business Tax Certificate Transfer Program.

Quantitative and Qualitative Disclosure about Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. We had cash and cash equivalents on hand of $2.4 million, $2.9 million and $15.1 million as of June 30, 2013, December 31, 2012 and 2011, respectively. Given the short-term nature of our cash equivalents, we believe that our interest rate risk is not significant to our financial statements. We do not engage in any hedging activities against changes in interest rates. Our outstanding notes carry a fixed interest rate and, as such, are not subject to interest rate risk. We do not have any foreign currency or other derivative financial instruments.

Jumpstart Our Business Startups Act of 2012

As a company with less than $1 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;
- reduced disclosure about our executive compensation arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal controls over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenue, we have more than $700 million in market value of our stock held by non-affiliates or we issue more than $1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of certain reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Recent Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board, or the FASB, issued ASU 2013-02 Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income which requires that public and non-public companies present information about reclassification adjustments for accumulated other comprehensive income in their annual financial statements in a note or on the face of the financial statements. Public companies will also have to provide this information in interim financial statements. The new disclosure requirements are effective for fiscal years, and interim periods within those years, beginning after December 15, 2012. The adoption of the provisions of this guidance will not have a material impaction on our results of operations, cash flows and financial position.

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In June 2011, the FASB issued amended guidance intended to increase the prominence of items reported on other comprehensive income (loss). This amended guidance requires that all non-owner changes in stockholders equity (deficit) be presented in a single continuous statement of comprehensive income (loss) or in two separate but consecutive statements. The amended guidance became effective for periods beginning after December 15, 2011. We applied this guidance beginning with our financial information for the year ended December 31, 2012. This amended guidance effects presentation, but does not have a material effect on our financial statements.

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BUSINESS

Overview

We are a clinical-stage pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with glaucoma and other diseases of the eye. Our strategy is to advance our product candidates, including dual-action AR-13324 and triple-action PG324, to regulatory approval, and commercialize these products ourselves in the United States. We plan to build a commercial team of approximately 100 sales representatives to target approximately 10,000 high prescribing eye-care professionals throughout the United States. For certain key markets outside the United States, including Europe, Japan and emerging markets, we intend to explore partnership opportunities through collaboration and licensing arrangements. We plan to further maximize our commercial potential by identifying and advancing additional product candidates, both through our internal discovery efforts and through possible in-licensing or acquisitions of additional ophthalmic products or product candidates that would complement our current product portfolio. Our senior leadership team has extensive experience in the ophthalmology market and has overseen the development and commercialization at major pharmaceutical companies of several successful ophthalmic products, including *Acular*, *Alphagan P*, *Bepreve*, *Besivance*, *Bromday*, *Istalol*, *Ocuflox*, *Retisert*, *Vitrase*, *Xibrom* and *Zylet*. If our products are approved and we are commercially successful, we believe Aerie could become a market-leading ophthalmic company.

Our lead product candidate, once-daily, dual-action AR-13324, recently completed a Phase 2b clinical trial in patients with open-angle glaucoma and ocular hypertension. We are developing AR-13324 as the first of a new class of compounds that is designed to lower intraocular pressure, or IOP, in patients through a novel dual mechanism of action, or MOA. We believe that, if approved, AR-13324 will represent the first new MOAs for lowering IOP in patients with glaucoma in nearly 20 years. Based on clinical data to date, we expect AR-13324 to compete successfully in the non-prostaglandin analogue, or PGA, market segment due to its strong and consistent IOP-lowering effect with once-daily dosing, favorable tolerability profile, lack of systemic side effects and novel dual-action MOA relative to currently marketed non-PGA products. We are currently planning two Phase 3 registration trials for AR-13324, which we expect to commence in mid-2014 upon completion of Phase 3-enabling toxicology studies.

We are also developing a second product candidate, once-daily, triple-action PG324, which is a single drop fixed-dose combination of AR-13324 and latanoprost, the most commonly prescribed drug for the treatment of patients with glaucoma. Based on our preclinical data to date, we believe PG324 has the potential to provide a greater IOP-lowering effect than any currently approved glaucoma product. Therefore, we believe that PG324 could compete with both PGA and non-PGA therapies. We are currently planning a Phase 2b clinical trial for PG324, which we expect to commence by early 2014.

Glaucoma is one of the largest segments in the global ophthalmic market. In 2012, branded and generic glaucoma product sales exceeded $4.5 billion in the United States, Europe and Japan in aggregate, according to IMS, and prescription volume is expected to grow, driven in large part by the aging population. The non-PGA market segment represents approximately half of the prescription volume in the glaucoma market, with the remainder accounted for by PGA products as shown in the following pie chart, which is based on IMS data.

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According to the Glaucoma Research Foundation, it is estimated that over 2.2 million Americans suffer from glaucoma. Glaucoma is a progressive and highly individualized disease, in which elevated levels of IOP are associated with damage to the optic nerve, which results in irreversible vision loss and potentially blindness. Patients may suffer the adverse effects of glaucoma across a wide range of IOP levels. The level of IOP in healthy individuals is generally accepted to be 10 to 21 millimeters of mercury, or mmHg. The majority of glaucoma patients have an IOP of 26 mmHg or below at the time of diagnosis, which we refer to as low to moderately elevated IOP. Glaucoma is treated by the reduction of IOP, which has been shown to slow the progression of vision loss. In a healthy eye, fluid is continuously produced and drained in order to maintain pressure equilibrium and provide nutrients to the eye tissue. The FDA recognizes sustained lowering of IOP as the primary clinical endpoint for the approval of drugs to treat patients with glaucoma and ocular hypertension. The primary drainage mechanism of the eye is the trabecular meshwork, or TM, which accounts for approximately 80% of fluid drainage, while the secondary drainage mechanism, the uveoscleral pathway, is responsible for the remaining drainage. In glaucoma patients, damage to the TM results in insufficient drainage of fluid from the eye, which causes increased IOP and damage to the optic nerve.

Once glaucoma develops, it is a chronic condition that requires life-long treatment. The initial treatment for glaucoma patients is typically the use of a prescription eye drop. PGAs have become the most widely prescribed glaucoma drug class. The most frequently prescribed PGA is once-daily latanoprost. The most commonly prescribed non-PGA drugs belong to the beta blocker class. The most frequently prescribed beta blocker is twice-daily timolol. Other non-PGA drug classes include the alpha agonists and carbonic anhydrase inhibitors. When PGA monotherapy is insufficient to control IOP, non-PGA products are used either as add-on therapy to the PGA or as an alternative monotherapy.

Our product candidates represent a new class of drugs utilizing novel MOAs that are applied topically as once-daily eye drops. Currently approved drugs mainly reduce IOP by increasing fluid outflow through the eye s secondary drain with once-daily dosing or reducing fluid inflow by decreasing fluid production with multiple doses per day. AR-13324 lowers IOP through a dual MOA that relaxes the contracted tissue of the TM to improve fluid outflow through the eye s primary drain while also decreasing fluid production in the eye. PG324, our triple-action fixed-

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combination product candidate, combines AR-13324 s dual action with latanoprost, a PGA that increases fluid drainage through the uveoscleral pathway. In addition to our primary product candidates, we are in preclinical development with AR-13533, our second generation dual-action ROCK/NET inhibitor.

We believe that significant unmet needs exist in the non-PGA market segment and that eye-care professionals are eager for new therapy choices. Many of the currently marketed non-PGA drugs have modest efficacy, require two to three doses daily and have tolerability and safety issues. None of the most commonly prescribed non-PGA drugs target the diseased TM. Despite these limitations, the most commonly prescribed non-PGA drugs each generated over $400 million of peak annual global revenues prior to the introduction of their generic equivalents. As a result, we believe there is significant market opportunity for AR-13324 as a non-PGA drug, if approved. In addition, based on our preclinical data to date, we believe that PG324 may have potentially superior efficacy to all currently marketed drugs, including PGAs. If we are able to demonstrate this in clinical trials and PG324 is approved for commercialization, we believe this new triple-action therapy could become an initial glaucoma treatment of choice for eye-care professionals.

We own the worldwide rights to all indications for our current product candidates. Our intellectual property portfolio contains patents and pending patent applications related to composition of matter, pharmaceutical compositions and methods of use for our product candidates. We have patent protection for our primary product candidates, AR-13324 and PG324, in the United States through at least 2030.

Our Product Pipeline

Our product candidates are once-daily eye drops that lower IOP through novel MOAs. Our product candidates are designed to inhibit both Rho Kinase, or ROCK, and the norepinephrine transporter, or NET. Through ROCK inhibition, they reduce IOP by increasing fluid outflow through the TM, the diseased tissue responsible for elevated IOP in glaucoma. Through NET inhibition, they also lower IOP by reducing the production of eye fluid.

We discovered and developed our product candidates internally through a rational drug design approach that

coupled medicinal chemistry with high content screening of compounds in proprietary cell-based assays. We selected and formulated our product candidates for preclinical *in vivo* testing following a detailed characterization of over 1,500 synthesized ROCK inhibitors, including ROCK/NET inhibitors. We continue to

discover and develop new compounds in our research laboratories and employ a scientific staff with expertise in medicinal chemistry, analytical chemistry, biochemistry, cell biology, pharmacology and pharmaceutical science.

The following table summarizes each of our existing product candidates, their MOAs, and their development status, as well as our intellectual property rights for these product candidates.

	Product Candidate and Mechanism	Phase of Development	Intellectual Property Rights
AR-13324	Dual-action ROCK/NET inhibitor	Phase 3 registration trial expected to begin mid-2014	Wholly-Owned
PG324	Triple-action Combination of dual-action AR-13324 and latanoprost, a PGA	Phase 2b clinical trial expected to begin by early 2014	Wholly-Owned
AR-13533	Dual-action Second generation ROCK/NET inhibitor	Preclinical	Wholly-Owned

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Dual-Action AR-13324

AR-13324 is the first of a new dual-action class of glaucoma drugs that was discovered by our scientists. It increases fluid outflow through the primary drain of the eye while also reducing eye fluid production. It acts through the inhibition of both ROCK and NET.

ROCK is a protein kinase, which is an enzyme that modifies other proteins by chemically adding phosphate groups to them. Specifically, ROCK regulates actin and myosin, which are proteins that are responsible for cellular contraction. ROCK activity also promotes the production of extracellular matrix proteins. ROCK inhibitors block TM cell contraction and reduce the production of extracellular matrix, thereby improving fluid outflow and consequently decreasing IOP.

NET is a protein that transports norepinephrine across neuronal cell membranes. Norepinephrine is a chemical released by neurons to communicate with targeted cells. NET returns excess norepinephrine back into the neuron, which helps end the signaling between the neuron and the neuron s target cells. We believe the inhibition of NET prolongs the activation of target cells in the ciliary body of the eye, which reduces the production of eye fluid and thereby lowers IOP.

In addition to its dual MOA, AR-13324 has a number of characteristics that distinguish it from our previously developed products, including single-action ROCK-selective drug AR-12286 and its fixed-dose combination product PG286, and other clinical-stage ROCK inhibitors, which together we refer to as comparator ROCK inhibitors. AR-13324 has a unique chemical composition that was specifically designed to allow maximal efficacy of the drug in the eye. Enzymatic conversion of AR-13324 produces two separate molecules, one of which is approximately ten to 160 times more potent at inhibiting ROCK than comparator ROCK inhibitors. This contributes to AR-13324 s greater efficacy and longer duration of effect relative to comparator ROCK inhibitors that we observed in preclinical models. In addition, AR-13324 has inhibitory activity against a secondary kinase target, Protein Kinase C, or PKC, which is known to act in parallel with ROCK to promote cell contraction. Compounds that inhibit ROCK without inhibiting PKC may allow PKC activity to increase in TM cells over time, resulting in a loss of IOP-lowering efficacy. We believe the ability of AR-13324 to inhibit both the primary, ROCK, and secondary, PKC, signaling pathways that lead to TM cell contraction contributes to the ability of AR-13324 to maintain its efficacy.

AR-13324 is expected to compete against non-PGA products, the significant majority of which have been in the market for at least 20 years. The most commonly prescribed non-PGA drugs each generated peak annual global revenues over $400 million prior to the introduction of their generic equivalents. The non-PGA market segment represents approximately half of the prescription volume and the remainder is accounted for by PGA products. We believe there is a significant unmet need in the non-PGA market segment due to the multiple daily dosings, side effects and contraindications of non-PGA products. We believe that AR-13324 has several significant differentiating characteristics that would make it a strong competitor in the non-PGA market segments, if approved, including:

Strong IOP-Lowering Effect In our Phase 2b clinical trial, once-daily AR-13324 demonstrated mean IOP reductions of 5.7 and 6.2 mmHg on days 28 and 14, respectively. Studies have shown that a sustained 5 mmHg reduction in IOP reduces risk of disease progression by approximately 50%. If confirmed in our planned Phase 3 registration trials, we believe this level of IOP reduction would equal or exceed that of all currently marketed non-PGA drugs.

Once-Daily Dosing Advantage The most commonly prescribed non-PGA drugs are dosed two to three times daily. AR-13324 is being developed as a once-daily dosed glaucoma therapy. This more convenient dosing regimen is expected to result in higher patient compliance, which may lead to improved outcomes.

Favorable Tolerability Profile Currently marketed non-PGA drugs have several tolerability issues indicated on their product labels, including blurred vision, unusual tastes, ocular allergic reaction and itching of the eye. In our Phase 2a and 2b clinical trials for AR-13324, a total of 209 patients were

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exposed to the drug. The main tolerability finding for AR-13324 was transient, or temporary, hyperemia, which is a cosmetic asymptomatic redness of the eye. Most hyperemia was scored as mild. Hyperemia is a common tolerability finding associated with the most widely prescribed glaucoma drugs.

Lack of Systemic Side Effects AR-13324 has demonstrated a lack of systemic side effects in clinical trials to date. The currently marketed non-PGA drugs have systemic side effect issues indicated on their product labels, including among others, lethargy, reduced heart rate, Stevens Johnson syndrome and blood dyscrasias. Further, the most widely prescribed non-PGA drug, timolol, has contraindications, including bronchospasm, arrhythmia and heart failure.

Novel Dual-Action MOA If approved, we believe AR-13324 would be the only once-daily drug available that specifically targets the TM, the diseased tissue responsible for elevated IOP in glaucoma. We believe AR-13324 will also be the first glaucoma drug to inhibit NET, which reduces fluid production in the eye. In addition, we believe the AR-13324 dual-action MOA is highly complementary to the MOA of the market-leading PGAs, which increase fluid outflow through the uveoscleral pathway.

Consistent IOP-Lowering Effect Across Various Baseline IOPs In our Phase 2b clinical trial, AR-13324 demonstrated a distinct ability to reduce IOP at consistent levels across all baseline IOPs tested in the trial. Published studies have indicated that currently marketed PGA and non-PGA drugs do not lower IOP as effectively in patients with low to moderately elevated baseline IOPs relative to patients with higher IOPs. Patients with low to moderately elevated IOPs represent the significant majority of glaucoma patients.

Based on the Phase 2b clinical trial results, and the several positive differentiating attributes of AR-13324, we believe AR-13324 has the potential to be a strong competitor in the non-PGA market segment. Our Phase 3 registration trials are designed to use timolol as the comparator, as timolol represents the most widely used comparator in registration trials in glaucoma, and is also the most widely prescribed non-PGA drug.

AR-13324 Phase 2 Efficacy Results

In May 2013, we completed a 28-day AR-13324 Phase 2b clinical trial. This trial included 224 patients who were treated once daily with AR-13324 0.01%, AR-13324 0.02% or latanoprost. Although AR-13324 is expected to compete primarily against other non-PGA drugs, latanoprost was used as the comparator because it is the most widely prescribed drug of all currently marketed glaucoma products. The primary efficacy endpoint for this Phase 2b clinical trial was mean diurnal IOP across subjects within each treatment group on day 28. We observed statistically significant decreases in mean diurnal IOP in all treatment groups on day 28 as compared to unmedicated baseline.

Baseline IOP was measured prior to treatment. Following treatment, IOP was measured on day seven at 8 a.m. and on days 14 and 28 at 8 a.m., 10 a.m. and 4 p.m. On day 14, mean diurnal IOP (which refers to the average of mean IOPs measured at 8 a.m., 10 a.m. and 4 p.m.) decreased to 19.8, 19.5 and 18.4 mmHg in the AR-13324 0.01%, AR-13324 0.02% and latanoprost groups, respectively, representing a decrease from unmedicated baseline of 5.9, 6.2 and 7.1 mmHg. On day 28, mean diurnal IOP was 20.1, 20.0 and 18.7 mmHg, respectively, representing a decrease from unmedicated baseline of 5.5, 5.7 and 6.8 mmHg. These decreases from unmedicated baseline were statistically significant with p-values < 0.001. P-value, or probability value, is a statistical measure that helps scientists determine if their hypotheses are correct. It is directly related to the statistical significance level of the results, which is an important component in determining whether the data obtained from scientific research support the hypothesis being tested.

The statistical significance level is determined by the researcher and is customarily set at 0.05, or 5%. Essentially, this means that 5% of the time, the results in the study would be derived by complete chance, but 95% of the time, the variable in the study would be directly related to the results of the study. Efficacy results from the Phase 2b trial are further described below.

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Efficacy Results of the 28-day Phase 2b Clinical Trial Comparing AR-13324 to Latanoprost

Showing Mean Diurnal IOP for Days 14 and 28 Compared to Baseline

AR-13324 maintained consistent efficacy from day seven to day 28. For AR-13324 0.02%, which is the concentration we intend to use in our planned Phase 3 trials, at the 8 a.m. time point, the time of highest baseline IOP, the IOP reductions achieved on day seven and day 28 were 6.0 and 5.9 mmHg, respectively. The level of IOP reduction achieved by AR-13324 0.02% in our Phase 2b study was clinically significant, since previously published long-term studies have demonstrated that a sustained 5 mmHg reduction in IOP reduces the risk of disease progression by approximately 50%.

Clinical significance means that the effect is large enough to be important to patients and physicians. An effect that is clinically significant may or may not also be statistically significant. In glaucoma, the Early Manifest Glaucoma Trial, a large long-term study evaluating the effect of IOP lowering in patients with glaucoma, concluded that each 1 mmHg reduction in IOP lowered the risk of progression of optic nerve damage by 10%, indicating that each 1 mmHg reduction in IOP provides a meaningful level of protection to the patient.

IOP-Lowering Effect of AR-13324 0.02% at 8 a.m. on Days 7, 14 and 28

In the full Phase 2b trial population, which consisted of patients with unmedicated baseline IOPs ranging from 22 to 36 mmHg, the IOP-lowering effect of our once-daily AR-13324 0.02% was 1.2 mmHg less than that of latanoprost on day 28 and did not show non-inferiority. However, AR-13324 0.02% efficacy relative to latanoprost was in line with published historical data for twice-daily timolol relative to latanoprost. Timolol is the most commonly prescribed non-PGA drug and the comparator for our planned Phase 3 non-inferiority registration trial.

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A study by Hedman and Alm, which reports on the pooled data from three registration trials of latanoprost versus timolol, showed the IOP-lowering effect of timolol to be 1.2 mmHg less than that of latanoprost, as reflected in the graph on the following page under the heading Comparison of Latanoprost and Timolol from Pooled Data of Three Registration Trials. Our AR-13324 Phase 2b clinical trials similarly showed AR-13324 to have an IOP-lowering effect of 1.2 mmHg less than that of latanoprost.

An additional protocol-specified analysis that compared the results for the patients who entered the trial with moderately elevated baseline IOPs (22 to 26 mmHg) to patients with highly elevated baseline IOPs (greater than 26 mmHg) revealed a differentiated efficacy profile of AR-13324 compared to latanoprost. Consistent with previous scientific literature, latanoprost produced smaller IOP reductions in patients with moderately elevated IOPs than in patients with highly elevated IOPs. In contrast, AR-13324 maintained essentially the same IOP-lowering effect in patients with moderately elevated IOPs as in patients with highly elevated IOPs ($p>0.30$). As a result, the IOP-lowering effect of AR-13324 was equivalent to latanoprost in patients with moderately elevated baseline IOPs and AR-13324 thereby demonstrated statistical non-inferiority to latanoprost in this sub-group. A non-inferiority trial is a type of clinical trial performed to see if a new drug or treatment is *not inferior* to a current active treatment or to determine if a new treatment is *at least as good as,* or *not unacceptably worse than*, the active comparator treatment. A non-inferiority trial aims at demonstrating that the test product is not worse than the comparator by more than a small pre-specified amount. This amount is known as the non-inferiority margin, which for the AR-13324 Phase 2b trial was 1.5 mmHg.

IOP-Lowering Effect of AR-13324 0.02% and Latanoprost in the Full Patient Population Compared to the Subgroup with Moderately Elevated IOP*

* Based on diurnal measurements.

A study published in 2000, which pooled data from three latanoprost registration trials, demonstrated that both latanoprost and timolol lose approximately 0.5 mmHg in efficacy for every 1 mmHg lower baseline IOP, as illustrated in the chart below. Additional publications have indicated similar declining efficacy results for other currently marketed non-PGA glaucoma drugs, including the alpha agonist brimonidine and the carbonic anhydrase inhibitor dorzolamide.

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Comparison of Latanoprost and Timolol from Pooled Data of Three Registration Trials

Source: Hedman and Alm (Eur J Ophthalmol 2000; 10:95-104)

We believe the ability of AR-13324 to maintain a consistent IOP-lowering effect on baseline IOP will place AR-13324 in a favorable competitive position relative to current non-PGA drugs because a significant majority of glaucoma patients have baseline IOPs of 26 mmHg or below. Results from a large epidemiological survey published in 1991, the Baltimore Eye Survey, demonstrated that greater than 78% of patients have unmedicated baseline IOPs of 26 mmHg or below when first diagnosed with glaucoma.

Prevalence of Glaucoma by Baseline IOP at the Time of Diagnosis

Adapted from Baltimore Eye Survey in which 10,444 subjects were screened for the prevalence of Open-Angle Glaucoma (OAG)

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AR-13324 Phase 2a Efficacy Results

In August 2012, we completed a 7-day AR-13324 Phase 2a clinical trial. This trial included 85 patients who were treated once-daily with AR-13324 0.01%, AR-13324 0.02%, AR-13324 0.04% or AR-13324 s vehicle. Vehicle refers to the formulation without the active ingredient. Baseline IOP was measured prior to treatment. IOP was measured following seven days of dosing at 8 a.m., 10 a.m., 12 p.m. and 4 p.m. The primary efficacy endpoint for this Phase 2a clinical trial was the mean diurnal IOP (which refers to the average of mean IOPs measured at 8 a.m., 10 a.m., 12 p.m. and 4 p.m.) across subjects within each treatment group on day eight. We observed statistically significant decreases in mean diurnal IOP in all AR-13324 treatment groups following seven days of dosing compared to unmedicated baseline. Additionally, each concentration of AR-13324 was shown to be statistically superior to the vehicle following seven days of dosing with p-values ranging from 0.018 to <0.001.

AR-13324 Phase 2 Safety Data

In our 7-day Phase 2a and 28-day Phase 2b clinical trials for AR-13324 a total of 209 patients were exposed to AR-13324. In these trials, AR-13324 was well tolerated. The main adverse event was transient hyperemia, or asymptomatic redness of the eye, with all hyperemia scored as mild or moderate. This cosmetic tolerability finding is based on the MOA of the drug, which induces a transient dilation of small blood vessels located over the sclera, or white part of the eye.

The biomicroscopy findings in the Phase 2b trial for the vast majority of patients who experienced ocular hyperemia were mild and transient, and there were no observations of severe ocular hyperemia. Biomicroscopy refers to the observation by a masked examiner of the anterior part of the eye. On day 28 at 8 a.m., mild and moderate conjunctival hyperemia was observed in 18% and 24% of patients in the AR-13324 0.01% and 0.02% treatment groups, respectively, and in 11% of patients in the latanoprost group. The incidence of conjunctival hyperemia decreased throughout the study for AR-13324 and increased for latanoprost.

Published data indicate that latanoprost generates the lowest rate of hyperemia among the commonly prescribed PGAs. In a study that compared the relative frequency of hyperemia for bimatoprost, travaprost and latanoprost after 12 weeks of treatment, the largest proportion of patients reporting redness was found in the bimatoprost group with 35%, followed by the travoprost and latanoprost groups with 27% and 16%, respectively.

AR-13324 Comparison to AR-12286

We have analyzed our clinical and preclinical data for AR-13324, the lead candidate from our dual-action ROCK/NET inhibitor class, relative to our clinical and preclinical data for AR-12286, our single-action ROCK-selective compound that we were previously evaluating for further clinical development in addition to AR-13324. We conducted similarly designed 28-day Phase 2 clinical trials for each of AR-13324 and AR-12286, the comparative results of which are presented in the chart below. AR-13324 0.02% maintained stable efficacy on day 28 relative to day seven in its 28-day Phase 2 clinical trial. In contrast, AR-12286 0.5% lost 1.4 mmHg of IOP-lowering efficacy from day seven to day 28 in its 28-day Phase 2 clinical trial.

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IOP-Lowering Effect of Dual-Action AR-13324 and Single-Action AR-12286

at 8 a.m. on Days 7, 14 and 28

We subsequently completed a three-month Phase 2 clinical trial for AR-12286, for which data were available in June 2013. This trial confirmed the trend observed in the 28-day trial discussed above. In the three-month trial, the efficacy of AR-12286 continued to decline over the trial period such that it failed to meet its primary efficacy endpoint, non-inferiority to timolol.

Our lead product candidate, AR-13324, has a number of characteristics that distinguish it from AR-12286. AR-13324 lowers IOP through a dual mechanism of action by inhibiting both ROCK and NET, whereas AR-12286 has a single mechanism of action inhibiting only ROCK. In addition, AR-13324 has a unique chemical composition that was specifically designed to allow maximal efficacy of the drug in the eye. Enzymatic conversion of AR-13324 produces two separate molecules, one of which is approximately ten times more potent at inhibiting ROCK than AR-12286. AR-13324 s more potent ROCK inhibition, as well as its ability to inhibit NET, contributes to its greater efficacy and longer duration of effect relative to AR-12286.

In addition, the analyses of our data suggest that there is a secondary signaling pathway that is activated by a protein called PKC that also leads to contraction of the TM. Our preclinical analyses show that AR-13324 is a potent inhibitor of both ROCK and PKC, whereas AR-12286 is a potent inhibitor of ROCK but not of PKC. We believe that the ability of AR-13324 to inhibit both the primary ROCK and the secondary PKC signaling pathways also contributes to AR-13324 s ability to maintain its efficacy over time.

Furthermore, in a six-month toxicology study with exaggerated dosing of AR-12286, lens opacities, otherwise known as cataracts, were observed in rabbit eyes beginning at three months. In a similar six-month toxicology study with exaggerated dosing of AR-13324, no adverse lens effects were observed.

As a result of these observations, in June 2013, we selected dual-action AR-13324 for advancement to Phase 3 clinical development and discontinued development of AR-12286 and its related fixed-dose combination product PG286.

AR-13324 Development Strategy

Registration trials for AR-13324 are expected to begin mid-2014 upon completion of three-month interim study reports from our six-month and nine-month Phase 3-enabling ocular toxicology studies. The AR-13324 doses and dosing frequencies being tested in these studies have previously been shown to be well tolerated in 28-day and six-month ocular toxicology studies. We plan to run two pivotal trials that will include at least 1,200 patients in total. The entry criteria for our Phase 3 trials are planned to include a minimum IOP of 21 mmHg and a likely maximum of 26 to 30 mmHg. Based on discussions with the FDA, we believe that the planned entry criteria for

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our Phase 3 trials is acceptable to the FDA and will not impact the product label. The entry criteria for our Phase 2 trials were 22 to 36 mmHg. Lowering the IOP entry criteria for our Phase 3 trials will increase the representation of patients with moderately elevated IOPs in the trials and thereby provide a more representative cross-section of the glaucoma patient population. The registration trials will be non-inferiority trials comparing AR-13324 0.02% taken once daily in the evening to twice-daily timolol, the standard comparator for glaucoma registration trials and also the most widely prescribed non-PGA glaucoma drug. Phase 3 efficacy results will be determined after three months of treatment and safety results will be analyzed and submitted following 12 months of treatment. Assuming we commence the Phase 3 trials in mid-2014 and fully enroll the trials within our anticipated timeframe, we would expect efficacy data from the two trials in mid-2015 and that, if the results of the Phase 3 trials are positive, that we would make an NDA filing by mid-2016. We intend to explore the potential for priority review with the FDA, although there can be no assurance that such priority review will be granted by the FDA.

Triple-Action PG324

Our once-daily, triple-action product candidate PG324 is a combination of our dual-action compound AR-13324 formulated with latanoprost in a single eye drop. If approved, we believe that PG324 would be the first glaucoma product to lower IOP through all three MOAs:

- increasing fluid outflow through the TM, the eye s primary drain,
- increasing fluid outflow through the uveoscleral pathway, the eye s secondary drain, and
- reducing fluid production in the eye.

In the PG324 fixed-combination product, AR-13324 is responsible for increasing fluid outflow through the TM and reducing fluid production in the eye. Latanoprost is responsible for increasing fluid outflow through the uveoscleral pathway.

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Triple-action PG324 has been tested in a preclinical primate model to assess its effectiveness at lowering IOP. The graph below presents the data from dosing PG324 and latanoprost once daily for three days (at hours 0, 24 and 48). The results of the study show that at all time points measured, PG324 reduced IOP substantially more than latanoprost alone. No IOP measurements were taken on day two of the study between hours 24 and 48.

* SEM refers to Standard Error of the Mean.

In addition, we have established human proof of concept in prior ROCK inhibitor/PGA combination trials with our discontinued PG286 product, which demonstrated significant IOP lowering beyond the PGA alone at 28 days.

We believe PG324, if approved, would be the only glaucoma product that covers the full spectrum of IOP-lowering mechanisms, giving it the potential to provide a greater IOP-lowering effect than any currently approved glaucoma product. Therefore, we believe that PG324 could compete with both PGA and non-PGA therapies.

PG324 Development Strategy

In light of the clinical experience with AR-13324 to date and the extensive clinical experience with latanoprost, which has been used in patients for approximately 20 years, we plan to advance PG324 directly into a Phase 2b clinical trial. PG324 is covered by the investigational new drug application, or IND, for AR-13324. We have 28-day toxicology data to support a 28-day clinical trial. The process to be followed for the planned Phase 2b clinical trial will be consistent with normal FDA guidelines, including the submission of the protocol to the FDA. We expect to commence this trial by early 2014. The trial is planned to be a randomized, controlled 28-day trial in approximately 300 patients. The trial will be designed to measure the efficacy of two concentrations of PG324 (with 0.01% and 0.02% concentrations) compared to latanoprost and AR-13324 0.02%, all dosed once daily. The efficacy endpoint will be superiority of PG324 to each of its components. The Phase 3 registration trial for PG324 is expected to mirror the planned Phase 2b trial but with three-month efficacy and a 12-month safety trial, and will only test one concentration of PG324. Assuming we commence the Phase 2b trial by early 2014 and fully enroll the trial within our anticipated timeframe, we would expect results mid-2014.

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Second-Generation, Dual-Action AR-13533

In addition to our primary product candidates, AR-13324 and PG324, we are in the preclinical development stage with AR-13533, our second generation dual-action ROCK/NET inhibitor. AR-13533 does not require enzymatic conversion in the eye to deliver maximal ROCK inhibitor activity, and therefore AR-13533 may provide additional IOP-lowering effect in patients beyond that obtained with AR-13324. We have not submitted an IND for AR-13533 to the FDA and there can be no assurance that an IND will be submitted.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of innovative pharmaceutical products for the treatment of patients with glaucoma and other diseases of the eye. We believe our product candidates have the potential to address many of the unmet medical needs in the glaucoma market. Key elements of our strategy are to:

Advance the development of our product candidates to approval. Based on the results from our Phase 2b clinical trial for dual-action AR-13324, we plan to proceed into Phase 3 registration trials for this drug. Additionally, we plan to initiate a Phase 2b clinical trial for PG324, our triple-action combination of AR-13324 and latanoprost and, over the longer term, also to evaluate opportunities associated with preclinical-stage AR-13533, our second generation dual-action ROCK/NET inhibitor.

Establish internal sales capabilities to commercialize our product candidates in the United States. We own worldwide rights to all indications for our product candidates and we plan to retain U.S. commercialization rights. Ultimately, if our product candidates are approved, we plan to build a commercial team of approximately 100 sales representatives. We expect our sales organization to target approximately 10,000 high prescribing eye-care professionals throughout the United States.

Explore partnerships with leading pharmaceutical and biotechnology companies to maximize the value of our product candidates outside the United States. We currently plan to explore the licensing of commercialization rights or other forms of collaboration with qualified potential partners for the commercialization of our product candidates in certain key markets outside of the United States, including Europe, Japan and emerging markets.

Continue to leverage and strengthen our intellectual property portfolio. We believe we have a strong intellectual property position relating to our product candidates. Our intellectual property portfolio contains U.S. patents and pending U.S. and foreign patent applications related to composition of matter, pharmaceutical compositions and methods of use for our product candidates. We have patent protection for our primary product candidates in the United States through at least 2030.

Expand our product portfolio through internal discovery efforts and possible in-licensing or acquisitions of additional ophthalmic product candidates or products. We continually seek to discover and develop new compounds in our research laboratories and employ a scientific staff with expertise in medicinal chemistry, analytical chemistry, biochemistry, cell biology, pharmacology and pharmaceutical science. In addition, we also plan to evaluate the expansion of our product portfolio through in-licensing or acquisitions of additional ophthalmic product candidates or products.

Glaucoma Overview

Glaucoma is generally characterized by relatively high IOP as a result of impaired drainage of fluid, known as aqueous humor, from the eye. The FDA recognizes sustained lowering of IOP, measured in terms of mmHg, as the primary clinical endpoint for regulatory approval, making clinical trials for this indication relatively straight-forward due to easily measured objective parameters.

In a healthy eye, aqueous humor is continuously produced and drained from the eye in order to maintain pressure equilibrium and provide micronutrients to various tissues in the eye. The normal range of IOP is generally

between 10 and 21 mmHg. Several studies have demonstrated that the significant majority of glaucoma patients have IOPs below 26 mmHg at the time of diagnosis. An insufficient drainage of fluid can increase IOP above normal levels, which can eventually cause damage to the optic nerve. Once damaged, the optic nerve cannot regenerate and thus, damage to vision is permanent.

The most common form of glaucoma is open-angle glaucoma, which is characterized by abnormally high IOP as a result of impaired drainage of fluid from the eye s primary drain, the TM. Open-angle glaucoma is a progressive disease leading to vision loss and blindness for some patients as a result of irreversible damage to the optic nerve.

Studies of the disease have demonstrated that reducing IOP in patients with glaucoma can help slow or halt further damage to the optic nerve and help preserve vision. Once diagnosed, glaucoma requires life-long treatment to maintain IOP at lower levels based on the individual patient s risk of disease progression. Ophthalmologists will routinely determine a target IOP, which represents the desired IOP level to achieve with glaucoma therapy for an individual patient. Should the disease progress even once the initial target IOP is reached, further lowering of the IOP has been shown to help in preventing additional damage to the optic nerve and further vision loss. This may require lowering IOP until it is in the so called low normal range of 12 to 14 mmHg to protect the optic nerve from further damage.

There are multiple factors that could lead to open-angle glaucoma, including age and family history of glaucoma, and there is a higher incidence and severity of the disease in African-American and Hispanic populations.

Some patients with high IOP are diagnosed with a condition known as ocular hypertension. Patients with ocular hypertension have high IOP without the loss of visual fields or observable damage to the optic nerve, and are at an increased risk of developing glaucoma. These patients are commonly treated in the same manner as glaucoma patients.

The following diagram illustrates how increased IOP eventually leads to increased pressure on the optic nerve, resulting in gradual loss of vision and ultimately visual disability and blindness.

The ciliary body in the eye is the tissue that produces aqueous humor, the production of which is commonly referred to as fluid inflow. The fluid leaves the eye primarily through the TM, the process of which is commonly referred to as fluid outflow. The healthy eye maintains a state of IOP homeostasis through a constant physiological process of aqueous humor production and drainage. The deteriorating function of the TM in glaucoma leads to increased resistance to fluid outflow and higher IOP. There is also a secondary drain for the fluid in the eye known as the uveoscleral pathway, which is typically responsible for approximately 20% of fluid drainage.

Patients are diagnosed through measurements of IOP using Goldmann applanation tonometry, the standard device used by clinicians to measure IOP, along with an evaluation of visual fields and observing the appearance of the optic nerve. These tests are routinely carried out by eye-care professionals. The initial treatment for

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patients diagnosed with open-angle glaucoma or ocular hypertension is typically a PGA eye drop. PGAs are designed to lower IOP by increasing outflow through the eye s secondary fluid drain. An eye-care professional will then measure a patient s response to the drug over the first few months. It has been shown that up to 50% of glaucoma patients require more than one drug to treat their IOP. This may occur as early as three to six months after initiating treatment with a PGA. The eye-care professionals may then add a second drug from one of the non-PGA classes, to be used together with the initial drug, or switch to a fixed-combination of two drugs in a single eye drop, or select an alternative single treatment. The reason so many patients eventually need more than one drug is generally considered to be a reflection of the progressive nature of the disease at the TM.

In severe glaucoma cases, patients may need to undergo an invasive surgical procedure. Trabeculectomy is the most common glaucoma-related surgical procedure, also referred to as filtration surgery, in which a piece of tissue in the drainage angle of the eye is removed, creating an opening to the outside of the eye. The opening is partially covered with a scleral flap, the white part of the eye, and the conjunctiva, the thin membrane covering the sclera. This new opening allows fluid to drain out of the eye, bypassing the clogged drainage channels of the TM to maintain a lowered IOP. Devices called shunts are used in glaucoma surgery to divert fluid in a controlled manner from the inside of the eye to the subconjunctival space bypassing the blocked TM. Generally, the shunts reduce IOP to the extent that the use of drops can be reduced, but often not completely eliminated. Many patients continue to require eye drops even following surgery.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our experience and scientific knowledge provide us with competitive advantages, we face competition from established branded and generic pharmaceutical companies, such as Bausch + Lomb, Inc. (recently acquired by Valeant Pharmaceuticals International, Inc.), Merck & Co., Inc., Novartis International AG, Allergan, Inc., Santen Inc. and smaller biotechnology and pharmaceutical companies as well as from academic institutions, government agencies and private and public research institutions, which may in the future develop products to treat glaucoma. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that the key competitive factors affecting the success of our product candidates, if approved, are likely to be efficacy, safety, convenience, price, tolerability and the availability of reimbursement from government and other third-party payors.

We expect to compete directly against companies producing existing and future glaucoma treatment products. The most commonly approved classes of eye drops to lower IOP in glaucoma are discussed below:

PGA Drug Class

Prostaglandin Analogues (PGAs). Most PGAs are once-daily dosed eye drops generally prescribed as the initial drug to reduce IOP by increasing fluid outflow through the eye s secondary drain. PGAs represent up to half of the U.S. and European prescription volume for the treatment of glaucoma.

Xalatan (latanoprost), the best-selling PGA, and Xalacom, its fixed-combination with a beta blocker, which is not available in the U.S., had worldwide peak sales of $1.7 billion before its patent expired in 2012, according to publicly reported sales. The adverse effects of PGAs include hyperemia or eye redness, irreversible change in iris color, discoloration of the skin around the eyes, and droopiness of eyelids. PGAs should be used with caution in patients with a history of intraocular inflammation.

Non-PGA Drug Class

Beta Blockers. Beta blockers, with their MOA designed to inhibit aqueous production, are one of the oldest approved drugs for the lowering of IOP. The most commonly used drug in this class is timolol. Beta blockers are less effective than PGAs in terms of IOP lowering and are typically used twice daily. Beta blockers are the most commonly used non-PGA drug. They are used as an initially prescribed

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monotherapy and as an adjunct therapy to PGAs when the efficacy of PGAs is insufficient. Beta blocker eye drops have contraindications in their label as a result of systemic exposure from topical application of the eye drops, potentially leading to cardio-pulmonary events such as bronchospasm, arrhythmia and heart failure.

Carbonic Anhydrase Inhibitors. Carbonic anhydrase inhibitors, with their MOA designed to inhibit aqueous production, are less effective than PGAs and are required to be dosed three times daily in order to obtain the desired IOP lowering. In published clinical studies of carbonic anhydrase inhibitors, the most frequently reported adverse events reported were blurred vision and bitter, sour or unusual taste. Carbonic anhydrase inhibitors are sulfonamides and, as such, systemic exposure increases risk of adverse responses such as Stevens Johnson syndrome and blood dyscrasias.

Alpha Agonists. Alpha agonists, with their MOA designed to inhibit aqueous production plus have an effect on uveoscleral outflow, are less effective than PGAs and need to be dosed three times daily in order to obtain the desired IOP lowering. In clinical studies, the most frequently reported adverse reactions that occurred in individuals receiving brimonidine ophthalmic solution, a commonly prescribed alpha agonist, included allergic conjunctivitis, conjunctival hyperemia, eye pruritus, burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness and visual disturbance.

Despite their modest efficacy, safety and tolerability profiles, and the requirement for two to three doses per day, the beta blocker, carbonic anhydrase inhibitor and alpha agonist products account for up to half of the total prescription volume for the treatment of glaucoma based on historical prescription patterns, with beta blocker timolol being the most widely prescribed non-PGA drug. This is driven by the PGA products not being sufficiently effective as monotherapy for up to half of all glaucoma patients. Among the non-PGA drug classes, brands such as Allergan s Alphagan / Combigan franchise generated combined global revenues in 2012 of over $420 million, and prior to the introduction of generics, the branded beta blockers and carbonic anhydrase inhibitors generated peak annual product revenues of over $400 million. Fixed-combination glaucoma products are currently marketed in the United States, including Cosopt, the combination of a beta blocker with a carbonic anhydrase inhibitor, and Combigan, the combination of a beta blocker with an alpha agonist. There are no fixed-combinations of PGAs with other glaucoma drugs currently available in the United States.

In addition to demonstrating suboptimal efficacy and safety profiles, many of the older glaucoma drugs are associated with compliance issues. For example, non-compliance can result from the difficulty of administering multiple eye drops in a single day. Challenges such as this are magnified for elderly patients, who constitute a large and growing proportion of the glaucoma population.

Administering multiple eye drops two or three times daily also increases exposure of patients to the preservatives in eye drops. Over time, this increased exposure may lead to damage to the surface of the cornea resulting in discomfort and symptoms of dry eye disease.

New eye drops for the treatment of glaucoma continue to be developed by our competitors. The following table outlines publicly disclosed development programs for the treatment of glaucoma of which we are aware.

Brand	New PGA*	Trial Stage
BOL-303259 (Bausch + Lomb)	NO-donating latanoprost (qd)	Phase 3
DE-117 (Santen)	EP2 agonist (qd)	Phase 2a
ONO-9054 (Ono)	FP/EP3 agonist (qd)	Phase 1
Brand	**New non-PGA***	**Trial Stage**
AR-13324 (Aerie)	ROCK/NET inhibitor (qd)	Phase 2b
K-115 (Kowa)	ROCK inhibitor (bid)	Phase 3 (Japan)
AMA0076 (Amakem)	ROCK inhibitor (bid)	Phase 2a
INO-8875 (Inotek)	Adenosine-A1 agonist (bid)	Phase 2
LX7101 (Lexicon)	LIMK2 inhibitor (bid)	Phase 1/2
SYL040012 (Sylentis)	RNAi beta blocker (bid)	Phase 2

* References to qd are to once daily-dosed products, and bid are to twice-daily products.

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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. Sucampo Pharmaceuticals, Inc. recently commercially relaunched Rescula, a twice-daily dosed PGA, with the claim that it reduces elevated IOP by increasing the outflow of aqueous humor through the TM. In addition, early-stage companies that are also developing glaucoma treatments, such as Inotek Pharmaceuticals, which is developing an adenosine receptor agonist, may prove to be significant competitors. We expect that our competitors will continue to develop new glaucoma treatments, which may include eye drops, oral treatments, surgical procedures, implantable devices or laser treatments. Alternative treatments beyond eye drops continue to develop.

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

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer adverse effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors encourage the use of generic products. Our industry is highly competitive and is currently dominated by generic drugs, such as latanoprost and timolol, and additional products are expected to become available on a generic basis over the coming years. If any of our product candidates are approved, we expect that they will be priced at a premium over competitive generic products and consistent with other branded glaucoma drugs.

Manufacturing

AR-13324 is a small molecule and capable of being manufactured in reliable and reproducible synthetic processes from readily available starting materials. We believe the chemistry used to manufacture AR-13324 is amenable to scale up and does not require unusual equipment in the manufacturing process. We do not currently operate manufacturing facilities for clinical or commercial production of our product candidates. We currently rely on third-party manufacturers to produce the active pharmaceutical ingredient and final drug product for our clinical trials. We manage such production with all our vendors on a purchase order basis in accordance with applicable master service and supply agreements. We do not have long-term agreements with any of these or any other third-party suppliers. Latanoprost, used in the manufacture of PG324, is available in commercial quantities from multiple reputable third-party manufacturers. We intend to procure quantities on a purchase order basis for our clinical and commercial production. If any of our existing third-party suppliers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might experience a delay in our ability to obtain alternative suppliers. We also do not have any current contractual relationships for the manufacture of commercial supplies of our product candidates if they are approved. With respect to commercial production of our potential products in the future, we plan on outsourcing production of the active pharmaceutical ingredients and final drug product manufacturing if they are approved for marketing by the applicable regulatory authorities.

We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities. However, should a supplier or manufacturer on which we have relied to produce a product candidate provide us with a faulty product or such product is later recalled, we would likely experience delays and additional costs, each of which could be significant.

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Intellectual Property

We have obtained patent protection for our primary product candidates, AR-13324 and PG324 (patent protection for PG324 arises from the patent protection we have secured for AR-13324), in the United States and are seeking patent protection in a number of foreign jurisdictions for these product candidates. We intend to maintain and defend our patent rights to protect our technology, inventions, processes and improvements that are commercially important to the development of our business. We cannot be sure that any of our existing patents or patents we obtain in the future will be commercially useful in protecting our technology. We cannot be sure that our patents will issue on any of our pending patent applications or patent applications we file in the future. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, see Risk Factors Risks Related to Intellectual Property.

Our intellectual property consists of issued patents, and pending patent applications for compositions of matter and methods of use, for our product candidates and other proprietary technology. For our primary product candidates AR-13324 and PG324, we hold U.S. Patent 8,450,344, which is scheduled to expire in 2026, and U.S. Patent 8,394,826, which is scheduled to expire in 2030, each of which has composition of matter and method use of claims for composition of matter. We hold additional patents for other ROCK Inhibitor molecules.

We have established and continue to build proprietary positions for our product candidates and related technology in the United States and other jurisdictions. As of June 30, 2013, we had nine United States or foreign issued patents that cover previously discontinued product candidates and 33 U.S. patent applications or foreign national patent applications that, if patents were to issue based on the existing claims, would cover various aspects of our current and previously discontinued product candidates.

In October 2012, our board of directors authorized the divestiture of certain non-core intellectual property relating to implantable ophthalmic devices for future development by Novaer Holding, Inc., or Novaer, an independent company. In addition, as part of this transaction, we also licensed the non-ophthalmic rights to our intellectual property portfolio to Novaer. See Note 13 to our financial statements appearing elsewhere in this prospectus.

On September 6, 2013, we terminated our agreement to exclusively license to Novaer our intellectual property for non-ophthalmic indications. No consideration, or future obligation thereof, was exchanged in connection with this termination. As of September 6, 2013, we own all of the worldwide rights to our current product candidates for all indications, both ophthalmic and non-ophthalmic.

Regulatory Matters

FDA Regulation and Marketing Approval

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Failure to comply with the applicable United States regulatory requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions and non-approval of product candidates. These sanctions could include the imposition by the FDA or an Institutional Review Board, or IRB, of a clinical hold on trials, the FDA s refusal to approve pending applications or related supplements, withdrawal of an approval, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, restitution, disgorgement, civil penalties or criminal prosecution. Such actions by government agencies could also require us to expend a large amount of resources to respond to the actions. Any agency or judicial enforcement action could have a material adverse effect on us.

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products.

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These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, post-approval monitoring, advertising, promotion, sampling and import and export of our products. Our drugs must be approved by the FDA through the NDA process before they may be legally marketed in the United States. See The NDA Approval Process below.

The process required by the FDA before drugs may be marketed in the United States generally involves the following:

- completion of non-clinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices or other applicable regulations;
- submission of an IND, which allows clinical trials to begin unless FDA objects within 30 days;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use or uses conducted in accordance with FDA regulations, Good Clinical Practices, or GCP, which are international ethical and scientific quality standards meant to assure the rights, safety and well-being of trial participants are protected and to define the roles of clinical trial sponsors, administrators, and monitors;
- pre-approval inspection of manufacturing facilities and clinical trial sites; and
- FDA approval of an NDA, which must occur before a drug can be marketed or sold.

IND and Clinical Trials

Prior to commencing the first clinical trial, an initial IND, which contains the results of preclinical tests along with other information, such as information about product chemistry, manufacturing and controls and a proposed protocol, must be submitted to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA unless the FDA within the 30-day time period raises concerns or questions about the conduct of the clinical trial. In such a case, the IND sponsor must resolve any outstanding concerns with the FDA before the clinical trial may begin. A separate submission to the existing IND must be made for each successive clinical trial to be conducted during product development. Further, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that site. Informed written consent must also be obtained from each trial subject. Regulatory authorities, including the FDA, an IRB, a data safety monitoring board or the sponsor, may suspend or terminate a clinical trial at any time on various grounds, including a finding that the participants are being exposed to an unacceptable health risk or that the clinical trial is not being conducted in accordance with FDA requirements.

For purposes of NDA approval, human clinical trials are typically conducted in sequential phases that may overlap:

- Phase 1 the drug is initially given to healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. These trials may also provide early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational drug s pharmacokinetics and pharmacologic effects may be obtained to permit the design of well- controlled and scientifically valid Phase 2 clinical trials.
- Phase 2 trials are conducted in a limited number of patients in the target population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. Throughout this prospectus, we refer to our initial Phase 2 clinical trials as Phase 2a clinical trials and our

subsequent Phase 2 clinical trials as Phase 2b clinical trials.

Phase 3 when Phase 2 evaluations demonstrate that a dosage range of the product appears effective and has an acceptable safety profile, and provide sufficient information for the design of Phase 3

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registration trials, Phase 3 registration trials are undertaken to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to further evaluate dosage, effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug and to provide an adequate basis for product labeling and approval by the FDA. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug.

All clinical trials must be conducted in accordance with FDA regulations, GCP requirements and their protocols in order for the data to be considered reliable for regulatory purposes.

An investigational drug product that is a combination of two different drugs in the same dosage form must comply with an additional rule that requires that each component make a contribution to the claimed effects of the drug product. This typically requires larger studies that test the drug against each of its components. In addition, typically, if a drug product is intended to treat a chronic disease, as is the case with our products, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more. Government regulation may delay or prevent marketing of product candidates or new drugs for a considerable period of time and impose costly procedures upon our activities.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

The NDA Approval Process

In order to obtain approval to market a drug in the United States, a marketing application must be submitted to the FDA that provides data establishing to the FDA s satisfaction the safety and effectiveness of the investigational drug for the proposed indication. Each NDA submission requires a substantial user fee payment (currently exceeding $2,100,000 for fiscal year 2014) unless a waiver or exemption applies. The application includes all relevant data available from pertinent non-clinical, preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product s chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators that meet GCP requirements.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meetings to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 registration trial that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with current Good Manufacturing Practice, or cGMP, requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and

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the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf-life.

The results of product development, non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept a NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA has 60 days from its receipt of an NDA to conduct an initial review to determine whether the application will be accepted for filing based on the agency s threshold determination that the application is sufficiently complete to permit substantive review. If the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product s identity, strength, quality and purity. The FDA has agreed to specific performance goals on the review of NDAs and seeks to review standard NDAs in 12 months from submission of the NDA. The review process may be extended by the FDA for three additional months to consider certain late submitted information or information intended to clarify information already provided in the submission. After the FDA completes its initial review of an NDA, it will communicate to the sponsor that the drug will either be approved, or it will issue a complete response letter to communicate that the NDA will not be approved in its current form and inform the sponsor of changes that must be made or additional clinical, non-clinical or manufacturing data that must be received before the application can be approved, with no implication regarding the ultimate approvability of the application or the timing of any such approval, if ever. If, or when, those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two to six months depending on the type of information included. The FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and, if so, 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 facilities at which the product is manufactured. The FDA will not approve the product 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 may inspect one or more clinical sites to assure compliance with GCP. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will request additional testing or information. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the NDA. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 trials may be made a condition to be satisfied for continuing drug approval. The results of Phase 4 trials can confirm the effectiveness of a product candidate and can provide important safety information. In addition, the FDA now has express statutory authority to require sponsors to conduct post-marketing trials to specifically address safety issues identified by the agency. See Post-Marketing Requirements below.

The FDA also has authority to require a Risk Evaluation and Mitigation Strategy, or an REMS, from manufacturers to ensure that the benefits of a drug outweigh its risks. A sponsor may also voluntarily propose a

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REMS as part of the NDA submission. The need for a REMS is determined as part of the review of the NDA. Based on statutory standards, elements of a REMS may include dear doctor letters, a medication guide, more elaborate targeted educational programs, and in some cases elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. These elements are negotiated as part of the NDA approval, and in some cases if consensus is not obtained until after the PDUFA review cycle, the approval date may be delayed. Once adopted, REMS are subject to periodic assessment and modification.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of onerous risk management plans, restrictions on distribution, or post-marketing trial requirements. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delay in obtaining, or failure to obtain, regulatory approval for our products, or obtaining approval but for significantly limited use, would harm our business. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

The Hatch-Waxman Amendments

Under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, a portion of a product s U.S. patent term that was lost during clinical development and regulatory review by the FDA may be restored. The Hatch-Waxman Amendments also provide a process for listing patents pertaining to approved products in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book) and for a competitor seeking approval of an application that references a product with listed patents to make certifications pertaining to such patents. In addition, the Hatch-Waxman Amendments provide for a statutory protection, known as non-patent exclusivity, against the FDA s acceptance or approval of certain competitor applications.

Patent Term Restoration

Patent term restoration can compensate for time lost during product development and the regulatory review process by returning up to five years of patent life for a patent that covers a new product or its use. This period is generally one-half the time between the effective date of an IND (falling after issuance of the patent) and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, provided the sponsor acted with diligence. Patent term restorations, however, cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended and the extension must be applied for prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant s product. Upon approval of a drug, each of the patents listed in the application for the drug are then published in the FDA s Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and

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dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA s Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a Section VIII statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product s listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

An applicant submitting an NDA under Section 505(b)(2) of the FDCA, which permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference, is required to certify to the FDA regarding any patents listed in the Orange Book for the approved product it references to the same extent that an ANDA applicant would.

Market Exclusivity

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing 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 ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a Paragraph IV certification. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing 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 or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. 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 non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

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Post-Marketing Requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug s approved labeling (known as off-label use), limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, who may or may not grant approval or may include in a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such product or may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

In addition, the manufacturer and/or sponsor under an approved NDA are subject to annual product and establishment fees, currently exceeding $104,000 per product and $554,000 per establishment for fiscal year 2014. These fees are typically increased annually.

The FDA also may require post-marketing testing, also known as Phase 4 testing, REMS to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, withdrawal of approval, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new

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government requirements, including those resulting from new legislation, may be established, or the FDA s policies may change, which could delay or prevent regulatory approval of our products under development.

Reimbursement, Anti-Kickback and False Claims Laws and Other Regulatory Matters

In the United States, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, state Attorneys General and other state and local government agencies. For example, sales, marketing and scientific/educational grant programs must comply with the Federal Anti-Kickback Statute, the False Claims Act, as amended, the privacy regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive regulatory approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, 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 payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-government payors.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidate, if any such product or the condition that it is intended to treat is the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor s product could adversely affect the sales of our product candidate. If 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 on a profitable basis.

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In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

As noted above, in the United States, we are subject to complex laws and regulations pertaining to healthcare fraud and abuse, including, but not limited to, the Federal Anti-Kickback Statute, the Federal False Claims Act, and other state and federal laws and regulations. The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the Federal Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws, the absence of guidance in the form of regulations or court decisions, and the potential for additional legal or regulatory change in this area, it is possible that our future sales and marketing practices and/or our future relationships with eye-care professionals might be challenged under anti-kickback laws, which could harm us. Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we plan to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we will or may become subject.

The Federal False Claims Act prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to cause the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been found liable under the Federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the Federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the Federal False Claims Act and certain states have enacted laws modeled after the Federal False Claims Act.

There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, as discussed below, beginning in 2013, a similar federal requirement will require manufacturers to track and report to the federal government certain payments made to physicians and teaching

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hospitals made in the previous calendar year. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state, and soon federal, authorities.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by required, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Patient Protection and Affordable Care Act

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, PPACA) was enacted, which includes measures that have or will significantly change the way healthcare is financed by both governmental and private insurers. Among the provisions of PPACA of greatest importance to the pharmaceutical industry are the following:

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services a condition for states to receive federal matching funds for the manufacturer s covered outpatient drugs furnished to Medicaid patients. Effective in 2010, PPACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic agents to 23.1% of AMP and adding a new rebate calculation for line extensions (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. PPACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits, to be phased-in by 2014. The Centers for Medicare & Medicaid Services, or CMS, have proposed to expand Medicaid rebate liability to the territories of the United States as well. In addition, PPACA provides for the public availability of retail survey prices and certain weighted average AMPs under the Medicaid program. The implementation of this requirement by the CMS may also provide for the public availability of pharmacy acquisition of cost data, which could negatively impact our sales.

In order for a pharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. Effective in 2010, PPACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children s hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs when used for the orphan indication. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

Effective in 2011, PPACA imposed a requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (i.e., donut hole).

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Effective in 2011, PPACA imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

Effective in 2012, PPACA required pharmaceutical manufacturers to track certain financial arrangements with physicians and teaching hospitals, including any transfer of value made or distributed to such entities, as well as any investment interests held by physicians and their immediate family members. Manufacturers are required to track this information beginning in 2013 and make their first reports in March 2014. The information reported will be publicly available on a searchable website in September 2014.

As of 2010, a new Patient-Centered Outcomes Research Institute was established pursuant to PPACA to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.

PPACA created the Independent Payment Advisory Board, which, beginning in 2014, will have authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.

PPACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Many of the details regarding the implementation of PPACA are yet to be determined, and at this time, it remains unclear the full effect that PPACA would have on our business.

European Union Drug Development

In the European Union, our products will also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained, and the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trial regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. In addition, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the NDCA and ECs of the Member State where they occurred.

The EU clinical trials legislation is currently undergoing a revision process mainly aimed at making more uniform and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials and increasing the transparency of clinical trials.

European Union Drug Review Approval

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations: the Community MA, which is issued by the European Commission through the Centralized Procedure based on the opinion of the Committee

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for Medicinal Products for Human Use, or CHMP, a body of the European Medicines Agency, or the EMA, and which is valid throughout the entire territory of the EEA; and the National MA, which is issued by the competent authorities of the Member States of the EEA and only authorized marketing in that Member State s national territory and not the EEA as a whole.

The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union. The National MA is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member state, or RMS. If the RMS proposes to authorize the product, and the other Member States do not raise objections, the product is granted a national MA in all the Member States where the authorization was sought. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

We had 23 full-time employees as of September 30, 2013. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Property and Facilities

Our headquarters is currently located in Bedminster, New Jersey, and consists of approximately 6,800 square feet of leased office space under a lease that expires on July 30, 2018. Our research and development facility is located in Research Triangle Park, North Carolina and consists of approximately 7,000 square feet of leased laboratory space under an annual leasing arrangement. We recently opened an office in Newport Beach, California, which consists of approximately 400 square feet of leased office space. We may require additional space and facilities as our business expands.

Legal Proceedings

We are not currently subject to any material pending legal proceedings.

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MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information about our executive officers and directors as of September 30, 2013.

NAME	AGE	POSITION(S)
Executive Officers		
Vicente Anido, Jr., PhD	60	Chief Executive Officer and Chairman of the Board
Casey C. Kopczynski, PhD	52	Chief Scientific Officer
Brian Levy, OD, MSc	62	Chief Medical Officer
Thomas A. Mitro	56	President and Chief Operating Officer
Richard J. Rubino	56	Chief Financial Officer
Non-Employee Directors		
Gerald D. Cagle, PhD	69	Director
Janet L. Conway, PhD	63	Director
Geoffrey Duyk, MD, PhD	54	Director
Murray A. Goldberg	68	Director
David W. Gryska	57	Director
Dennis Henner, PhD	62	Director
David Mack, PhD	51	Director
Anand Mehra, MD	37	Director

The following includes a brief biography for each of our executive officers and directors, with each director biography including information regarding the experiences, qualifications, attributes or skills that caused our board of directors to determine that each member of our board of directors should serve as a director as of the date of this prospectus. There are no family relationships among any of our directors or executive officers.

Executive Officers

Vicente Anido, Jr., PhD has served as our Chief Executive Officer since July 2013 and as a Chairman and member of our board of directors since April 2013. Dr. Anido is the former President, Chief Executive Officer and Director of ISTA Pharmaceuticals, Inc., which was acquired by Bausch + Lomb, Inc. in 2012. Prior to joining ISTA Pharmaceuticals, Dr. Anido served as general partner of Windamere Venture Partners from 2000 to 2001. From 1996 to 1999, Dr. Anido served as President and Chief Executive Officer of CombiChem, Inc., a drug discovery company. From 1993 to 1996, Dr. Anido served as President of the Americas Region of Allergan, Inc., where he was responsible for Allergan s commercial operations for North and South America. Prior to joining Allergan, Dr. Anido spent 17 years at Marion Laboratories and Marion Merrell Dow, Inc., including as Vice President, Business Management of Marion s U.S. Prescription Products Division. Dr. Anido currently serves as a member of the boards of directors of QLT Inc. and Depomed, Inc. and is a nominee to the board of directors for Nicox S.A. In addition, from 2002 to 2008, Dr. Anido served as a member of the boards of directors of Apria Healthcare, Inc. Dr. Anido holds a BS and a MS from West Virginia University and a PhD from the University of Missouri, Kansas City. We believe Dr. Anido s experience in the pharmaceutical industry, sales and marketing, business development and pharmaceutical product launch and his experience serving as a director of other public companies provide him with the qualifications and skills to serve as a member of our board of directors.

Casey C. Kopczynski, PhD has served as our Chief Scientific Officer since co-founding our company in 2005. From 2002 to 2005, he was the Managing Partner at Biotech Initiative, LLC, a consulting practice dedicated to emerging biotech companies. He was also previously the Vice President of Research at Ercole Biotech, Inc. from 2003 to 2004, a company developing drugs for the treatment of cancer, inflammation and orphan genetic diseases. Prior to Ercole Biotech, Inc., Dr. Kopczynski was Director of Research and a founding member of the

scientific staff at Exelixis, Inc. from 1996 to 2002. Dr. Kopczynski received his PhD in Molecular, Cellular and Developmental Biology from Indiana University and was a Jane Coffin Childs Research Fellow at the University of California, Berkeley.

Brian Levy, OD, MSc has served as our Chief Medical Officer since January 2012. From 1994 to 2008, Dr. Levy was at Bausch + Lomb, Inc. where he served in various roles including Vice President of Research & Development, Corporate Vice President of Research & Development and Chief Medical Officer. Prior to joining Bausch + Lomb, Inc., Dr. Levy was in private clinical practice in Toronto, Ontario from 1980 to 1989, and from 1989 to 1994 he served as an Associate Professor in the Department of Ophthalmology at California Pacific Medical Center in San Francisco. He has also served as Chief Operating Officer at Danube Pharmaceuticals from 2008 to 2010 and Chief Scientific Officer at Nexis Vision from 2010 to 2011, both small venture-backed companies developing products in Ophthalmology. Dr. Levy currently holds an appointment as Clinical Professor in the Department of Ophthalmology at the University of Rochester s School of Medicine. Dr. Levy received his Doctor of Optometry degree from the University of California at Berkeley and did his post-graduate work in comparative anatomy and physiology of the eye at the University of Waterloo in Canada, where he received a MS degree.

Thomas A. Mitro has served as our President and Chief Operating Officer since August 2013. From November 2012 to August 2013, Mr. Mitro served as Vice President, Sales and Marketing at Omeros Corporation, a publicly traded clinical-stage biopharmaceutical company. Prior to this, Mr. Mitro was Vice President, Sales and Marketing at ISTA Pharmaceuticals from July 2002 to July 2012, where he was instrumental in building ISTA s commercial operations and launching several eye-care products, including *Bromday* (bromfenac ophthalmic solution) 0.09% and *Bepreve* (bepotastine besilate ophthalmic solution) 1.5%. Previously, Mr. Mitro held various positions at Allergan, Inc., including Vice President, Skin Care; Vice President, Business Development; and Vice President, e-Business. Mr. Mitro received his B.S. degree from Miami University.

Richard J. Rubino has served as our Chief Financial Officer since October 2012. From March 2008 to April 2012, Mr. Rubino served as Senior Vice President, Finance and Chief Financial Officer of Medco Health Solutions, Inc. and from May 1993 to March 2008 served as Controller and Vice President of Planning, with responsibilities for financial, business and strategic planning. Previously, Mr. Rubino held various positions at International Business Machines Corporation from 1983 to May 1993 and PricewaterhouseCoopers LLP (formerly Price Waterhouse & Co.) from 1979 to 1983. Mr. Rubino is a Certified Public Accountant and a member of the American Institute of Certified Public Accountants. Mr. Rubino received his BS in Accounting from Manhattan College. He has been a director of the Northside Center for Child Development since 2009, the Treasurer since 2012 and also currently serves as a member of the Finance Committee.

Directors

Gerald D. Cagle, PhD has served as a member of our board of directors since September 2013. Dr. Cagle is currently Chief Operating Officer at Cognoptix, lnc., focused on the diagnosis of Alzheimer s disease. He also is Senior Advisor and Head of Business Development for GrayBug, LLC, a platform drug delivery company. Previously, Dr. Cagle served as Senior Vice President of Research & Development at Alcon Laboratories lnc. from 1997 to 2008, assuming the responsibility of Chief Scientific Officer in 2006. Dr. Cagle has served on the Wilmer Eye Institute Advisory Council and is a member of the ARVO Foundation Board of Governors. Dr. Cagle received his BS degree from Wayland College and earned both his MS and PhD degrees from the University of North Texas. We believe that Dr. Cagle s scientific background and experience provides him with the qualifications and skills to serve as a member of our board of directors.

Janet L. Conway, PhD has served as a member of our board of directors since 2005. Dr. Conway has served as head of Wyoming Ophthalmic Consulting since 2005. Since 2010, Dr. Conway has also provided scientific, preclinical and clinical assistance and analysis to The Magnum Group. From 2003 to 2005, Dr. Conway was Director of Licensing and Development at Pfizer, Executive Director of Ophthalmology Licensing at Pharmacia

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from 2000 to 2003, Director of Global Business Development for Johnson & Johnson s Vision Care franchise from 1995 to 1999 and Vice President of Product Development and co-founder of M6 Pharmaceuticals from 1993 to 1995. From 1983 to 1993, she held similar positions at VimRx Pharmaceuticals, Olympus Corporation (Medical Device Division) and at Johnson & Johnson s ophthalmic pharmaceutical and medical device company, IOLAB, and was a Senior Scientist in Allergan s Discovery Research organization. Dr. Conway holds BA and MA degrees from Northeastern University and a PhD in ocular physiology from the Massachusetts Institute of Technology. Dr. Conway also completed a post-doctoral fellowship in visual neurochemistry at the University of California, Irvine. We believe that Dr. Conway s scientific background and experience provide her with the qualifications and skills to serve as a member of our board of directors.

Geoffrey Duyk, MD, PhD has served as a member of our board of directors since 2005. Dr. Duyk is a Managing Director of TPG Biotech. Dr. Duyk is a member of numerous NIH panels and oversight committees focused on the planning and execution of the Human Genome Project. Previously, he served on the board of directors and was President of Research and Development at Exelixis, Inc., a biopharmaceutical company focusing on drug discovery, from 1996 to 2003. Prior to Exelixis, Dr. Duyk was Vice President of Genomics and one of the founding scientific staff at Millennium Pharmaceuticals, from 1993 to 1996. Before that, Dr. Duyk was an Assistant Professor at Harvard Medical School in the Department of Genetics and Assistant Investigator of the Howard Hughes Medical Institute. Dr. Duyk currently serves on the board of directors of Amyris, Inc., which he joined in May 2012 (and was previously on the board from May 2006 to May 2011), and is also currently on the boards of directors of several private companies and the non-profit Wesleyan University Board of Trustees. He served on the board of directors of Agria Corporation from August 2007 to May 2009, Cardiovascular Systems, Inc. (formerly Replidyne, Inc.) from 2004 to February 2009 and Exelixis, Inc. from 1996 to 2003. Dr. Duyk holds a BA in Biology from Wesleyan University and a PhD and an MD from Case Western Reserve University. We believe that Dr. Duyk s experience with the pharmaceutical industry provides him with the qualifications and skills to serve as a member of our board of directors.

Murray A. Goldberg has served as a member of our board of directors since August 2013. Mr. Goldberg is Senior Vice President, Administration, at Regeneron Pharmaceuticals, Inc. Previously, Mr. Goldberg served as Senior Vice President, Finance and Administration, Chief Financial Officer, and Assistant Secretary, positions he held from December 2000 to September 2013. Prior to that date, Mr. Goldberg was Vice President, Finance and Administration, Chief Financial Officer and Treasurer, positions he held since March 1995, and Assistant Secretary, a position he held since January 2000. Mr. Goldberg served as Vice President of Finance and Administration and Treasurer at Regeneron Pharmaceuticals, Inc. since March 1995. Prior to joining Regeneron Pharmaceuticals Inc., Mr. Goldberg served as Vice President of Finance, Treasurer, and Chief Financial Officer of PharmaGenics Inc., since February 1991 and served as a Director since May 1991. From 1987 to 1990, Mr. Goldberg served as Managing Director in the Structured Finance Group at the Chase Manhattan Bank, N.A. and from 1973 to 1987 he served in various managerial positions in finance and corporate development at American Cyanimid Company. Mr. Goldberg received his BE in Industrial Engineering from New York University, his MBA from the University of Chicago and an MSc in Economics from the London School of Economics. We believe that Mr. Goldberg s business and finance experience at various companies in the pharmaceutical industry provides him with the qualifications and skills to serve as a member of our board of directors.

David W. Gryska has served as a member of our board of directors since March 2012. From May 2012 until December 2012, Mr. Gryska served as Chief Operating Officer and a director of Myrexis Inc., a biotechnology company. From December 2006 to October 2010, he served as Senior Vice President and Chief Financial Officer of Celgene Corporation, a biopharmaceutical company. From October 2004 to December 2006, he was a principal at Strategic Consulting Group, where he provided strategic consulting to early-stage biotechnology companies. Prior to the Strategic Consulting Group, Mr. Gryska was employed by Scios, Inc., a biopharmaceutical company, as Senior Vice President and Chief Financial Officer from November 2000 to October 2004 and as Vice President of Finance and Chief Financial Officer from December 1998 to November 2000. Scios was acquired by Johnson & Johnson in 2003. From 1993 to December 1998, he served as Vice President, Finance and Chief Financial Officer at Cardiac Pathways Corporation, a medical device company, which was later acquired by Boston Scientific Corporation. Prior to joining Cardiac Pathways, Mr. Gryska served

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as a partner at Ernst & Young LLP, an accounting firm, with an emphasis on biotechnology and healthcare companies. Mr. Gryska currently serves as a member of the boards of directors of Hyperion Therapeutics, Inc. since November 2010 and Seattle Genetics Inc. since March 2005. Mr. Gryska received a BA in accounting and finance from Loyola University and an MBA from Golden Gate University. We believe that Mr. Gryska s business experience as a senior financial executive at a life sciences and biotechnology company and his experience serving as a director of other public companies provide him with the qualifications and skills to serve as a member of our board of directors.

Dennis Henner, PhD has served as a member of our board of directors since 2011. Dr. Henner has served as managing director of Clarus Ventures, LLC since the firm s inception in 2005. He has over 27 years of healthcare industry and investment experience, including as a partner at MPM Capital from 2001 to 2005. From 1978 to 2001, Dr. Henner was a scientist and executive at Genentech, Inc. where he held various positions, including Senior Vice President of Research, and was a member of Genentech s executive committee. In addition to serving on our board of directors, Dr. Henner currently serves as a member of the boards of directors of several private companies, as well as the board of directors of KaloBios Pharmaceuticals, Inc. since March 2005. He is a member of the Board of Trustee of Reed College. Dr. Henner received his PhD from the Department of Microbiology at the University of Virginia and completed his post-graduate training at the Scripps Clinic and Research Foundation. We believe that Dr. Henner s experience in the healthcare industry provides him with the qualifications and skills to serve as a member of our board of directors.

David Mack, PhD has served as a member of our board of directors since 2005. Dr. Mack currently serves as Chief Executive Officer and President of PMV Pharma, which he co-founded in 2013. Dr. Mack was previously a Director at Alta Partners from 2002 to 2013 and currently serves as a consultant for Alta Partners. Dr. Mack was Chief Executive Officer and director of Angiosyn from 2003 to 2005. In 1997, Dr. Mack co-founded and served as Vice President of Genomics Research at Eos Biotechnology from 1997 to 2002. From 1994 to 1997, Dr. Mack served at Affymetrix Inc. as Head of Cancer Biology. Dr. Mack currently serves as a member of the boards of directors of several private companies. Dr. Mack holds a BA in Molecular Biology from the University of California, Berkeley and received his PhD from the University of Chicago where he was a Howard Hughes fellow in Molecular Genetics and Cell Biology. He was an American Cancer Society postdoctoral fellow at Stanford University School of Medicine in Microbiology and Immunology. We believe that Dr. Mack s management experience in the pharmaceuticals industry and scientific background provides him with the qualifications and skills to serve as a member of our board of directors.

Anand Mehra, MD has served as a member of our board of directors since August 2010. Dr. Mehra has ten years of experience as a management consultant and biotech investor and currently serves as a General Partner at Sofinnova Ventures, which he joined in 2007 as a principal, a healthcare focused investment firm specializing in clinical-stage pharmaceutical companies. Prior to joining Sofinnova Ventures, Dr. Mehra worked at JP Morgan Partners, and consulted at McKinsey and Company. Dr. Mehra currently serves as a member of the boards of directors of several private companies. Dr. Mehra graduated Phi Beta Kappa from the University of Virginia with a BA in government and foreign affairs and received his MD from Columbia University s College of Physicians and Surgeons. We believe that Dr. Mehra s directorship experience and scientific background provides him with the qualifications and skills to serve as a member of our board of directors.

Board Composition and Election of Directors

Our board of directors currently consists of nine members. Messrs. Duyk, Henner, Mack and Mehra were elected as directors pursuant to a voting agreement that we have entered into with the holders of our outstanding series of preferred stock. The voting agreement will terminate upon the closing of this offering and there will be no further contractual obligations regarding the election of our directors. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective prior to the closing of this offering provide that the authorized number of directors may be changed only

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by resolution of the board of directors. Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective prior to the closing of this offering also provide that our directors may be removed only for cause, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective prior to the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the Class I directors will be Dr. Anido, Dr. Mack and Dr. Conway, and their terms will expire at the annual meeting of stockholders to be held in 2014;
- the Class II directors will be Mr. Gryska, Mr. Goldberg and Dr. Duyk; and their terms will expire at the annual meeting of stockholders to be held in 2015; and
- the Class III directors will be Dr. Henner, Dr. Mehra and Dr. Cagle, and their terms will expire at the annual meeting of stockholders to be held in 2016.

The classification of the board of directors may have the effect of delaying or preventing changes in control of our company. We expect that additional directorships resulting from an increase in the number of directors, if any, will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors.

Director Independence

Under the listing requirements and rules of the NASDAQ Global Market, or NASDAQ, independent directors must compose a majority of a listed company s board of directors within a one year period following the completion of this offering. In addition, applicable NASDAQ rules require that, subject to specified exceptions, each member of a listed company s audit, compensation and nominating and corporate governance committees must be independent within the meaning of applicable NASDAQ rules. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act.

In October 2013, our board of directors undertook a review of the independence of each director and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director and the association of our directors with the holders of more than 5% of our common stock. As a result of this review, our board of directors determined that Dr. Mack, Dr. Conway, Dr. Duyk, Mr. Gryska, Mr. Goldberg, Dr. Henner, Dr. Mehra and Dr. Cagle qualify as independent directors within the meaning of the NASDAQ rules. Although NASDAQ rules require that a majority of the board of directors and each member of our audit, compensation and nominating and corporate governance committees must be independent, under special phase-in rules applicable to new public companies, we will have until one year from the effective date of our initial public offering to comply with these independence requirements. We intend to rely on these phase-in rules with respect to the composition of our audit committee. As required under applicable NASDAQ rules, we anticipate that our independent directors will meet in regularly scheduled executive sessions at which only independent directors are present.

Lead Independent Director

Our corporate governance guidelines provide that one of our independent directors should serve as a lead independent director at any time when the Chief Executive Officer serves as the Chairman of our board of directors, or if the Chairman is not otherwise independent. Because Dr. Anido is our Chairman and Chief Executive Officer, our board of directors has appointed Mr. Gryska to serve as our lead independent director. As

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lead independent director, Mr. Gryska presides over periodic meetings of our independent directors, serves as a liaison between our Chairman and the independent directors and performs such additional duties as our board of directors may otherwise determine and delegate.

Committees of the Board of Directors

Our board of directors has an audit committee, a compensation committee and a nominating and corporate governance committee. The composition and responsibilities of each committee are described below. Members serve on these committees until their resignation or until otherwise determined by our board.

Audit Committee

The members of our audit committee following the offering will be Mr. Goldberg, Mr. Gryska and Dr. Duyk. Mr. Goldberg will serve as chair of the audit committee. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ and which will be available on our website prior to the completion of this offering at www.aeriepharma.com. The inclusion of our website address here and elsewhere in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

Under the applicable NASDAQ rules, we are permitted to phase in our compliance with the independent audit committee requirements set forth in Rule 5605 of the NASDAQ listing standards on the same schedule as we are permitted to phase in our compliance with the independent audit committee requirement pursuant to Rule 10A-3 under the Exchange Act, which require (1) one independent member at the time of listing; (2) a majority of independent members within 90 days of listing; and (3) all independent members within one year of listing.

Our board of directors has determined that two members of our audit committee who will continue to be on the audit committee following our initial public offering are independent as independence is currently defined in Rule 5605 of the NASDAQ listing standards and Rule 10A-3 under the Exchange Act. We expect that membership of this committee will be changed to comply with independence requirements prior to the end of the phase-in period permitted by NASDAQ.

In addition, our board of directors has determined that each member of the audit committee is financially literate and that Mr. Goldberg and Mr. Gryska each qualifies as an audit committee financial expert as defined in applicable SEC rules. In making this determination, our board has considered the formal education and nature and scope of his previous experience, coupled with past and present service on various audit committees.

The responsibilities of our audit committee include, among other things:

- reviewing our annual and quarterly financial statements and reports, discussing the statements and reports with our independent registered public accounting firm and management and recommending to the board whether to include the financial statements in the annual reports filed with the SEC;

- discussing the type of information to be disclosed and the type of presentation to be made regarding financial information and guidance to analysts and ratings agencies;

- overseeing our disclosure controls and procedures, including internal controls over our financial reporting, and reviewing and discussing our management s periodic review of the effectiveness of our internal control over financial reporting;

- reviewing with our independent registered public accounting firm and management significant issues that arise regarding accounting principles and financial statement presentation, matters concerning the scope, adequacy and effectiveness of our financial controls, effects of alternative accounting principles generally accepted in the United States of America, methods on our financial statements and any

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correspondence or reports that raise issues with or could have a material effect on our financial statements;

retaining, appointing, setting compensation of and evaluating the performance, independence, internal quality control procedures and qualifications of our independent auditors;

reviewing and approving in advance the engagement of our independent registered public accounting firm to perform audit services and any permissible non-audit services;

reviewing with our independent registered public accounting firm the planning and staffing of the audit, including the rotation requirements and other independence rules;

reviewing and, if acceptable, approving any related person transactions;

overseeing and discussing with management our policies with respect to risk assessment and risk management, and our significant financial and operational risk exposures;

setting policies for our hiring of employees or former employees of our independent registered public accounting firm;

reviewing and assessing the adequacy of our audit committee charter periodically; and

establishing procedures for receipt, retention and treatment of complaints regarding accounting, internal controls and auditing matters, and for confidential, anonymous submissions of accounting and auditing concerns by employees.

Compensation Committee

The members of our compensation committee are Dr. Mehra, Mr. Gryska, Dr. Mack and Dr. Cagle. Mr. Gryska serves as chair of the compensation committee. All members of our compensation committee are independent as independence is currently defined in Section 5605 of the NASDAQ listing standards and qualify as outside directors under Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code. The compensation committee operates under a written charter that satisfies the applicable standards of NASDAQ and which will be available on our website prior to the completion of this offering at www.aeriepharma.com. The inclusion of our website address here and elsewhere in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

The responsibilities of our compensation committee include, among other things:

approving the compensation and other terms of employment of our chief executive officer, which are then reviewed and ratified by our board of directors;

approving or recommending to our board of directors the compensation and other terms of employment of our senior executives;

approving annually the corporate goals and objectives relevant to the compensation of our chief executive officer and assessing at least annually our chief executive officer s performance against these goals and objectives;

reviewing annually our compensation strategy, including base salary, incentive compensation and equity-based grants, as well as adoption, modification or termination of this compensation;

evaluating at least annually and recommending to our board of directors the type and amount of compensation to be paid or awarded to non-employee board members;

reviewing the competitiveness of our executive compensation programs and evaluating the effectiveness of our compensation policy and strategy in achieving expected benefits to us;

approving the terms of any employment agreements, severance arrangements, change in control protections and any other compensatory arrangements for our executive officers;

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reviewing at least annually the adequacy of our compensation committee charter; and

reviewing and evaluating, at least annually, the performance of the compensation committee.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Dr. Henner and Dr. Conway. Dr. Henner serves as chair of this committee. Currently, our board of directors has determined that both members of our nominating and corporate governance committee are independent as independence is currently defined in Section 5605(a)(2) of the NASDAQ listing standards. The nominating and corporate governance committee operates under a written charter that satisfies the applicable standards of NASDAQ and which will be available on our website prior to the completion of this offering at www.aeriepharma.com. The inclusion of our website address here and elsewhere in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

The responsibilities of our nominating and corporate governance committee include, among other things:

identifying, considering and nominating candidates to serve on our board of directors;

developing and recommending the minimum qualifications for service on our board of directors;

overseeing the evaluation of the board and management on an annual basis;

considering nominations by stockholders of candidates for election to the board of directors;

reviewing annually the independence of the non-employee directors and members of the independent committees of the board;

developing and recommending to our board of directors a set of corporate governance guidelines, and reviewing and recommending to our board of directors any changes to such principles;

developing and recommending to our board of directors a code of business conduct and ethics, and reviewing and recommending to our board of directors any changes to the code; and

reviewing the adequacy of its charter, our corporate governance guidelines and our code of business conduct and ethics on an annual basis.

Code of Business Conduct and Ethics

We adopted a code of business conduct and ethics that applies to all of our employees, officers and directors including those officers responsible for financial reporting. Upon the completion of this offering, the code of business conduct and ethics will be available on our website at www.aeriepharma.com. We intend to disclose future amendments to the code or any waivers of its requirements on our website to the extent permitted by the applicable rules and exchange requirements.

Compensation Committee Interlocks and Insider Participation

No member of the Compensation Committee has ever been one of our officers or employees. In addition, during fiscal year 2012, none of our executive officers served as a member of a compensation committee or board of directors of an entity that had an executive officer serving as a

member of our board of directors.

Executive Officers

Each of our executive officers has been elected by our board of directors and serves until his or her successor is duly elected and qualified.

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EXECUTIVE COMPENSATION

The discussion and tabular disclosure that follows describes our executive compensation program during the fiscal year ended December 31, 2012, our most recently completed fiscal year, with a focus on our executive compensation program relating to the following individuals: Thomas J. van Haarlem, Richard J. Rubino and Brian Levy (our named executive officers).

Summary Compensation Table

The following table sets forth the portion of compensation paid to the named executive officers that is attributable to services performed during the fiscal year ended December 31, 2012.

NAME AND PRINCIPAL POSITION	YEAR	SALARY ($)	BONUS ($) [1]	OPTION AWARDS ($) [2]	TOTAL ($)
Thomas J. van Haarlem [3] President & Chief Executive Officer	2012	$ 389,622	$ 146,108		$ 535,730
Richard J. Rubino Chief Financial Officer	2012	$ 62,500[4]	$ 10,080	$ 700,000	$ 772,580
Brian Levy Chief Medical Officer	2012	$ 285,000	$ 57,000	$ 202,000	$ 544,000

(1) Amounts reflected in this column are bonus amounts awarded at the discretion of the board of directors after its assessment of our and the executive s performance in the fiscal year. The amount reported will be paid in November 2013.

(2) The amounts included in the Option Awards column represent the grant date fair value computed in accordance with FASB ASC Topic 718. The valuation assumptions used in determining such amounts are described in Note 11 to our financial statements included elsewhere in this prospectus.

(3) Thomas J. van Haarlem resigned from his position as President & Chief Executive Officer on July 25, 2013. In connection with his separation, Dr. van Haarlem entered into a separation agreement and release pursuant to which he will receive base salary continuation and other benefits, and also entered into a consulting agreement, which agreements are described below under Executive Agreements 2013 Agreements.

(4) For Mr. Rubino, represents solely the pro-rated amount of his annual base salary earned commencing October 15, 2012, his employment start date.

Executive Agreements

On July 25, 2013, Vicente Anido, Jr., Ph.D., Chairman of our board of directors, was named Chief Executive Officer and will continue as our Chairman. Dr. Anido replaced our founding Chief Executive Officer Thomas J. van Haarlem, M.D., who resigned from his positions as our President, Chief Executive Officer and Director. Dr. van Haarlem serves as a consultant to us pursuant to the terms of the consulting agreement described below. The following summary for Dr. van Haarlem reflects the terms and conditions of his employment prior to the separation date.

Thomas J. van Haarlem. On July 5, 2005, we entered into a letter agreement with Dr. van Haarlem, which was amended effective September 28, 2009. The initial employment term, and the subsequent renewal term entered into pursuant to the amendment effective September 28, 2009, concluded on July 5, 2008 and December 31, 2010, respectively. The letter agreement provided that Dr. van Haarlem was entitled to base salary of $389,622 per annum as of December 31, 2012. Dr. van Haarlem was eligible to receive an annual performance bonus of up

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to 50% of his base salary for the relevant calendar year. His letter agreement also provided for severance upon certain terminations of employment, as described below under Potential Payments Upon Termination or Change in Control.

Dr. van Haarlem s letter agreement provided that for the one-year period following his termination of employment, he is prohibited from (i) soliciting any of our competitors, customers, or employees, and (ii) inducing or encouraging any of our third-party licensors, licensees, distributors, or research, development or commercialization collaborators to terminate or reduce its business activities with us. In connection with the execution of his letter agreement, Dr. van Haarlem also entered into a confidentiality, inventions and noncompetition agreement, which provided that for a period of one year following his termination he is prohibited from (i) engaging in any business related to our fields of interest anywhere in the Noncompetition Area (as defined in the agreement), (ii) from interfering with the relationship between us (and any of our affiliates) and our customers then existing or existing at any time within one year prior to termination and (iii) from interfering with the relationship between us and our suppliers then existing or existing at any time within one year prior to termination.

Richard J. Rubino. On September 24, 2012, we entered into a letter agreement with Mr. Rubino, pursuant to which his initial employment term commenced on October 15, 2012 and will expire on October 15, 2015, unless extended by mutual written agreement between us and Mr. Rubino. The letter agreement provides that Mr. Rubino is entitled to base salary of $300,000 per annum as of December 31, 2012, which may be increased at the board of director s or the CEO s discretion and may be decreased by the board of directors only in connection with an overall reduction in executive officer salaries. Mr. Rubino is eligible to receive an annual performance bonus of up to 20% of his base salary for the relevant calendar year.

Mr. Rubino s letter agreement provides that for the one-year period following his termination of employment, he is prohibited from (i) soliciting any of our competitors, customers, or employees, and (ii) inducing or encouraging any of our third-party licensors, licensees, distributors, or research, development or commercialization collaborators to terminate or reduce its business activities with us. In connection with the execution of his letter agreement, Mr. Rubino also entered into a confidentiality, inventions and noncompetition agreement which provides that for a period of one year following his termination he is prohibited from (i) engaging in any business related to our fields of interest anywhere in the Noncompetition Area (as defined in the agreement), (ii) from interfering with the relationship between us (and any of our affiliates) and our customers then existing or existing at any time within one year prior to termination and (iii) from interfering with the relationship between us and our suppliers then existing or existing at any time within one year prior to termination.

Brian Levy. On December 15, 2011, we entered into a letter agreement with Dr. Levy, pursuant to which his initial employment term commenced on January 2, 2012 and will expire January 2, 2016, and will thereafter be subject to automatic one-year extensions unless either we or Dr. Levy provide at least 90 days written notice of non-extension. The letter agreement provides that Dr. Levy is entitled to base salary of $285,000 per annum as of December 31, 2012 which may be increased at the board of director s or the CEO s discretion, and may be decreased only in connection with an overall reduction in executive officer salaries. Dr. Levy is eligible to receive an annual performance bonus of up to 20% of his base salary for the relevant calendar year. His employment agreement also provides for severance upon certain terminations of employment, as described below under Potential Payments Upon Termination or Change in Control.

Dr. Levy s letter agreement provides that for the one-year period following his termination of employment, he is prohibited from (i) soliciting any of our employees and (ii) inducing or encouraging any of our third-party licensors, licensees, distributors, or research, development or commercialization collaborators to terminate or reduce its business activities with us. In connection with the execution of his letter agreement, Dr. Levy also entered into a confidentiality, inventions and noncompetition agreement which provides that for a period of one year following his termination he is prohibited from (i) engaging in any business related to our fields of interest anywhere in the Noncompetition Area (as defined in the agreement), (ii) from interfering with the relationship

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between us (and any of our affiliates) and our customers then existing or existing at any time within one year prior to termination and (iii) from interfering with the relationship between us and our suppliers then existing or existing at any time within one year prior to termination.

2013 Agreements

Vicente Anido, Jr. On September 20, 2013, we entered into an employment agreement with Vicente Anido, Jr. to memorialize his appointment as our Chief Executive Officer, which appointment was effective as of July 25, 2013. The employment agreement provides for a four-year term during which Dr. Anido will receive an annual base salary of $475,000, which may be increased annually at the board of director s discretion, and may be decreased only in connection with an overall reduction in executive officer salaries. Dr. Anido is eligible to receive an annual performance bonus of up to 50% of his base salary for the relevant calendar year. The employment agreement also provides that Dr. Anido will be granted an option to purchase 922,468 shares of common stock which will vest, subject to his continued employment with (or provision of services to) us through the applicable vesting date, 25% on July 25, 2014, and thereafter will vest ratably on each of the 36 monthly anniversaries of July 25, 2014. For the four-year period commencing on September 20, 2013, in the event that any of the payments or benefits provided by us to Dr. Anido would constitute a parachute payment within the meaning of Section 280G of the Code and would be subject to the excise tax imposed under Section 4999 of the Code, Dr. Anido will entitled to a gross-up payment equal to the sum of such excise tax and related interest or penalties (the Excise Tax) plus the amount necessary to put him in the same after-tax position that he would have been in had he not incurred any tax liability under Section 4999 of the Code.

In the event of a termination of Dr. Anido s employment by us without Cause or by Dr. Anido for Good Reason, Dr. Anido will be entitled to (i) a lump sum severance payment equal to six months of base salary, (ii) commencing on the date that is six months following the termination date, continued payment of Dr. Anido s base salary at the rate in effect at the time of termination for a period of six months, (iii) 12 months of Company-paid COBRA continuation coverage less the amount payable by an active employee for such coverage, and (iv) payment of the greater of (x) the target annual performance bonus for the year in which termination occurs and (y) the average of the annual performance bonus received by Dr. Anido for the three years immediately preceding the year in which termination occurs (together with the payments provided under (i), (ii) and (ii), the Severance Payments). In the event Dr. Anido s employment is terminated by us with or without Cause, or he resigns for or without Good Reason, he will have a post-termination exercise period of 90 days during which he may exercise the portion of the options that was vested as of the termination date. In the event of a termination by us without Cause or by Dr. Anido for Good Reason at any time during the 12 months following a Transfer of Control, he will be entitled to (i) the Severance Payments (which Severance Payments shall be made for a period of 18 months following termination if we are a publicly reporting company at the time of the Transfer of Control) and (ii) full vesting of all options and other equity incentive awards which were unvested immediately prior to such termination. In the event that the Board approves a decision to liquidate, dissolve, or terminate our business or operations (other than in connection with the sale of the assets or merger of our company), Dr. Anido will immediately resign from all then-held employment, officer and director positions, and will not be required to oversee, participate or assist in any in such liquidation, provided, however, that in the event of such resignation, Dr. Anido would not be entitled to any severance benefits or payments.

Dr. Anido s employment agreement also provides that he shall not (and shall not assist any person to), directly or indirectly, without our prior written consent (a) during the employment term and for a period of 6 months thereafter contact, induce or solicit for employment any person who is, or within three month prior to such hiring, contacting, inducing or soliciting, was an employee of us or any of our affiliates; (b) during the employment term and for a period of 12 months thereafter, induce or solicit any customer, client or vendor of, or other person having a business relationship with us or any of our affiliates to terminate its relationship or otherwise cease doing business in whole or in part with us or any of our affiliates; or (c) during the employment term and for a period of 12 months thereafter, interfere with any relationship between us or any of our affiliates and any of our respective customers, clients, vendors or any other business contacts.

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Thomas J. van Haarlem. On July 25, 2013, or the Separation Date, we entered into a Separation and General Release Agreement with Dr. Thomas van Haarlem, pursuant to which Dr. van Haarlem resigned from his positions as President, Chief Executive Officer and director. Pursuant to the terms of the Separation Agreement, Dr. van Haarlem has released us from any and all claims, known or unknown, that he had, has or may have against us up until the Separation Date. In consideration for such release, we have agreed to provide: (a) payment of base salary of $397,414 for a period of 12 months, payable in regular installments in accordance with our usual payroll practices; (b) reimbursement for any unreimbursed business expenses incurred by him prior to the Separation Date in accordance with Company policy; (c) 12 months of benefits continuation under our health and dental plan; and (d) reimbursement for the pro-rata number of unused vacation days during 2013. The Separation Agreement also provides that Dr. van Haarlem will be paid an amount equal to $146,108 within 30 days following the earliest to occur of the following, provided that such event occurs on or before June 30, 2014 (i) the closing of an initial public offering in which we receive gross proceeds of at least $50,000,000; (ii) the closing of an equity financing in which we receive gross proceeds of no less than $20,000,000; and (iii) a merger, acquisition or transfer of all or substantially all of our business assets. In addition, we have released Dr. van Haarlem from the non-competition obligations in his confidentiality, inventions and noncompetition agreement.

In accordance with the terms of the Separation Agreement, we and Dr. van Haarlem have also entered into a consulting agreement, or the Consulting Agreement, effective as of the Separation Date through June 30, 2014 (the Expiration Date). The Consulting Agreement provides for (i) the payment of $100.00 per month; (ii) the continuation of the vesting of options to purchase 41,678 shares of common stock held by Dr. van Haarlem in accordance with the vesting schedule applicable immediately prior to the Separation Date until the Expiration Date; and (iii) the extension of the exercise period of options to purchase 443,623 shares of common stock, all of which were vested on or prior to the Separation Date, until the Expiration Date, following which date all then unexercised options shall automatically expire. Dr. van Haarlem will be entitled to exercise his vested options prior to the Expiration Date by means of a cashless exercise. The Consulting Agreement also provides that during the term and for a period of 12 months thereafter, Dr. van Haarlem shall not, directly or indirectly, without our prior written consent (a) solicit or induce any of our employees to leave our company; or (b) solicit the business of any of our agents, clients or customers with respect to products or services similar to and competitive with those provided or supplied by us. Dr. van Haarlem also agreed to maintain the confidentiality of any of our proprietary information at all times during and after the term, and to assign to us all rights in any inventions conceived by him during the term of the agreement. Moreover, pursuant to the terms of each of the Consulting Agreement and Separation Agreement, we and Dr. van Haarlem each agree to refrain from making or encouraging any other individual to make any public or private comments that would disparage the other, and in the case of us, our officers, directors or managers.

Thomas A. Mitro. On July 31, 2013, we entered into an employment agreement with Thomas A. Mitro, effective as of August 5, 2013, pursuant to which Mr. Mitro was appointed as our President and Chief Operating Officer. The employment agreement provides for a four-year term during which Mr. Mitro will receive an annual base salary of $335,000, which may be increased annually at the board of director s discretion, and may be decreased only in connection with an overall reduction in executive officer salaries. Mr. Mitro is eligible to receive an annual performance bonus of up to 20% of his base salary for the relevant calendar year. The employment agreement also provides that Mr. Mitro will be granted an option to purchase 380,483 shares of common stock, which will vest, subject to his continued employment with (or provision of services to) us through the applicable vesting date, 25% on August 5, 2014, and thereafter will vest ratably on each of the 36 monthly anniversaries of August 5, 2014. For the two-year period commencing on the date of the agreement, in the event that any of the payments or benefits provided by us to Mr. Mitro would constitute a parachute payment within the meaning of Section 280G of the Code and would be subject to the excise tax imposed under Section 4999 of the Code, Mr. Mitro will be entitled to a gross-up payment equal to the sum of such excise tax and related interest or penalties (the Excise Tax) plus the amount necessary to put him in the same after-tax position that he would have been in had he not incurred any tax liability under Section 4999 of the Code. In the event of a termination by us without Cause or by Mr. Mitro for Good Reason, Mr. Mitro will be entitled to

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six months of (i) base salary continuation and (ii) benefits continuation. In the event Mr. Mitro is terminated by us with or without Cause, or resigns for or without Good Reason, he will have a post-termination exercise period of 90 days during which he may exercise the portion of the option which was vested as of the termination date. In the event he terminates for Good Reason or is terminated by us without cause, at any time during the 12 months following a Transfer of Control, he will be entitled to six months of (i) base salary continuation and (ii) benefits continuation, and full vesting of all options and other equity incentive awards which were unvested immediately prior to such termination.

Mr. Mitro s employment agreement also provides that during the term and for a period of 12 months thereafter, he shall not, directly or indirectly, without our prior written consent (a) solicit or induce any of our employees to leave us; or (b) solicit the business of any of our agents, clients or customers with respect to products or services similar to and competitive with those provided or supplied by us.

Equity Incentive Awards

Our named executive officers are eligible to receive long-term equity-based incentive awards under the 2005 Plan. While we believe that long-term equity awards are an important element of the mix of compensation paid to our named executive officers, we do not maintain any formal grant-making policy. Instead, the board of directors (or the compensation committee) periodically reviews the total level and mix of compensation paid to each of our named executive officers in order to determine the appropriate timing and amounts of long-term equity awards so as to continue to promote the alignment of our executive officers interests with those of our stockholders.

Richard J. Rubino. Pursuant to the terms of an incentive stock option agreement, on October 15, 2012, we granted Mr. Rubino an option to purchase 345,000 shares of common stock scheduled to vest over a period of four years beginning on the anniversary of the date of grant, which option agreement was subsequently amended on March 21, 2013 to provide that (i) the option would no longer be an incentive stock option as described in Section 422 of the Code, (ii) the option would be fully vested and (iii) Mr. Rubino may elect to net exercise his option such that the number of shares delivered would reflect the total number of shares underlying the option reduced by the number of shares of common stock having a fair market value on the date of exercise equal to the aggregate exercise price for the total number of shares underlying the option (net exercise). As described in greater detail in footnote 5 to the Outstanding Equity Awards at Fiscal Year-End table, this option was exercised in full by Mr. Rubino in March 2013. We also made an additional option grant to purchase 174,939 shares of common stock, which was the equivalent number of shares he surrendered to us in connection with the cashless exercise of his October 2012 option. On September 12, 2013, we granted Mr. Rubino an option to purchase 25,000 shares of common stock scheduled to vest 25% on or after September 12, 2014 and 75% in 36 equal monthly installments on the corresponding day of each successive month thereafter.

Brian Levy. Pursuant to the terms of an incentive stock option agreement, on January 1, 2012, we granted Dr. Levy an option to purchase 154,000 shares of common stock scheduled to vest 25% on or after December 31, 2012, and 75% in 36 equal monthly installments on the corresponding day of each successive month thereafter. The option terminates on the earliest to occur of (i) January 1, 2022, (ii) the expiration of the post-termination exercise period or (iii) upon a Transfer of Control. On September 12, 2013, we granted Dr. Levy an option to purchase 50,000 shares of common stock scheduled to vest 25% on or after September 12, 2014 and 75% in 36 equal monthly installments on the corresponding day of each successive month thereafter.

The treatment of Dr. van Haarlem s, Mr. Rubino s and Dr. Levy s equity awards upon a termination of employment (as applicable) or a Transfer of Control is described below in the section entitled Potential Payments Upon Termination or Change in Control.

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Outstanding Equity Awards at Fiscal Year-End

The following table provides information concerning outstanding equity awards for each of our named executive officers as of December 31, 2012.

	OPTION AWARDS			
NAME	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS EXERCISABLE (#)	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS UNEXERCISABLE (#)	OPTION EXERCISE PRICE ($)	OPTION EXPIRATION DATE
Thomas J. van Haarlem	42,073[1]		$ 0.0050	8/12/2015
	56,000[2]		$ 0.3950	2/19/2018
	228,286	52,681[3]	$ 0.4050	12/3/2019
	57,217	73,565[4]	$ 0.1960	4/28/2021
Richard J. Rubino		345,000[5]	$ 1.4705	10/15/2022
Brian Levy	38,500	115,500[6]	$ 1.4245	1/1/2022

(1) This option was granted on July 5, 2005 and was fully vested as of July 5, 2010.

(2) This option was granted on February 19, 2008 and was fully vested as of December 29, 2012.

(3) This option was granted on December 3, 2009 and, by its original terms, was scheduled to vest in equal monthly installments such that the option would have fully vested on September 22, 2013. Pursuant to the terms of the Consulting Agreement, this option will continue to vest until June 30, 2014, and any portion of the option unvested as of such date shall be forfeited.

(4) This option was granted on April 28, 2011 and, by its original terms, was scheduled to vest in equal monthly installments such that the option would have fully vested on March 25, 2015. Pursuant to the terms of the Consulting Agreement, this option will continue to vest until June 30, 2014, and any portion of the option unvested as of such date shall be forfeited.

(5) This option was granted on October 15, 2012 and was scheduled to vest 25% on October 14, 2013, and thereafter in equal monthly installments such that the option would have been fully vested on October 14, 2016. This option is no longer outstanding and is considered cancelled for accounting purposes. Pursuant to an amendment to the option agreement, in March 2013, the option was fully exercisable and Mr. Rubino exercised the option in full on a net exercise basis such that he acquired 170,061 shares of common stock. The resulting 170,061 shares are subject to the original vesting terms and are considered restricted stock until vesting occurs. In order to cover Mr. Rubino s out-of-pocket tax costs associated with the exercise of his option, on March 21, 2013 we made an additional grant of 200,973 shares of restricted stock which is scheduled to vest over a two-year period in equal monthly installments. We also made an additional option grant to purchase 174,939 shares of common stock, which was the equivalent number of shares he had surrendered to us in connection with the cashless exercise of the October 2012 option. This option is scheduled to vest 25% on October 14, 2013, and thereafter in equal monthly installments such that the option will be fully vested on October 14, 2016.

(6) This option was granted on January 1, 2012. The option vested 25% on December 31, 2012 and thereafter is scheduled to vest in equal monthly installments such that the option will be fully vested on December 31, 2015.

Retirement Benefit Programs

Our named executive officers are entitled, on the same basis as our other employees, to participate in our 401(k) plan, a tax-qualified defined contribution plan under Section 401 of the Code. Pursuant to the 401(k) plan, participants may contribute an amount of his or her pre-tax compensation up to the statutory limit, which limit in 2013 is $17,500.

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Potential Payments Upon Termination or Change in Control

A description of Dr. van Haarlem s entitlements following his resignation, as provided under the terms of his Separation Agreement and Consulting Agreement, are described above in the section Executive Agreements 2013 Agreements.

Brian Levy. Upon termination by us without Cause or by Dr. Levy in connection with a Constructive Termination Event (as defined in his letter agreement), Dr. Levy would be entitled to six months of annual base salary, at the rate in effect immediately prior to the date of such termination (the Severance Amount). The Severance Amount will be paid in installments in accordance with our normal payroll practices or, at our election, in a lump sum. Notwithstanding the foregoing, if we elect to pay the Severance Amount in a lump sum pursuant to Dr. Levy s determination that such payment would have resulted in the avoidance of the imposition of excise taxes, and we subsequently determine either that (i) the payment of the Severance Amount in installments would not result in the imposition of excise taxes upon Dr. Levy or (ii) payment of the Severance Amount in a lump sum would adversely affect our ability to pay our debts as they come due or would otherwise violate any of our obligations or covenants under any written agreement with any third party, we shall not be obligated to pay the Severance Amount in a lump sum and may continue to pay the Severance Amount in installments.

In the event of Dr. Levy s termination for any reason other than for Cause (as defined in the letter agreement), the vested portion of his outstanding option shall remain exercisable until the earlier of (i) expiration of the three- month period (in the case of termination due to death or disability, the twelve-month period) beginning on the date following the termination date and (ii) the option expiration date. In the event of termination for Cause, the option may not be exercised after the date on which Dr. Levy s employment terminates.

Richard J. Rubino. Mr. Rubino s employment may be terminated by us for any reason, and may be voluntarily terminated by him with 30 days prior written notice, which notice period may be waived or shortened by us. Upon his termination of employment for any reason, Mr. Rubino would be entitled to payment by us of amounts of base salary and bonus (if any) accrued under any bonus plan through, and payable at, the date of such termination.

In the event of Mr. Rubino s termination for any reason other than for cause, the vested portion of his option shall remain exercisable until the earlier of (i) expiration of the three-month period (in the case of termination due to death or disability, the twelve-month period) beginning on the date following the termination date and (ii) the option expiration date. In the event of termination for cause (as determined in the sole discretion of the board of directors), the option may not be exercised after the date on which Mr. Rubino s employment terminates.

Messrs. van Haarlem, Rubino and Levy Treatment of Equity in the Event of a Transfer of Control. The 2005 Plan provides that in the event of a Transfer of Control (as defined in the 2005 Plan), each outstanding option shall be assumed or an equivalent option substituted by the successor corporation (or a parent or subsidiary of the successor corporation). If the successor corporation in a Transfer of Control refuses to assume or substitute for any outstanding option, the option shall fully vest and become exercisable. An option shall be considered assumed if, following the Transfer of Control, the option confers upon the holder the right to receive, in respect of each share underlying such option, the per share consideration (whether in the form of stock, cash or other securities or property) received by holders of our common stock (as of the effective date of the transaction) in the Transfer of Control, provided, however, that if such consideration received in the Transfer of Control is not solely capital stock of the successor corporation (or parent thereof), the board of directors may, with the consent of the successor corporation, provide for the consideration to be received upon the exercise of the option, for each share subject to the option, to be solely capital stock of the successor corporation (or parent thereof) equal in fair market value to the per share consideration received by holders of our common stock in the Transfer of Control. Upon occurrence of a Transfer of Control, each outstanding option, to the extent not exercised prior to or concurrently with the Transfer of Control, shall terminate as of the effective time of the Transfer of Control, unless such option is assumed or replaced with an option to purchase shares of capital stock in the successor corporation.

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Notwithstanding the foregoing, if the successor corporation (or a parent or subsidiary of the successor corporation), either (A) does not offer employment to the executive on terms comparable to his then existing terms of employment (as determined by the board of directors) or (B) terminates the executive s employment without cause (as such term is defined in the letter agreement, option agreement or 2005 Plan, as applicable) within one year after the Transfer of Control, then the entire unexercisable portion of the outstanding option that would become exercisable during the twelve months following the occurrence of either of the events set forth in clauses (A) or (B) above, shall become immediately exercisable.

2005 Equity Incentive Plan

On July 13, 2005, the board of directors adopted the Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan. As of September 30, 2013, we have outstanding options to purchase 3,189,660 shares of our common stock at exercise prices ranging from $0.005 to $3.15 (with a weighted average exercise price of $0.21634). Total shares of 3,586,227 of our common stock are reserved for issuance, of which 68,492 shares are available for grant. Following this offering, no additional awards will be made under the 2005 Plan, and any subsequent awards will be made under our new 2013 Omnibus Incentive Plan, as described below. All outstanding awards in respect of the 2005 Plan will continue to be governed by their existing terms.

The 2005 Plan is administered by the board of directors or by a duly appointed committee of the board of directors (in either case, referred to hereinafter as the board of directors). The board of directors has the authority to make final and binding determinations with respect to all questions of interpretation of the plan and any awards granted under the plan.

The board of directors may grant options to purchase shares of our authorized but unissued common stock, which options may be either incentive stock options as defined in Section 422 of the Code (an Incentive Stock Option) or nonqualified stock options. The board of directors, in its sole discretion, shall determine:

(i) to whom options are granted;

(ii) the number of shares of stock into which the option is exercisable;

(iii) whether the option is to be treated as Incentive Stock Option or as a nonqualified stock option;

(iv) the exercise price for each option;

(v) the schedule upon which an option becomes exercisable; and

(vi) all other terms and conditions with respect to an option.

In the event of a Transfer of Control (as defined in the plan), each outstanding option shall be assumed or substituted by the successor corporation. Any outstanding option which is not assumed or substituted by the successor corporation shall become fully vested and exercisable. For purposes of this paragraph, an option shall be considered assumed if, following the Transfer of Control, the holder of such option receives, in respect of each option outstanding prior to the Transfer of Control, the per share transaction consideration received by holders of common stock in connection with the Transfer of Control. Upon the occurrence of the Transfer of Control, each outstanding option, to the extent not exercised prior to or concurrently with the Transfer of Control, shall terminate as of the effective time of the Transfer of Control (unless assumed or substituted by the successor corporation).

Notwithstanding the foregoing, if the successor corporation (A) does not offer employment to the option holder on terms comparable to his or her then existing terms of employment with the Company (as determined in the sole discretion of the board of directors); or (B) terminates the option holder s employment without Cause (as defined in the plan or applicable agreement) within one year after the Transfer of Control, then that unexercisable portion of an outstanding option that would become exercisable during the next twelve months following the occurrence of

either of the events set forth in clauses (A) or (B) above, shall become immediately exercisable.

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The board of directors shall make appropriate adjustments in the number and class of shares of the stock subject to the plan and to any outstanding options and in the option price of any outstanding options in the event of a stock dividend, stock split, reverse stock split, combination, reclassification or similar change in the capital structure of the Company.

The board of directors may amend, suspend or terminate the Plan or any portion thereof at any time. The board of directors may also amend, modify or terminate any outstanding option, provided however, that the board of directors shall not be authorized to make any amendment which would materially adversely affect the rights of the option holder without his or her consent.

2013 Omnibus Incentive Plan

On September 12, 2013, the board of directors adopted the Aerie Pharmaceuticals, Inc. Omnibus Incentive Plan (the 2013 Equity Plan) under which equity awards may be made in respect of 3,229,068 shares of common stock of the Company (Shares). Under the 2013 Equity Plan, awards may be granted in the form of options, restricted stock, restricted stock units, stock appreciation rights, dividend equivalent rights and performance-based awards (including performance units, performance share units and performance-based restricted stock).

Administration. The 2013 Equity Plan will be administered by a committee appointed by the board of directors (the Committee). The Committee shall consist of at least two directors of the board and may consist of the entire board of directors. The Committee will generally consist of at least two directors considered to be non-employee directors for purposes of Section 16 of the Exchange Act, and to the extent that an award is intended to qualify as performance based compensation within the meaning of Section 162(m) of the Code, the Committee will consist of at least two directors of the board, each of whom shall be an outside director as defined within the meaning of Section 162(m) of the Code.

Plan Term. The 2013 Equity Plan became effective on September 12, 2013, subject to stockholder approval, and will terminate on the tenth (10th) anniversary thereof, unless earlier terminated by the board.

Eligibility. Under the 2013 Equity Plan, the Eligible Individuals includes officers, employees, consultants and non-employee directors providing services to the Company and its subsidiaries and affiliates. The Committee will determine which Eligible Individuals will receive grants of stock options or other awards.

Incentives Available. Under the 2013 Equity Plan, the Committee may grant any of the following types of awards to an Eligible Individual: incentive stock options (ISOs) and nonqualified stock options (Nonqualified Stock Options, and together with ISOs, Options); stock appreciation rights (SARs); restricted stock grants (Restricted Stock Grants); restricted stock units (RSUs); Performance Awards; Dividend Equivalent Rights; and Share Awards, as defined below, (each type of grant, considered an Award).

Shares Available. Subject to any adjustment as provided in the 2013 Equity Plan, the maximum number of Shares that may be issued pursuant to Awards granted under the Plan shall not exceed 3,229,068, no more than 3,229,068 of which may be issued upon the exercise of ISOs. With respect to Awards granted following the last day of the Transition Period (or, if later, the date the 2013 Equity Plan is approved by the Company s stockholders for purposes of Section 162(m)), (a) the aggregate number of Shares that may be the subject of Options, SARs, Performance-Based Restricted Stock and Performance Share Units, as defined below, granted to an Eligible Individual in any calendar year may not exceed 1,200,000 and (b) the maximum dollar amount of cash or the fair market value of Shares that any individual may receive in any calendar year in respect of Performance Units may not exceed $5,000,000.

Stock Options. The Committee may grant Options (which may be ISOs or Nonqualified Stock Options) to Eligible Individuals. An ISO is an Option intended to qualify for tax treatment applicable to ISOs under Section 422 of the Code. An ISO may only be granted to Eligible Individuals that are employees of the Company

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or any of its subsidiaries. A Nonqualified Stock Option is an Option that is not subject to statutory requirements and limitations required for certain tax advantages allowed under Section 422 of the Code.

Vesting and Exercise Periods. Each Option granted under the 2013 Equity Plan may be subject to certain vesting requirements and will become exercisable in accordance with the specific terms and conditions of the Option, as determined by the Committee at the time of grant and set forth in an award agreement. The term of an Option generally may not exceed ten years from the date it is granted (five years in the case of an ISO granted to a ten-percent stockholder); provided, however, that upon the death of a participant prior to the expiration of the Option, the Option may be exercised for up to one year following the date of the participant s death, even if such period extends beyond ten years. Each Option, to the extent it becomes exercisable, may be exercised at any time in whole or in part until its expiration or termination, unless otherwise provided in applicable award agreement.

Exercise Price. The purchase price per Share with respect to any Option granted under the 2013 Equity Plan may be not less than 100 percent (100%) of the fair market value of a share of Common Stock on the date the Option is granted (110 percent (110%) in the case of an incentive stock option granted to a ten-percent stockholder).

Limits on Incentive Stock Options. In order to comply with the requirements for ISOs in the Code, no person may receive a grant of an ISO for stock that would have an aggregate fair market value in excess of $100,000, determined when the ISO is granted, that would be exercisable for the first time during any calendar year. If any grant of an ISO is made in excess of such limit, the portion that is over the $100,000 limit would be a Nonqualified Stock Option.

Stock Appreciation Rights. The Committee may grant SARs to Eligible Individuals on terms and conditions determined by the Committee at the time of grant and set forth in an award agreement. An SAR may be granted (a) at any time if unrelated to an Option or (b) if related to an Option, either at the time of grant or at any time thereafter during the term of the Option.

Amount Payable. An SAR is a right granted to a participant to receive an amount equal to the excess of the fair market value of a Share on the last business day preceding the date of exercise of such SAR over the fair market value of a Share on the date the SAR was granted. A SAR may be settled or paid in cash, Shares, or a combination of each, in accordance with its terms.

Duration. Each SAR will be exercisable or be forfeited or expire on such terms as the Committee determines. Except in limited circumstances, an SAR shall have a term of no greater than ten years; provided, however, that upon the death of a participant prior to the expiration of the SAR, the SAR may be exercised for up to one year following the date of the participant s death, even if such period extends beyond ten years.

Prohibition on Repricings. The Committee will have no authority to make any adjustment or amendment (other than in connection with certain changes in capitalization or certain corporate transactions in accordance with the terms of the 2013 Equity Plan, as generally described below) that reduces, or would have the effect of reducing, the exercise price of an Option or SAR previously granted under the 2013 Equity Plan, unless the Company s stockholders approve such adjustment or amendment.

Dividend Equivalent Rights. The Committee may grant dividend equivalent rights (Dividend Equivalent Rights), either in tandem with an Award or as a separate Award, to Eligible Individuals on terms and conditions determined by the Committee at the time of grant and set forth in an award agreement. A Dividend Equivalent Right is a right to receive cash or Shares based on the value of dividends that are paid with respect to the Shares. Amounts payable in respect of Dividend Equivalent Rights may be payable currently or, if applicable, deferred until the lapsing of restrictions on such dividend equivalent rights or until the vesting, exercise, payment, settlement or other lapse of restrictions on the Award to which the Dividend Equivalent Rights relate, subject to compliance with Section 409A of the Code. Dividend Equivalent Rights may be settled in cash or shares of Common Stock or a combination thereof, in a single installment or multiple installments, as determined by the Committee.

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Restricted Stock; Restricted Stock Units. The Committee may grant either Shares (Restricted Stock) or phantom Shares (RSUs), in each case subject to certain vesting requirements, on terms and conditions determined by the Committee at the time of grant and set forth in an award agreement.

Restricted Stock. Unless the Committee determines otherwise, upon the issuance of shares of Restricted Stock, the participant shall have all of the rights of a shareholder with respect to such Shares, including the right to vote the Shares and to receive all dividends or other distributions made with respect to the Shares. The Committee may determine that the payment to the participant of dividends, or a specified portion thereof, declared or paid on such Shares shall be deferred until the lapsing of the restrictions imposed upon such Shares and held by the Company for the account of the participant until such time. Payment of deferred dividends in respect of shares of Restricted Stock shall be made upon the lapsing of restrictions imposed on the shares of Restricted Stock in respect of which the deferred dividends were paid, and any dividends deferred in respect of any shares of Restricted Stock shall be forfeited upon the forfeiture of such shares of Restricted Stock.

Restricted Stock Units. Each RSU shall represent the right of the participant to receive a payment upon vesting of the RSU, or on any later date specified by the Committee, of an amount equal to the fair market value of a Share as of the date the RSU becomes vested, or such later date as determined by the Committee at the time the RSU is granted (and which will be set forth in the applicable grant agreement). An RSU may be settled or paid in cash, Shares, or a combination of each, as determined by the Committee.

Performance Awards. Performance awards (Performance Awards) (including performance units (Performance Units), performance share units (Performance Share Units) and performance-based restricted stock (Performance-Based Restricted Stock)) may be granted to Eligible Individuals on terms and conditions determined by the Committee and set forth in an award agreement.

Performance Units and Performance Share Units. Performance Units shall be denominated in a specified dollar amount and, contingent upon the attainment of specified performance objectives within a performance cycle and such other vesting conditions as may be determined by the Committee (including without limitation, a continued employment requirement following the end of the applicable performance period), represent the right to receive payment of the specified dollar amount or a percentage of the specified dollar amount depending on the level of performance objective attained; provided, however, that the Committee may at the time a Performance Unit is granted specify a maximum amount payable in respect of a vested Performance Unit. Performance Share Units shall be denominated in Shares and, contingent upon the attainment of specified performance objectives within a performance cycle and such other vesting conditions as may be determined by the Committee (including without limitation, a continued employment requirement following the end of the applicable performance period), represent the right to receive payment of the fair market value of a Share on the date the Performance Share Unit was granted, the date the Performance Share Unit became vested or any other date specified by the Committee or a percentage of such amount depending on the level of performance objective attained; provided, however, that the Committee may at the time a Performance Share Unit is granted specify a maximum amount payable in respect of a vested Performance Share Unit. The award agreement for each Performance Unit and Performance Share Unit shall specify the number of Performance Units or Performance Share Units to which it relates, the performance objectives and other conditions which must be satisfied in order for the Performance Unit or Performance Share Unit to vest and the performance cycle within which such performance objectives must be satisfied (which will not be less than one (1) year) and the circumstances under which the award will be forfeited.

Performance-Based Restricted Stock. Performance-Based Restricted Stock shall consist of an award of shares of Restricted Stock, issued in the participant s name and subject to appropriate restrictions and transfer limitations. Unless the Committee determines otherwise and as set forth in the applicable award agreement, upon issuance of shares of Performance-Based Restricted Stock, the participant shall have all of the rights of a shareholder with respect to such Shares, including the right to vote the Shares and to receive all dividends or other distributions paid or made with respect to Shares. The award agreement for each award of Performance-Based Restricted Stock will specify the number of shares of Performance-Based Restricted Stock to which it relates, the performance objectives and other conditions that must be satisfied in order for the Performance-Based Restricted

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Stock to vest, the performance cycle within which the performance objectives must be satisfied (which will not be less than one (1) year) and the circumstances under which the award will be forfeited. At the time the Award of Performance-Based Restricted Stock is granted, the Committee may determine that the payment to the participant of dividends, or a specified portion thereof, declared or paid on Shares represented by such Award which have been issued by the Company to the participant shall be deferred until the lapsing of the restrictions imposed upon such Performance-Based Restricted Stock and held by the Company for the account of the participant until such time. Payment of deferred dividends in respect of Shares of Performance-Based Restricted Stock shall be made upon the lapsing of restrictions imposed on the Performance-Based Restricted Stock in respect of which the deferred dividends were paid, and any dividends deferred in respect of any Performance-Based Restricted Stock shall be forfeited upon the forfeiture of such Performance-Based Restricted Stock.

Share Awards. The Committee may grant an award of Shares (Share Awards) to an Eligible Individual on such terms and conditions as the Committee may determine at the time of grant. A Share Award may be made as additional compensation for services rendered by the Eligible Individual or may be in lieu of cash or other compensation to which the Eligible Individual is entitled from the Company.

Adjustments. In the event of a Change in Capitalization (as defined in the 2013 Equity Plan) the Committee shall conclusively determine the appropriate adjustments, if any, to (a) the maximum number and class of shares or other stock or securities with respect to which Awards may be granted under the 2013 Equity Plan, (b) the maximum number and class of shares or other stock or securities that may be issued upon exercise of ISOs, (c) the number and kind of Shares or other securities covered by any or all outstanding Awards that have been granted under the 2013 Equity Plan, (d) the option price of outstanding Options and the base price of outstanding SARs, and (e) the Performance Objectives applicable to outstanding Performance Awards.

Effect of Change in Control or Certain Other Transactions. Generally, the award agreement evidencing each Award will provide any specific terms applicable to that award in the event of a Change in Control of the Company (as defined below). Unless otherwise provided in an award agreement, in connection with a merger, consolidation, reorganization, recapitalization or other similar change in the capital stock of the Company, or a liquidation or dissolution of the Company or a change in control (each a Corporate Transaction), Awards shall either: (a) continue following such Corporate Transaction, which may include, in the discretion of the Committee or the parties to the Corporate Transaction, the assumption, continuation or substitution of the Awards, in each case with appropriate adjustments to the number, kind of shares, and exercise prices of the awards; or (b) terminate.

For purposes of the 2013 Equity Plan, Change in Control generally means the occurrence of any of the following events with respect to the Company: (a) any person (other than directly from the Company) acquires securities of the Company representing fifty percent or more of the combined voting power of the Company s then outstanding voting securities; (b) a majority of the members of the board of directors is replaced by directors whose appointment or election is not endorsed by a majority of the members of the board of directors serving immediately prior to such appointment or election; (c) any merger, consolidation or reorganization, unless stockholders immediately before such merger, consolidation or reorganization continue to own at least a majority of the combined voting power of such surviving entity following the transaction; (d) a complete liquidation or dissolution or (e) sale or disposition of all or substantially all of the assets. A non-control transaction generally includes any transaction in which (a) stockholders immediately before such transaction continue to own at least a majority of the combined voting power of such resulting entity following the transaction; (b) a majority of the members of the board of directors immediately before such transaction continue to constitute at least a majority of the board of the surviving entity following such transaction or (c) with certain exceptions, no person other than any person who had beneficial ownership of more than fifty percent of the combined voting power of the Company s then outstanding voting securities immediately prior to such transaction has beneficial ownership of more than fifty percent of the combined voting power of the surviving entity s outstanding voting securities immediately after such transaction.

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Options and SARs. If Options or SARs are to terminate in the event of a corporate transaction, the holders of vested Options or SARs must be provided either (a) fifteen days to exercise their Options or SARs or (b) payment (in cash or other consideration) in respect of each Share covered by the Option of SAR being cancelled in an amount equal to the excess of the per share price to be paid to stockholders in the Corporate Transaction over the price of the Option or the SAR. If the per share price to be paid to stockholders in the Corporate Transaction is less than the exercise price of the Option or SAR, the Option or SAR may be terminated without payment of any kind. The holders of unvested Options or SARs may also receive payment, at the discretion of the Committee, in the same manner as described above for vested Options and SARs. The Committee may also accelerate the vesting on any unvested Option or SAR and provide holders of such Options or SARS a reasonable opportunity to exercise the award.

Other Awards. If Awards other than Options and SARs are to terminate in connection with a corporate transaction, the holders of vested Awards will be provided, and holders of unvested Awards may be provided, at the discretion of the Committee, payment (in cash or other consideration upon or immediately following the Corporate Transaction, or, to the extent permitted by Section 409A of the Code, on a deferred basis) in respect of each Share covered by the Award being cancelled in an amount equal to the per share price to be paid to stockholders in the Corporate Transaction, where the value of any non-cash consideration will be determined by the Committee in good faith.

The Committee may, in its sole discretion, provide for different treatment for different Awards or Awards held by different parties, and where alternative treatment is available for a participant s Awards, may allow the participant to choose which treatment will apply to his or her Awards.

Transferability. The 2013 Equity Plan generally restricts the transfer of any Awards, except (a) transfers by will or the laws of descent and distribution or (b) to a beneficiary designated by the participant, to whom any benefit under the 2013 Equity Plan is to be paid or who may exercise any rights of the participant in the event of the participant s death before he or she receives any or all of such benefit or exercises an award.

Amendment or Termination of the 2013 Equity Plan. The 2013 Equity Plan may be amended or terminated by the board without shareholder approval unless shareholder approval of the amendment or termination is required under applicable law, regulation or exchange requirement. No amendment may impair or adversely impact any Awards that had been granted under the 2013 Equity Plan prior to the amendment without the impacted participant s consent. The 2013 Equity Plan will terminate on the tenth anniversary of its effective date; however, when the 2013 Equity Plan terminates, any applicable terms will remain in effect for administration of any Awards outstanding at the time of the 2013 Equity Plan s termination.

2013 Employee Stock Purchase Plan

On September 12, 2013, the board of directors adopted the Aerie Pharmaceuticals, Inc. Employee Stock Purchase Plan (the ESPP) which is intended to qualify as an employee stock purchase plan under Section 423 or any successor provision of the Code and the related Treasury Regulations thereunder. The ESPP is intended to provide a method whereby eligible employees of the Company and its designated subsidiaries will have an opportunity to purchase Shares through accumulated payroll deductions and contributions (for purposes of the section below, such opportunity shall be defined as an option). A maximum of 645,814 Shares may be issued under the ESPP, which Shares may be authorized but unissued Shares or treasury shares.

Administration. The ESPP shall be administered by the compensation committee of the board of directors (the compensation committee). All decision and determinations by the compensation committee in the exercise of its powers hereunder shall be final, binding and conclusive upon all parties. The compensation committee may establish any policies or procedures that in its discretion are necessary or appropriate for the operation and administration of the ESPP and may adopt rules for the administration of the ESPP.

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Qualification. No eligible employee shall be granted an option to purchase Shares under the ESPP which permits such eligible employee s rights to purchase stock under all employee stock purchase plans of the Company or any subsidiary subject to Section 423 of the Code to accrue at a rate which exceeds $25,000 of fair market value of the common stock (determined at the time such option is granted) for each calendar year in which such option is outstanding at any time, in accordance with Section 423(b)(8) of the Code and the regulations thereunder.

Eligibility. An eligible employee under the ESPP is an employee of the Company or a designated subsidiary (i) who does not, immediately after the option is granted, own stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or a subsidiary (as determined under Section 423(b)(3) of the Code); (ii) whose customary employment is for more than twenty (20) hours per week; and (iii) whose customary employment is for more than five (5) months in any calendar year. Each employee who is an eligible employee on the first business day of each offering period (the offering date) shall be eligible to participate in the offering period commencing on such offering date.

Offering Period and Purchase Date. The offering period is each period of approximately six (6) months commencing on such dates as may be determined by the compensation committee from time to time. The purchase date is the last business day of each offering period, but in no event later than the date that is twenty-seven months from the date the option is granted. The compensation committee shall have the power to change the duration of offering periods, the offering dates and the purchase dates without stockholder approval if such change is announced prior to the commencement of the relevant offering period. Persons who are not eligible employees on an offering date shall not be eligible to participate in the ESPP with respect to that offering period.

Offering Price. On each offering date, each participant shall be deemed to have been granted an option to purchase a maximum number of Shares equal to (a) total of all payroll deductions from a participant s compensation during an offering period and all personal contributions (the contribution) divided by (b) the applicable offering price which shall be equal to the lesser of (x) eighty-five percent (85%) of the fair market value of the common stock on the offering date of such offering period; or (y) eighty-five percent (85%) of the fair market value of the common stock on the purchase date of such offering period. If the compensation committee desires to establish an offering price or a formula for setting the offering price for an offering period that is different than the offering price determined above, it shall do so in advance of the applicable offering period; provided, that, the offering price shall in no event be less than the offering price determined above. Any such offering price or formula for setting the offering price may, if the committee so determines, remain in effect for subsequent offering periods until modified by the compensation committee.

Payroll Deductions and Contributions. An eligible employee may become a participant by completing an authorization for payroll deductions or personal contributions on the form provided by the Company and filing the completed form with the compensation committee on or before the filing date set therefor by the compensation committee, which date shall be prior to the offering date for the next following offering period. Each participant shall be deemed to continue participation in the ESPP until the earlier of (a) the termination of the ESPP and (b) such eligible employee s termination of participation in the ESPP. A participant may reduce or increase future payroll deductions (in accordance with Section 423(b)(8) of the Code and the Treasury Regulations thereunder) pursuant to the form provided by the Company.

Automatic Exercise. Unless a participant withdraws from the ESPP in accordance with its terms or otherwise becomes ineligible to participate in the ESPP, each participant s option for the purchase of Shares with contributions made during any offering period shall be exercised automatically on the applicable purchase date, and the maximum number of full Shares subject to the option shall be purchased for the participant at the applicable offering price with the accumulated contributions in such participant s account.

Withholding. In connection with the exercise of an option (in whole or in part) or at the time of disposition of some or all of the common stock issued under the ESPP, a participant shall make adequate provision for any federal, state, local or other tax withholding obligations, if any, which arise upon such exercise or disposition. At

any time, the Company may, but shall not be obligated to, withhold from the participant s compensation an amount necessary for the Company to satisfy any applicable withholding obligations, including any withholding required to make available to the Company any tax deductions or benefits attributable to the early disposition of the common stock by the employee. Furthermore, the Company reserves the right to satisfy its applicable withholding obligations by any other means, as determined by the compensation committee.

Delivery of Shares. As promptly as practicable after each purchase date on which a purchase of Shares occurs, the Company shall arrange the delivery to each participant of the Shares purchased upon exercise of such participant s option.

Transfer Restrictions. Neither the option or rights with regard to the exercise of an option under the ESPP may be assigned, transferred, pledged or otherwise disposed of in any way by the participant other than by will or the laws of descent and distribution. During a participant s lifetime, options held by a participant shall be exercisable only by such participant.

Termination of Employment. Upon a participant s ceasing to be an eligible employee for any reason, including as a result of a termination of employment (including retirement or death), such Participant shall be deemed to no longer be a participant under the plan, and the contributions credited to such participant s account shall be refunded to him or her as soon as reasonably practicable, or, in the case of his or her death, to the participant s designated beneficiary under the ESPP.

Use of Funds. All contributions received or held by the Company under the ESPP may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such contributions.

Adjustments. In the event of an Adjustment Event (as defined in the ESPP), the compensation committee shall make such adjustments, if any, as it determines are equitable and appropriate to (a) the maximum number and class of Shares or other stock or securities with respect to which options may be granted under the ESPP, (b) the maximum number and class of Shares or other stock or securities that may be issued upon exercise of options, (c) the maximum number and class of Shares or other stock or securities with respect to which options may be granted to any eligible employee in any calendar year and (d) the number and class of Shares or other stock or securities which are subject to outstanding options granted under the ESPP and the offering price therefor, if applicable. Any such adjustment in the Shares or other stock or securities subject to outstanding options (including any adjustments in the offering price) shall be made in such manner as not to constitute a modification as defined by Section 424(h)(3) of the Code and only to the extent permitted by Sections 423 and 424 of the Code. If, by reason of any such adjustment, a participant shall be entitled to, or a participant shall be entitled to exercise an option with respect to, new, additional or different shares of stock or securities of the Company or any other corporation, such new, additional or different shares shall thereupon be subject to all of the conditions and restrictions that were applicable to the Shares subject to the option prior to such adjustment.

In the event of a Corporate Transaction (as defined in the ESPP), the compensation committee shall have the option, in its discretion, to (a) accelerate the purchase date with respect to the offering period then in progress to the last payroll date immediately preceding the Corporate Transaction or proposed dissolution or liquidation, and promptly refund (without interest) any cash balance remaining in a participant s account to such participant or (b) terminate the offering period then in progress immediately prior to the consummation of such Corporate Transaction or proposed dissolution or liquidation and refund (without interest) the entire cash balance of a participant s account to such participant as soon as reasonably practicable.

Amendment or Termination of the ESPP. The board of directors shall have complete power and authority to terminate or amend the ESPP; provided, however, that the board of directors shall not, without the approval of the stockholders of the Company, (a) increase the aggregate number of Shares which may be issued under the ESPP (except in connection with an Adjustment Event or Corporate Transaction) or (b) change the class of employees eligible to receive options under the ESPP; and provided, further, however, that no termination,

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modification or amendment of the ESPP may, without the consent of a participant then having an option under the ESPP to purchase Shares, adversely affect the rights of such participant under such option, except that the foregoing shall not prohibit the Company from terminating the ESPP at any time (including during an offering period) and applying the amounts theretofore withheld from a participant to the purchase of Shares as if the termination date of the plan were a purchase date and promptly refunding (without interest) any cash balance remaining in such participant s account to the participant.

Director Compensation for Fiscal Year 2012

The following table sets forth the compensation paid to our directors for the year ended December 31, 2012.

NAME	FEES EARNED OR PAID IN CASH	OPTION AWARDS [1] [2]	TOTAL
Janet L. Conway	$ 4,000		$ 4,000
Geoffrey Duyk			
David Epstein			
David W. Gryska	$ 30,000	$ 26,210[3]	$ 56,210
Dennis Henner			
David Mack			
Anand Mehra			

(1) The amounts included in the Option Awards column represent the grant date fair value computed in accordance with FASB ASC Topic 718. The valuation assumptions used in determining such amounts are described in Note 11 to our financial statements included elsewhere in this prospectus.

(2) As of December 31, 2012, Dr. Conway, Dr. Epstein and Mr. Gryska held outstanding options to purchase 17,435 shares, 49,600 shares and 20,000 shares, respectively.

(3) This option was granted on March 29, 2012 and is scheduled to vest ratably over three years.

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CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following is a description of transactions since January 1, 2010 to which we were a party in which the amount involved exceeded or will exceed $120,000, and in which any of our executive officers, directors or holders of more than 5% of any class of our voting securities, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or amounts that would be paid or received, as applicable, in arm s-length transactions with unrelated third parties.

Please see Description of Capital Stock Warrants for a more detailed description of our various series of outstanding warrants described below.

Participation in This Offering

Our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of approximately $10 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may determine to purchase fewer shares than they have indicated an interest in purchasing or not to purchase any shares in this offering. It is also possible that these stockholders could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these stockholders than the stockholders have indicated an interest in purchasing or not to sell any shares to these stockholders. Any shares purchased by these potential investors will be subject to lock-up restrictions described under Shares Eligible for Future Sale.

In addition, our directors and executive officers have indicated to us that they currently intend to purchase common stock in the directed share program in this offering at the initial public offering price. These prospective purchasers have the right to purchase these shares, but are under no obligation to purchase any shares in this offering and their interest in purchasing shares in this offering is not a commitment to do so. The underwriters will receive the same discount from shares of our common stock purchased by such directors and officers as they will from other shares of our common stock sold to the public in this offering. Any shares purchased by such directors and officers will be subject to lock-up restrictions described under Shares Eligible for Future Sales.

Convertible Note and Warrant Issuances

In 2010, we extended the maturity date of convertible notes previously issued in 2009 with an aggregate principal amount of $10.0 million (the 2009 Notes) to February 2013. The 2009 Notes accrued interest at a rate of 6% per annum. In connection with the issuance of the 2009 notes, we also issued warrants to purchase shares of our Series A-3 convertible preferred stock (the Series A-3 warrants). The Series A-3 warrants are exercisable at a price of $1.00 per share at any time during their ten year term, subject to adjustment. Upon completion of this offering, the Series A-3 warrants will automatically become exercisable for shares of our common stock at an exercise price of $5.00 per share. The Series A-3 warrants are currently outstanding and 150,000 of the Series A-3 warrants are expected to remain outstanding and exercisable for common stock following the completion of this offering.

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The aggregate principal amount of the 2009 Notes together with accrued interest was converted into 10,979,476 shares of Series A-3 Convertible Preferred Stock in February 2011 in connection with the issuance of our Series B Convertible Preferred Stock and none of the 2009 Notes remain outstanding. The following table summarizes the participation in the issuance of our 2009 Notes:

NAME	AGGREGATE PRINCIPAL AMOUNT OF 2009 NOTES	AMOUNT OF ACCRUED INTEREST ON 2009 NOTES	AGGREGATE SHARES OF SERIES A-3 CONVERTIBLE PREFERRED STOCK RECEIVED UPON CONVERSION OF 2009 NOTES	OUTSTANDING SERIES A-3 WARRANTS
ACP IV, L.P.	$ 5,000,000	$ 489,738	5,489,738	750,000
TPG Biotechnology Partners, L.P.	5,000,000	489,738	5,489,738	750,000
Total	$ 10,000,000	$ 979,476	10,979,476	1,500,000

In August 2010, we issued a new series of convertible promissory notes (the 2010 Notes) to existing investors identified in the table below for an aggregate principal amount of $5.25 million. The 2010 Notes accrued interest at a rate of 6% per annum. In connection with the issuance of the 2010 Notes, we also issued warrants to purchase shares of our Series A-4 convertible preferred stock (the Series A-4 warrants). The Series A-4 warrants are exercisable at a price of $1.00 per share at any time during their ten year term, subject to adjustment. Upon completion of this offering, the Series A-4 warrants will automatically become exercisable for shares of our common stock at an exercise price of $5.00 per share. The Series A-4 warrants are currently outstanding and are expected to remain outstanding and exercisable for common stock following the completion of this offering.

The aggregate principal amount of the 2010 Notes together with accrued interest thereon was converted to shares of our Series A-4 convertible preferred stock in February 2011 in connection with the issuance of our Series B Convertible Preferred Stock and none of the 2010 Notes remain outstanding. The following table summarizes the participation in the issuance of our 2010 Notes:

NAME	AGGREGATE PRINCIPAL AMOUNT OF 2010 NOTES	AMOUNT OF ACCRUED INTEREST ON 2010 NOTES	AGGREGATE SHARES OF SERIES A-4 CONVERTIBLE PREFERRED STOCK RECEIVED UPON CONVERSION OF 2010 NOTES	OUTSTANDING SERIES A-4 WARRANTS
Sofinnova Venture Partners VII, L.P.	$ 5,000,000	$ 129,041	4,662,765	750,000
Thomas J. van Haarlem	150,000	3,871	139,883	22,500
Casey C. Kopczynski	100,000	2,581	93,256	15,000
Total	$ 5,250,000	$ 135,493	4,895,904	787,500

In December 2012, we entered into a note and warrant purchase agreement with certain of our existing investors providing for the issuance from time to time of convertible notes up to a maximum of $15.0 million of aggregate principal amount. In August 2013, we amended the note and warrant purchase agreement allowing for the issuance of an additional $3.0 million of aggregate principal amount and extending the issuance period through November 30, 2013 as further described in Note 16 to our financial statements appearing elsewhere in this prospectus.

Concurrently with entering into the note and warrant purchase agreement in December 2012, we issued $3.0 million in aggregate principal amount of our outstanding notes to existing investors identified in the table below. In March 2013, May 2013, August 2013 and September 2013, we issued an additional $3.0 million, $4.5 million, $4.5 million and $3.0 million, respectively, in aggregate principal amount of our outstanding

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to these existing investors. Our outstanding notes accrue interest at a rate of 8% per annum. In connection with the issuances of the outstanding notes, we also issued warrants to purchase shares of our Series B convertible preferred stock (the Series B warrants). The Series B warrants are exercisable at a price of $0.01 per share at any time during their seven year term, subject to adjustment. Upon completion of this offering, the Series B warrants will automatically become exercisable for shares of our common stock at an exercise price of $0.05 per share.

We expect all outstanding notes and accrued interest thereon to be converted into 1,431,048 shares of our common stock in connection with this offering based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming, for illustrative purposes, that interest on the outstanding notes accrued through October 31, 2013. The Series B warrants are currently outstanding and 408,296 of the Series B warrants are expected to remain outstanding and exercisable for common stock following the completion of this offering. The following table summarizes the participation in the issuance of our outstanding notes and accrued interest thereon:

NAME	AGGREGATE PRINCIPAL AMOUNT OF 2012 NOTES	AMOUNT OF ACCRUED INTEREST AS OF SEPTEMBER 30, 2013	OUTSTANDING SERIES B WARRANTS
ACP IV, L.P.	$ 4,916,642	$ 137,585	1,117,415
TPG Biotech Reinvest AIV, L.P.	4,916,642	137,585	1,117,415
Clarus Lifesciences II, L.P.	4,065,869	113,778	924,060
Sofinnova Venture Partners VII, L.P.	3,423,202	95,794	778,000
Total	$ 17,322,355	$ 484,742	3,936,890

Preferred Stock Issuances

In February 2011, we issued and sold an aggregate 22,727,275 shares of our Series B convertible preferred stock in exchange for cash at a price of $1.10 per share. Simultaneously, we issued 10,979,476 shares and 4,895,905 hares of Series A-3 and A-4 convertible preferred stock, respectively, in connection with the conversion of the 2009 notes and the 2010 notes, as described above for no additional consideration. The following table summarizes the participation in this February 2011 transaction:

PARTICIPANTS	SHARES OF SERIES A-3 CONVERTIBLE PREFERRED STOCK [1]	SHARES OF SERIES A-4 CONVERTIBLE PREFERRED STOCK [2]	SHARES OF SERIES B CONVERTIBLE PREFERRED STOCK [3]	AGGREGATE PURCHASE PRICE OF SERIES B CONVERTIBLE PREFERRED STOCK
ACP IV, L.P.	5,489,738			
TPG Biotech Reinvest AIV, L.P.	5,489,738			
Clarus Lifesciences II, L.P.			13,636,364	$ 15,000,000
Sofinnova Venture Partners VII, L.P.		4,662,765	6,818,182	7,500,000
Thomas J. van Haarlem		139,883		
Casey C. Kopczynski		93,256		
Total	10,979,476	4,895,904	20,454,546	$ 22,500,000

(1) Upon completion of this offering, shares of our Series A-3 convertible preferred stock will automatically convert into shares of our common stock on a one-for-five basis.

(2) Upon completion of this offering, shares of our Series A-4 convertible preferred stock will automatically convert into shares of our common stock on a one-for-five basis.

(3) Upon completion of this offering, shares of our Series B convertible preferred stock will automatically convert into shares of our common stock on a one-for-five basis.

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Investor Rights Agreement

We are party to an amended and restated investor rights agreement, dated February 2011, as amended in December 2012, or the Investor Rights Agreement, with certain holders of our preferred stock. The Investor Rights Agreement provides that the holders of common stock issuable upon conversion of our convertible preferred stock have the right to demand that we file a registration statement or request that their shares of common stock be covered by a registration statement that we are otherwise filing. With respect to this offering, the registration rights have been validly waived. The registration rights will terminate upon the date three years following the closing of this offering. The Investor Rights Agreement also includes certain rights related to information and inspection, certain of our covenants and certain rights of first refusal, which will terminate upon the completion of this offering. The registration rights are described in more detail under Description of Capital Stock Registration Rights.

Voting Agreement

We have entered into an amended and restated voting agreement, dated February 2011 (the Voting Agreement), with certain holders of our common stock and certain holders of our convertible preferred stock. Pursuant to the Voting Agreement, holders of our preferred stock have agreed to vote such that: one director be a designee of TPG Biotech Reinvest AIV, L.P. or its affiliates, who is currently Dr. Geoffrey Duyk; one director be a designee of ACP IV, L.P. or its affiliates, who is currently Dr. David Mack; one director be a designee of Clarus Lifesciences II, L.P. or its affiliates, who is currently Dr. Dennis Henner; and one director be a designee of Sofinnova Venture Partners VII, L.P. or its affiliates, who is currently Dr. Anand Mehra. The provisions of the amended and restated voting agreement will terminate upon the completion of this offering.

Other Transactions

In October 2012, we formed Novaer, a wholly-owned entity, and contributed certain non-core, non-competitive intellectual property relating to certain ophthalmic implant technology, as well as an exclusive license for all of our intellectual property for non-ophthalmic indications, and $0.1 million in cash for initial funding. Our board of directors declared a dividend and distributed 100% of Novaer s equity interests to our stockholders and warrant holders of record as of September 6, 2012. Following this spin-off, Novaer is an independent company. We have no right to or ability to receive profits from the non-core intellectual property divested to Novaer. We also have no board seats or ongoing involvement with Novaer.

On September 6, 2013, we terminated our agreement to exclusively license to Novaer our intellectual property for non-ophthalmic indications. No consideration, or future obligation thereof, was exchanged in connection with this termination. As of September 6, 2013, we own all of the worldwide rights to our current product candidates for all indications, both ophthalmic and non-ophthalmic.

Policies and Procedures for Related Person Transactions

Prior to completion of this offering, we expect that our board of directors will adopt a policy providing that the audit committee will review and approve or ratify transactions in excess of $120,000 of value in which we participate and in which a director, executive officer or beneficial holder of more than 5% of any class of our voting securities has or will have a direct or indirect material interest. Under this policy, the board of directors is to obtain all information it believes to be relevant to a review and approval or ratification of these transactions. After consideration of the relevant information, the audit committee is to approve only those related party transactions that the audit committee believes are on their terms, taken as a whole, no less favorable to us than could be obtained in an arms-length transaction with an unrelated third party and that the audit committee determines are not inconsistent with the best interests of the Company. A related person is any person who is or was one of our executive officers, directors or director nominees or is a holder of more than 5% of our common stock, or their immediate family members or any entity owned or controlled by any of the foregoing persons. All of the transactions described above were entered into prior to the adoption of this policy and were approved by our board of directors.

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PRINCIPAL STOCKHOLDERS

The following table sets forth certain information known to us regarding beneficial ownership of our common stock as of September 30, 2013 by:

- our named executive officers;
- our directors;
- all of our executive officers and directors as a group; and
- each person, or group of affiliated persons, known by us to be the beneficial owner of more than 5% of our common stock.

We have based our calculation of beneficial ownership prior to the offering on 13,141,740 shares of common stock outstanding as of September 30, 2013, assuming the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,120,531 shares of common stock. We have based our calculation of beneficial ownership after the offering on 20,324,003 shares of our common stock outstanding immediately after the completion of this offering, which gives effect to (i) the issuance of 5,250,000 shares of common stock in this offering, (ii) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,120,531 shares of common stock, (iii) the conversion of the principal and accrued interest outstanding under our $18.0 million in aggregate principal amount of our outstanding notes into 1,431,048 shares of common stock immediately prior to the closing of this offering at a conversion price equal to the initial public offering price, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming, for illustrative purposes, the conversion occurred on October 31, 2013, and (iv) the net exercise immediately prior to the completion of this offering of warrants to purchase 2,506,075 shares of convertible preferred stock that will subsequently be automatically converted into 501,215 shares of common stock upon completion of this offering. The number of shares issued upon the conversion of the outstanding notes is based on the assumptions set forth above, and the actual number of shares issued upon such conversion will likely differ from the numbers appearing in this discussion and the following table and footnotes. See Prospectus Summary The Offering.

Information with respect to beneficial ownership has been furnished to us by each director, executive officer or stockholder listed in the table below, as the case may be. Beneficial ownership is determined in accordance with SEC rules. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include shares of common stock issuable upon the exercise of stock options or warrants that are immediately exercisable or exercisable within 60 days after September 30, 2013. Common stock subject to options or warrants that are currently exercisable or exercisable within 60 days of September 30, 2013 are deemed to be outstanding and beneficially owned by the person holding the options or warrants. These shares, however, are not deemed outstanding for the purposes of computing the percentage ownership of any other person.

Our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of approximately $10 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may determine to purchase fewer shares than they have indicated an interest in purchasing or not to purchase any shares in this offering. It is also possible that these stockholders could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these stockholders than the stockholders have indicated an interest in purchasing or not to sell any shares to these stockholders. The information set forth in the table below does not reflect any potential purchases of any shares in this offering by these stockholders or their affiliated entities .

In addition, the table below assumes that the underwriters do not exercise their option to purchase additional shares and does not reflect any shares of our common stock that our directors and executive officers may purchase in this offering through the directed share program described under Underwriting.

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Except as otherwise indicated, all of the shares reflected in the table are shares of common stock and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them. The information is not necessarily indicative of beneficial ownership for any other purpose. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Aerie Pharmaceuticals, Inc., 135 US Highway 206, Suite 15, Bedminster, New Jersey 07921.

	NUMBER OF SHARES BENEFICIALLY OWNED		PERCENTAGE OF SHARES BENEFICIALLY OWNED	
NAME OF BENEFICIAL OWNER	PRIOR TO THIS OFFERING	AFTER THIS OFFERING	PRIOR TO THIS OFFERING	AFTER THIS OFFERING
5% Stockholders				
Entities affiliated with ACP IV, L.P. [1]	3,671,432	4,062,318	27.17%	19.26%
Entities affiliated with Clarus Lifesciences II, L.P. [2]	2,912,085	3,235,333	21.85%	15.53%
Entities affiliated with Sofinnova Venture Partners VII, L.P. [3]	2,601,789	2,873,943	19.35%	13.75%
TPG Funds, L.P. [4]	3,671,432	4,062,318	27.17%	19.26%
Executive Officers and Directors				
Vicente Anido, Jr., PhD [5]	37,881	37,881	*	*
Thomas J. van Haarlem, MD [6]	733,908	733,908	5.39%	3.53%
Brian Levy, OD, MSc [7]	73,792	73,792	*	*
Richard J. Rubino [8]	117,757	117,757	*	*
Gerald D. Cagle, PhD [9]	2,333	2,333	*	*
Janet L. Conway, PhD [10]	17,927	17,927	*	*
Geoffrey Duyk, MD, PhD [11]	2,333	2,333	*	*
Murray A. Goldberg [12]	2,333	2,333	*	*
David W. Gryska [13]	14,781	14,781	*	*
Dennis Henner, PhD [14]	2,914,418	3,237,666	21.87%	15.54%
David Mack, PhD [15]	3,673,765	4,064,651	27.18%	19.27%
Anand Mehra, MD [16]	2,604,122	2,876,277	19.37%	13.76%
All executive officers and directors as a group (14 persons)	10,525,522	11,511,810	69.23%	52.60%

* Represents beneficial ownership of less than 1% of our outstanding common stock.

(1) Consists of (a) 373,484 shares of common stock issuable upon the exercise of warrants within 60 days as of September 30, 2013 (assuming the completion of this offering) and (b) 3,297,948 shares of common stock issuable upon conversion of our outstanding convertible preferred stock, all of which are held by ACP IV, L.P. In addition, the number of shares beneficially owned after the offering, assuming an initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, includes 390,886 shares of common stock issuable upon conversion of our outstanding notes. Alta Partners III, Inc. provides investment advisory services to several venture capital funds including ACP IV, L.P. Daniel Janney, David Mack, and Guy Nohra are directors of ACMP IV, LLC (which is the general partner of ACP IV, L.P). As directors of ACMP IV, LLC they may be deemed to share voting and investment powers over the shares held by the fund. The directors of ACMP IV, LLC disclaim beneficial ownership of all such shares held by ACP IV, L.P. except to the extent of their pecuniary interest therein. Alta Partners III, Inc. is a venture capital firm located at One Embarcadero Center, Suite 3700, San Francisco, CA 94111.

(2) Consists of (a) 184,812 shares of common stock issuable upon the exercise of warrants within 60 days as of September 30, 2013 (assuming the completion of this offering) and (b) 2,727,273 shares of common stock issuable upon conversion of our outstanding convertible preferred stock, all of which are held by Clarus Lifesciences II, L.P. In addition, the number of shares beneficially owned after the offering, assuming an initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, includes 323,248 shares of common stock issuable upon conversion of our outstanding notes. The voting and dispositive decisions with respect to the shares held by Clarus Lifesciences II, L.P. are made by the following managing members of the general partner, Clarus Ventures II, LLC, of the general

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partner of Clarus Lifesciences II, L.P.: Dennis Henner, Nicholas Galaktos, Robert Liptak, Nicholas Simon and Kurt Wheeler, each of whom disclaims beneficial ownership of such shares, except to the extent of his actual pecuniary interest therein. Dr. Henner is a member of our board of directors. The address for the funds affiliated with Clarus Lifesciences II, L.P., Clarus Ventures II, LLC and its managing members is c/o Clarus Lifesciences II, L.P., 101 Main Street, Suite 1210, Cambridge, MA 02142.

(3) Consists of (a) 305,600 shares of common stock issuable upon the exercise of warrants within 60 days as of September 30, 2013 (assuming the completion of this offering) and (b) 2,296,189 shares of common stock issuable upon conversion of our outstanding convertible preferred stock, all of which are held by Sofinnova Venture Partners VII, L.P. In addition, the number of shares beneficially owned after the offering, assuming an initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, includes 272,154 shares of common stock issuable upon conversion of our outstanding notes. The voting and dispositive decisions with respect to the shares held by Sofinnova Venture Partners VII, L.P. are made by the following managing members of its general partner, Sofinnova Management VII, L.L.C.: James Healy, Michael Powell and Eric Buatois, each of whom disclaims beneficial ownership of such shares, except to the extent of his actual pecuniary interest therein. The address for the funds affiliated with Sofinnova Venture Partners VII, L.P., Sofinnova Management VII, L.L.C. and its managing members is c/o Sofinnova Ventures, Inc., 2800 Sand Hill Road, Suite 150, Menlo Park, CA 94025.