AERIE PHARMACEUTICALS INC
Form 10-K
March 09, 2017
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016
or
o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from _____ to _____
Commission File Number: 001-36152

Aerie Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	20-3109565
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

2030 Main Street, Suite 1500
Irvine, California 92614
(949) 526-8700
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value per share	NASDAQ Global Market

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý No o
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes o No ý
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

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

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

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

Large accelerated filer o	Accelerated filer ý
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

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

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 30, 2016, based upon the closing price of $17.60 of the registrant's common stock as reported on the NASDAQ Global Market, was $437,044,000.

As of February 28, 2017, the registrant had 33,626,226 shares of common stock, $0.001 par value, issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement (the "Proxy Statement") for the 2017 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K. The Proxy Statement will be filed with the Securities and Exchange Commission (the "SEC") within 120 days of the registrant's fiscal year ended December 31, 2016.

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Unless otherwise indicated or the context requires, the terms “Aerie,” “Company,” “we,” “us” and “our” refer to Aerie Pharmaceuticals, Inc. and its subsidiaries.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). We may, in some cases, use terms such as “predicts,” “believes,” “potential,” “proposed,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “would,” “could,” “might,” “will,” “should,” “exploring,” “pursuing” or ot convey uncertainty of future events or outcomes to identify these forward-looking statements.

Forward-looking statements appear in a number of places throughout this report 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 and anticipated preclinical studies and clinical trials for our current and potential future product candidates, including statements regarding the timing of initiation and completion of the studies and trials;
- our expectations regarding the clinical effectiveness of our product candidates and results of our clinical trials;
- the timing of and our ability to obtain and maintain U.S. Food and Drug Administration (“FDA”) or other regulatory authority approval of, or other action with respect, to our product candidates, in the U.S., Canada, Europe, Japan and elsewhere;
- our expectations related to the use of proceeds from our financing activities;
- our estimates regarding anticipated operating expenses and capital requirements and our needs for additional financing;
- the commercial launch and potential future sales of our current or any other future product candidates;
- our commercialization, marketing, manufacturing and supply management capabilities and strategy;
- third-party payor coverage and reimbursement for our product candidates;
- 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 plans to explore possible uses of our existing proprietary compounds beyond glaucoma;
- our ability to protect our proprietary technology and enforce our intellectual property rights;
- our expectations regarding collaborations, licensing, acquisitions and strategic operations, including our ability to in-license or acquire additional ophthalmic products or product candidates; and
- our stated objective of building a major ophthalmic pharmaceutical company.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, industry change and other factors beyond our control, and depend on regulatory approvals and economic and other environmental 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 greater detail under the heading “Risk Factors” in Part I, Item 1A of this report and elsewhere in this report. 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 report, 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 report. In addition, even if our results of operations, financial condition and liquidity, and

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events in the industry in which we operate are consistent with the forward-looking statements contained in this report, they may not be predictive of results or developments in future periods.

Any forward-looking statements that we make in this report speak only as of the date of this report. 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 report.

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PART I

ITEM 1. 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 stated objective is to build a major ophthalmic pharmaceutical company and our strategy is to advance our product candidates, including Rhopressa™ (netarsudil ophthalmic solution) 0.02% ("Rhopressa™"), and Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% ("Roclatan™"), to regulatory approval and commercialize these products ourselves in North American markets. If approved, 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. Our strategy includes developing our business outside of North America, including obtaining regulatory approval on our own for our product candidates in Europe and Japan. For commercialization outside of North America, we expect to explore partnership opportunities through collaboration and licensing arrangements in Europe and Japan. We are also enhancing our longer-term commercial potential by identifying and advancing additional product candidates and drug delivery technologies, including through our internal discovery efforts, and potential research collaborations, in-licensing or acquisitions of additional ophthalmic products or technologies or product candidates that would complement our current product portfolio.

We completed our IPO in October 2013 which raised net proceeds of approximately $68.3 million. Since our IPO we have raised additional net proceeds of approximately $122.9 million through the sale and issuance of the 2014 Convertible Notes in September 2014, and approximately $217.6 million through the issuance and sale of common stock under our shelf registration statements on Form S-3 and former "at-the-market" sales agreements. Our senior leadership team has extensive experience in the ophthalmology market and has overseen the development and commercialization of several successful ophthalmic products at major pharmaceutical companies. If our products are approved and we are commercially successful, we believe Aerie could become a major ophthalmic pharmaceutical company.

Our two advanced stage product candidates are designed to lower intraocular pressure, or IOP, in patients with open-angle glaucoma and ocular hypertension. Both product candidates are taken once-daily and have shown in preclinical and clinical trials to be effective in lowering IOP, with novel mechanisms of action, or MOAs, and a positive safety profile. Glaucoma is one of the largest segments in the global ophthalmic market. In 2015, branded and generic glaucoma product sales exceeded $4.6 billion in the United States, Europe and Japan in aggregate, according to IMS. Prescription volume for glaucoma products in the United States alone was 34 million in 2015 and is expected to grow, driven in large part by the aging population.

Our lead product candidate, Rhopressa™, is a novel once-daily eye drop designed to lower IOP in patients with open-angle glaucoma and ocular hypertension. We resubmitted our new drug application ("NDA") with the U.S. Food and Drug Administration ("FDA") for Rhopressa™ on February 28, 2017 and we expect a standard 12-month FDA review from the date of resubmission. Our initial submission, announced in September 2016, was withdrawn as a result of a contract manufacturer of our drug product not being prepared for pre-approval inspection by the FDA. We are developing Rhopressa™ as the first of a new class of compounds that is designed to lower IOP in patients through novel MOAs. We believe that, if approved, Rhopressa™ will represent the first new MOAs for lowering IOP in patients with glaucoma in over 20 years. Based on preclinical studies and clinical data to date, we expect that Rhopressa™, if approved, will have the potential to compete with non-PGA (prostaglandin analog) products as a preferred adjunctive therapy to PGAs, due to its targeting of the diseased tissue known as the trabecular meshwork, or TM, its demonstrated IOP-lowering ability at consistent levels across tested baselines with once-daily dosing relative to currently marketed non-PGA products, its potential synergistic effect with PGA products, its once-daily dosing, and its lack of serious drug related adverse events. Adjunctive therapies currently represent approximately one-half of the entire glaucoma therapy market in the United States, according to IMS. In addition, if approved, we believe that Rhopressa™ may also become a preferred therapy where PGAs are contraindicated, for patients who do not respond to

PGAs, for patients who have lower IOPs but nevertheless present with glaucomatous damage to the optic nerve, which is commonly referred to as “low-tension” or “normal tension” glaucoma, as well as for patients who choose to avoid the cosmetic issues associated with PGA products.

Our second product candidate is once daily Roclatan™, a fixed-dose combination of Rhopressa™ and latanoprost, the most commonly prescribed drug for the treatment of patients with open-angle glaucoma. We currently have two Phase 3 registration trials for Roclatan™ in process. The first Phase 3 registration trial for Roclatan™, named “Mercury 1,” commenced in September 2015 and in September 2016, we announced that Mercury 1 achieved its primary efficacy endpoint of demonstrating superiority of Roclatan™ to each of its components.

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The second Phase 3 registration trial for Roclatan™, named "Mercury 2," commenced in March 2016. We expect to report the topline 90-day efficacy data for Mercury 2 in the second quarter of 2017. If both Mercury 1 and Mercury 2 are successful, we expect to submit an NDA for Roclatan™ in late 2017 or early 2018, which may be prior to obtaining approval for Rhopressa™.

We believe our clinical plans for both Rhopressa™ and Roclatan™ are already in place to satisfy European regulatory requirements. In addition to Rocket 1 and Rocket 2, our initial Phase 3 registration trials for Rhopressa™, our Rocket 4 trial is designed to provide adequate six month safety data for Rhopressa™ to meet European requirements. Based on our Rhopressa™ clinical plan, we expect to file for regulatory approval in Europe in the second half of 2018. Additionally, we plan to initiate a third Phase 3 registration trial for Roclatan™, named "Mercury 3," in Europe in mid-2017. Mercury 3 will be designed to compare Roclatan™ to Ganfort®, a fixed-dose combination product of bimatoprost and timolol marketed in Europe, which if successful, should improve our commercialization prospects in that region.

We believe, based on our preclinical studies and clinical trials to date, that Roclatan™ has the potential to provide a greater IOP-lowering effect than any currently approved glaucoma product. Therefore, we believe that Roclatan™, if approved, could compete with both PGA and non-PGA therapies and become the product of choice for patients requiring maximal IOP lowering, including those with higher IOPs and those who present with significant disease progression despite currently available therapies.

We continue to explore the longer-term impact of Rhopressa™ on the diseased TM. We have issued several research updates on preclinical results demonstrating that Rhopressa™ may have the potential for disease modification, including stopping and reversing fibrosis in the TM, and also increasing perfusion in the trabecular outflow pathway thus increasing both drainage and the delivery of nutrients to the diseased tissue, which we believe would represent a breakthrough in the treatment of glaucoma. We are also conducting ongoing research to evaluate injectable sustained release formulation technologies with the potential capability of delivering Rhopressa™ internally in the eye over several months for the treatment of glaucoma.

We are also evaluating possible uses of our existing proprietary portfolio of Rho Kinase inhibitors beyond glaucoma. Our owned preclinical small molecule, AR-13154, has demonstrated the potential for the treatment of wet age-related macular degeneration (AMD) by inhibiting Rho kinase and Protein kinase C and has shown lesion size decreases in a model of wet AMD at levels similar to current market-leading products, and even greater lesion size reduction in combination with the market-leading wet AMD anti-VEGF product. As we look forward to next steps for AR-13154, we expect to continue evaluating sustained delivery systems and establish long-term efficacy and pharmacokinetics in preclinical models.

We may enter into research collaboration arrangements, license, acquire or develop additional product candidates and technologies to broaden our presence in ophthalmology, and continually explore and discuss potential additional opportunities for new ophthalmic products, delivery alternatives and new therapeutic areas with potential partners. Our approach has consistently been to explore opportunities with minimal initial investment allowing us to more fully evaluate the probability of success prior to making a material commitment. We are currently focused on the evaluation of delivery technologies for the delivery of our owned molecules to the front and back of the eye over sustained periods. In 2016, we terminated our collaboration and license arrangements with GrayBug, Inc. for drug delivery technology and elected not to extend our collaboration agreement with Ramot at Tel Aviv University, Ltd. for a preclinical anti-beta amyloid molecule. Neither of these collaborations represented a material financial commitment by Aerie.

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

As indicated earlier, glaucoma is one of the largest segments in the global ophthalmic market. In 2015, branded and generic glaucoma product sales exceeded $4.6 billion in the United States, Europe and Japan in aggregate, according to IMS. Prescription volume for glaucoma products in the United States alone was 34 million in 2015 and is expected to grow, driven in large part by the aging population. The PGA and non-PGA market segments each represent approximately one-half of the prescription volume in the U.S. glaucoma market, as shown in the following chart, which is based on IMS data.

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According to the National Eye Institute, it is estimated that over 2.7 million people in the United States suffer from glaucoma, a number that is expected to reach 4.3 million by 2030. Furthermore, The Eye Diseases Prevalence Research Group has estimated that only half of the nation's glaucoma sufferers know that they have the disease. Glaucoma is a progressive and highly individualized disease, in which elevated levels of IOP are associated with damage to the optic nerve, resulting in irreversible vision loss and potentially blindness. Patients may suffer the adverse effects of glaucoma across a wide range of IOP levels. There are multiple factors that can contribute to an individual getting glaucoma, including, but not limited to, age, family history and ethnicity. Based on data from the Baltimore Eye Survey, approximately 75% of glaucoma patients have low to moderately elevated IOP at the time of diagnosis and approximately 60% of glaucoma patients have IOP of 21 mmHg, or millimeters of mercury, or below at the time of diagnosis. Additionally, in Japan, the Tajimi Study found that approximately 92% of glaucoma patients had IOP of 21 mmHg or below at the time of diagnosis. In clinical trials to date, Rhopressa™ has demonstrated the ability to provide relatively consistent IOP lowering across all tested baseline IOP levels, which we believe differentiates it from currently marketed drugs that have shown reduced efficacy at lower baseline IOPs.

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 TM, which accounts for approximately 80% of fluid drainage in a healthy eye, 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. In addition to eye fluid production and drainage through the TM and uveoscleral pathway, episcleral venous pressure, or EVP, makes a significant contribution to IOP. EVP represents the pressure of the blood in the episcleral veins of the eye where the eye fluid drains into the bloodstream. Historical studies have shown that EVP accounts for approximately half of IOP in normotensive subjects and approximately one-third of IOP in patients with pressures of 24 mmHg to 30 mmHg. When EVP is lowered, fluid is able to flow more freely from the eye. Drugs that lower IOP without lowering EVP are most effective at high IOPs, where EVP is believed to contribute less to IOP, and are less effective at lower IOPs, where EVP is seen to account for a larger portion of IOP.

Once glaucoma develops, it is a chronic condition that requires life-long treatment. The initial treatment for glaucoma patients is typically the use of prescription eye drops. 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 or contraindicated due to concerns about side effects, non-PGA products are used either as add-on therapy to the PGA or as an alternative monotherapy. It is estimated that up to 50% of glaucoma patients receiving PGA monotherapy require add-on therapy within two years of initial prescription of the drug, in order to maintain adequate control of IOP. It is believed that this rise in IOP after a patient is on an initial therapy results from the lack of effect of current therapies on the TM, and as a result damage to the TM progresses and the IOPs begin to rise.

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We believe there are significant unmet needs in the glaucoma market and that eye-care professionals are eager for new therapy choices. None of the commonly prescribed PGAs or non-PGAs target the TM, the diseased tissue responsible for elevated IOP levels in glaucoma patients and the eye's primary drain. Moreover, PGAs have side effects, contraindications and reduced efficacy in patients with low to moderately elevated IOPs relative to patients with higher IOPs. Non-PGAs are less efficacious than PGAs, have more serious and a greater number of side effects and contraindications, and require multiple daily doses. As a result, we believe there is a significant unmet need in both the PGA and non-PGA market segments, each of which represents approximately one-half of the U.S. and European glaucoma market based on prescription volumes, according to IMS. Despite the limitations of existing glaucoma drugs, Xalatan® (latanoprost), the best-selling PGA, together with Xalacom®, its fixed-dose combination with a beta blocker, which is not available in the United States, generated peak annual global revenues of approximately $1.7 billion prior to the introduction of their generic equivalents, and the most commonly prescribed non-PGA drugs each generated peak annual global revenues of over $400 million prior to the introduction of their generic equivalents.

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. Based on our preclinical studies and clinical data to date, we believe our product candidates represent a new class of drugs utilizing novel MOAs that are applied topically as once-daily eye drops. Based on preclinical and clinical studies, we believe Rhopressa™, if approved, may become the only once-daily product that specifically targets the TM. Rhopressa™ has demonstrated that it lowers IOP by (i) relaxing the contracted tissue of the TM to improve fluid outflow through the eye's primary drain, (ii) potentially decreasing fluid production in the eye and (iii) lowering EVP, an MOA that we believe further differentiates Rhopressa™ from currently marketed glaucoma products. Roclatan™, our fixed-dose combination product candidate, combines the MOAs of Rhopressa™ with the MOA of latanoprost, a PGA that increases fluid drainage through the uveoscleral pathway.

We believe Rhopressa™, if approved, may be prescribed by eye-care professionals as a preferred adjunctive therapy for patients taking PGAs, due to the MOAs of Rhopressa™ being complementary to the MOA of PGAs, and due to its IOP-lowering ability, more convenient dosing and better tolerability profile compared to currently marketed non-PGA adjunctive products.

In addition, we believe Roclatan™, if approved, will be the only glaucoma product that, based on our preclinical studies and clinical trials to date, covers the full spectrum of currently known IOP-lowering MOAs, giving it the potential to provide a greater IOP-lowering effect than any currently approved glaucoma product. Therefore, we believe that if Roclatan™ is approved, it could compete with both PGA and non-PGA therapies and become the product of choice for patients requiring maximal IOP lowering, including those with higher IOPs and those who present with significant disease progression despite currently available therapies.

We currently plan to commercialize our products ourselves in North America. We expect to explore partnership opportunities through collaboration and licensing arrangements in certain key markets outside of North America, including Europe and Japan.

Our Product Pipeline

Our primary product candidates, Rhopressa™ and Roclatan™, are once-daily eye drops. Based on our studies, Rhopressa™ has been shown to inhibit Rho kinase, or ROCK, and the norepinephrine transporter, or NET, which are both novel biochemical targets for lowering IOP. By inhibiting these targets, we believe Rhopressa™ reduces IOP through the following MOAs: (i) through ROCK inhibition, it increases fluid outflow through the TM, which accounts for approximately 80% of fluid drainage from the eye; (ii) also through ROCK inhibition, as demonstrated in a preclinical study, it reduces EVP, which represents the pressure of the blood in the episcleral veins of the eye where eye fluid drains into the bloodstream; and (iii) through NET inhibition, it may potentially reduce the production of eye fluid. Roclatan™, a single-drop fixed-dose combination of Rhopressa™ and latanoprost, lowers IOP through the same MOAs as Rhopressa™ and, through a fourth MOA, utilizing the ability of latanoprost to increase fluid outflow through the uveoscleral pathway, the eye's secondary drain. All of these observations represent findings from our body of preclinical and clinical work to date.

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 3,000 synthesized ROCK-selective and ROCK/NET inhibitors. We continue to 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.

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The following table summarizes each of our current 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
Rhopressa™	ROCK/NET inhibitor	Submitted NDA	Wholly-Owned
Roclatan™	ROCK/NET inhibitor and latanoprost, a PGA	Phase 3	Wholly-Owned

Rhopressa™

Rhopressa™ is the first of a new class of glaucoma drug products that was discovered by our scientists. It is a once-daily eye drop designed to reduce IOP in patients with glaucoma or ocular hypertension by specifically targeting the TM, the eye's primary fluid drain and the diseased tissue responsible for elevated IOP in glaucoma. Based on our preclinical studies and clinical trials to date, Rhopressa™ increases fluid outflow through the primary drain of the eye through ROCK inhibition while also reducing eye fluid production through NET inhibition. Preclinical studies have also demonstrated that Rhopressa™ lowers EVP, as further described below, which contributes approximately half of IOP in healthy subjects.

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. In addition, we believe ROCK inhibition may also be responsible for reduction of EVP. EVP represents the pressure of the blood in the episcleral veins of the eye, where eye fluid drains into the bloodstream. When EVP is lowered, the fluid is able to flow more freely from the eye.

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. Based on our clinical trials, we have observed that Rhopressa™ may also have a potential synergisitic effect with PGAs, whereby its IOP-lowering ability is increased when patients take a PGA as a first line therapy.

Rhopressa™ is expected to compete primarily in the adjunctive therapy market, which represents approximately one-half of the U.S. glaucoma prescription market, which totaled approximately 34 million prescriptions in 2015 according to IMS. Currently marketed adjunctive therapies are older generation products that are generally dosed two to three times a day, have MOAs focused on reducing fluid production, often have lower efficacy levels and have systemic side effects. Based on preclinical studies and clinical trials to date, we believe Rhopressa™, if approved, has the potential to be the future drug of choice as an adjunctive therapy to PGAs due to its potential synergistic effect with PGAs and will also be able to separately compete with PGAs due to its several positive differentiating attributes, including its effective IOP-lowering at relatively consistent levels across tested IOPs, the ability to lower EVP, targeting of the diseased tissue, convenient once-daily dosing and favorable tolerability profile.

In addition to the expected primary use of Rhopressa™ as an adjunctive therapy, we also believe Rhopressa™ may be prescribed by eye-care professionals in the following circumstances:

•As a preferred alternative therapy for patients who do not respond to PGAs.

•As a preferred initial therapy for patients with low or normal-tension glaucoma.

- As a preferred initial therapy where PGAs are contraindicated and for patients who choose to avoid the cosmetic issues associated with PGAs, including iris color change in light-eyed patients, discoloration of tissue surrounding the eyes and eyelid droopiness and sunken eyes caused by loss of orbital fat.

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Rhopressa™ NDA

We resubmitted our NDA for Rhopressa™ with the FDA on February 28, 2017 and expect a standard 12-month FDA review period from the date of resubmission. Our initial submission, announced in September 2016, was withdrawn as a result of a contract manufacturer of our drug product not being prepared for pre-approval inspection by the FDA. The NDA submission included our second Phase 3 registration trial for Rhopressa™, named "Rocket 2," as the pivotal clinical trial and our initial Phase 3 registration trial, named "Rocket 1," as supportive in nature. We included as supportive data the 90-day efficacy results of Rocket 4 and Mercury 1, each as further discussed below, with the NDA submission for Rhopressa™.

Rhopressa™ Phase 3 Trials

Our initial Phase 3 registration trials commenced in July 2014 and 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. We had total enrollment of over 1,900 patients in our Phase 3 registrations trials of Rhopressa™. Phase 3 efficacy results are determined after three months of treatments and safety results are analyzed following six or 12 months of treatment depending on the trial design.

In April 2015, we completed Rocket 1, which was designed to measure efficacy over three months. Baseline IOP was measured prior to treatment. Following treatment, IOP was measured at 8 a.m., 10 a.m. and 4 p.m. at the end of week two, week four and day 90. This trial included 202 patients in the Rhopressa™ once-daily (QD) arm and 209 patients in the timolol twice-daily (BID) arm. The baseline IOPs tested in the trial ranged from above 20 to below 27 mmHg. Rhopressa™ did not achieve its primary endpoint of demonstrating non-inferiority of IOP lowering for Rhopressa™ compared to timolol for patients with IOP below 27 mmHg, but did achieve its pre-specified secondary endpoint, demonstrating non-inferiority of IOP lowering for Rhopressa™ compared to timolol for patients with IOP below 24 mmHg.

For the Rhopressa™ population of patients with IOP below 27 mmHg in Rocket 1, the mean difference from timolol ranged from -0.4 to +1.3 mmHg at a 95% confidence interval. For the population of patients with IOP below 26 mmHg, Rhopressa™ met the criteria for non-inferiority to timolol at all 9 time points and was numerically superior to timolol at the majority of time points. For the pre-specified population of patients with IOP below 24 mmHg, Rhopressa™ met the criteria for non-inferiority to timolol at all 9 time points and was numerically superior to timolol at all 9 time points.

No drug-related serious adverse events, or SAEs, were identified during the Rocket 1 trial. The primary adverse event was conjunctival hyperemia, or eye redness, which was reported in approximately 35% of the Rhopressa™ patients, of which approximately 80% was reported as mild. Conjunctival hyperemia was measured by biomicroscopy at 8am at the end of week two, week four and day 90. Across the population of patients on Rhopressa™, approximately 5% to 13% of subjects reported conjunctival hemorrhage, or petechiae, erythema of the eyelid, blurry vision and or corneal verticillata.

Rocket 2 was designed to measure efficacy over three months and safety over 12 months. The Rocket 2 trial included Rhopressa™ dosed both once-daily, or QD, and twice daily, or BID. After evaluating Rocket 1 efficacy results, we obtained agreement from the FDA to change the IOP range for the primary endpoint for the Rocket 2 trial to baseline IOP below 25 mmHg. This modified clinical endpoint range was set to a level where Rocket 1 would have been successful.

In September 2015, the Rocket 2 trial achieved its primary efficacy endpoint of demonstrating non-inferiority of IOP lowering for Rhopressa™ QD and BID compared to timolol BID. The baseline IOPs tested in the trial ranged from baseline IOPs of above 20 mmHg to below 25 mmHg. The study included a Rhopressa™ BID arm at the request of the

FDA, because it is known that PGAs are less efficacious when dosed BID, and we believe there was interest in discovering how Rhopressa™ BID would perform. Baseline IOP was measured prior to treatment. Following treatment, IOP was measured at 8 a.m., 10 a.m. and 4 p.m. at the end of week two, week six and day 90. The trial included 251 patients in the Rhopressa™ QD arm, 254 patients in the Rhopressa™ BID arm and 251 patients in the timolol twice-daily arm. The most common Rhopressa™ adverse event in the QD arm was conjunctival hyperemia, or eye redness, which was reported in approximately 50% of patients, of which 80% was reported as mild. Other ocular adverse events reported in approximately 5% to 15% of patients in the Rhopressa™ QD arm included conjunctival hemorrhage, or petechiae, corneal verticillata and blurry vision. The Rhopressa™ BID arm showed slightly higher efficacy, but had a higher incidence of adverse events which led to a greater number of early terminations in comparison to the Rhopressa™ QD arm. Other ocular adverse events reported in approximately 5% to 17% of patients in the Rhopressa™ QD arm included conjunctival hemorrhage, or petechiae, corneal verticillata, blurry vision, increased lacrimation, reduced visual acuity, eye pruritus, and conjunctival edema. In February 2016, safety data for the 12-month period of the Rocket 2 trial confirmed this positive safety profile for the drug and demonstrated a consistent IOP lowering effect throughout the 12-month period at the 8 a.m. timepoint, the only timepoint measured at months six, nine and 12.

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After detailed analysis of the Rocket 1 and Rocket 2 results, we observed higher levels of IOP lowering for Rhopressa™ at week two and to a lesser extent at week six stemming from patients who were previously on a PGA, pointing to the potential synergistic effect of PGAs and Rhopressa™, which decreases over the 90-day period as the residual PGA effect subsides. For all other patients, the IOP lowering was consistent across the 90 day measurement periods and from day 90 through month 12, as observed in the 12-month safety data. For illustrative purposes, the graph below shows the performance of Rhopressa™ in Rocket 1 and Rocket 2 at baselines above 20 mmHg and below 25 mmHg, compared to timolol.

Data on file; Based on Rocket 2 and Rocket 1 topline interim 3-month efficacy results

We are also conducting a third Phase 3 registration trial for Rhopressa™, named “Rocket 3,” in Canada, which is designed as a supplementary 12-month safety-only trial and was not required for NDA filing purposes. Rocket 3 commenced in September 2014 and patients are no longer being enrolled in this trial.

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Further, we are conducting a fourth Phase 3 registration trial for Rhopressa™, named "Rocket 4," in the U.S., which is designed to generate adequate six-month safety data for European regulatory approval, which we expect to file for in the second half of 2018. In October 2016, we announced the 90-day efficacy results from Rocket 4 where Rhopressa™ achieved its primary efficacy endpoint of demonstrating non-inferiority of Rhopressa™ compared to timolol for patients with baseline IOPs ranging from above 20 mmHg to below 25 mmHg, and also at a pre-specified secondary range from above 20 mmHg to below 28 mmHg. Rocket 4 is designed to measure efficacy over three months and safety over six months and includes Rhopressa™ dosed QD and BID. Baseline IOP was measured prior to treatment. Following treatment, IOP was measured at 8 a.m., 10 a.m. and 4 p.m. at the end of week two, week six and day 90. The trial includes 351 patients in the Rhopressa™ QD arm and 357 patients in the timolol BID arm. Based on the 90-day efficacy results, the most common Rhopressa™ adverse event observed in the QD and BID arms was conjunctival hyperemia, or eye redness, which was reported in approximately 40% of patients, of which 85% was reported as mild. Other ocular adverse events reported in approximately 5% to 12% of patients in the Rhopressa™ arm included conjunctival hemorrhage, cornea verticillata, increased lacrimation and blurred vision. While Rocket 4 was not required for NDA filing purposes, we included the 90-day efficacy results for Rocket 4 with the Rhopressa™ NDA as supportive data. The graph below shows the performance of Rhopressa™ in Rocket 4 at baseline IOPs above 20 mmHg and below 25 mmHg, compared to timolol.

Data on file; Based on Rocket 4 topline interim 3-month efficacy results

Rhopressa™ 24-Hour IOP Pilot Study

In a recent 24-hour, 16-patient pilot study comparing the efficacy of Rhopressa™ to that of placebo, Rhopressa™ demonstrated similar levels of IOP lowering during nocturnal and diurnal periods. This is potentially a further differentiating feature of Rhopressa™ when considering that currently marketed products have demonstrated little or no efficacy at night and eye pressure is typically highest when patients are asleep.

Rhopressa™ Preclinical Anti-Fibrotic and Perfusion Results

We continue to explore the potential longer-term impact of Rhopressa™ on the TM. By increasing trabecular outflow, as demonstrated in our preclinical studies, Rhopressa™ has the potential to stop the degeneration of outflow tissues. As part of the aging process, the TM becomes stiffened and clogged as fibrosis develops and progresses. Preclinical studies on human TM cells have demonstrated a meaningful anti-fibrotic effect from Rhopressa™. Further, additional preclinical experiments on human eyes have demonstrated the product candidate's potential ability to increase the perfusion of the TM and downstream outflow tissues. We believe this is possible because, as a result of the action of Rhopressa™, the TM becomes relaxed and opens, which increases the flow of eye fluid, or aqueous humor. This has the potential to increase the health of the trabecular outflow tissues, since it should increase the delivery of nutrients and antioxidants to the TM that were otherwise blocked from passage. The flow of fluid through the TM is the only known mechanism for delivering such nutrients to the diseased tissue, as there are no blood vessels present. Work is continuing as we explore whether our product candidates may be able to prevent, or possibly even reverse, damage to the TM pathway through this potential effect as well as the potential anti-fibrotic effect of our product candidates. If findings are positive and there is demonstrated disease modification, this could be a major breakthrough in the treatment of glaucoma and ocular hypertension.

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Roclatan™

Our once-daily, product candidate Roclatan™ is a combination of our compound netarsudil, the active ingredient in Rhopressa™, formulated with latanoprost in a single eye drop. Roclatan™ lowers IOP through the same MOAs as Rhopressa™ and, through a fourth MOA, utilizing the ability of latanoprost to increase fluid outflow through the uveoscleral pathway, the eye's secondary drain.

We believe, based on our preclinical studies and clinical trials to date, that Roclatan™, if approved, will be the only glaucoma product that covers the full spectrum of currently known IOP- lowering MOAs, giving it the potential to provide a greater IOP-lowering effect than any currently marketed glaucoma product. Therefore, we believe Roclatan™ could compete with both PGA and non-PGA therapies for patients requiring maximal IOP lowering, including those with higher IOPs and those who present with significant disease progression despite currently available therapies.

Roclatan™ Phase 3 Trials

Our current Phase 3 registration trials commenced in September 2015 and are designed to compare Roclatan™ to each of its components, including Rhopressa™ and market-leading latanoprost. We anticipate total enrollment of over 1,900 patients in our planned Phase 3 registrations trials. Phase 3 efficacy results are determined after three months of treatment and safety results are analyzed after six or 12 twelve months of treatment depending on the trial design.

Our initial Phase 3 registration trial, named "Mercury 1," which commenced in September 2015, is a 12-month safety trial with a 90-day efficacy readout. We had total enrollment of over 700 patients in this three-arm study, with all three arms dosed once daily. Baseline IOP was measured prior to treatment. Following treatment, IOP was measured at 8 a.m., 10 a.m. and 4 p.m. at week 2, week 6 and day 90 for the 90-day efficacy period of the trial. In September 2016, we announced that Mercury 1 achieved its primary efficacy endpoint of demonstrating superiority of Roclatan™ to each of its components. The trial is designed to evaluate patients with maximum baseline IOPs ranging from above 20 mmHg to below 36 mmHg. In the 90-day efficacy results, the IOP-lowering effect of Roclatan™ exceeded that of the latanoprost monotherapy in a range of 1.3 mmHg to 2.5 mmHg and that of the Rhopressa™ monotherapy in a range of 1.8 mmHg to 3.0 mmHg. Roclatan™ reduced mean diurnal IOPs to 16 mmHg or lower in 61% of patients, a significantly higher percentage than observed in the comparator arms in the study. We included the Mercury 1 90-day efficacy results with the Rhopressa™ NDA as supportive data. The graph below shows the performance of Roclatan™ in Mercury 1 compared to each of its components.

***p<0.0001 vs. Latanoprost and Rhopressa™

Data on file; Based on Mercury 1 topline interim 3-month efficacy results

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The graph below represents the responder analysis from Mercury 1 which shows the percentage of patients for whom IOP was reduced to 18 mmHg or lower, comparing Roclatan™ to Rhopressa™ and latanoprost.
***p<0.0001 vs. Latanoprost and Rhopressa™
###p<0.0001 vs. Rhopressa™, p<0.05 vs. Latanoprost

Data on file; Based on Mercury 1 topline interim 3-month efficacy results

The safety and tolerability results for Roclatan™ from the 90-day efficacy period of Mercury 1 showed no drug-related serious adverse events. The most common adverse event observed in the Roclatan™ arm was conjunctival hyperemia, or eye redness, which was reported in approximately 50% of patients, of which approximately 80% was reported as mild. Other ocular adverse events reported in approximately 5% to 11% of patients in the Roclatan™ arm included conjunctival hemorrhage, or petechiae, eye pruritus, increased lacrimation and corneal verticillata. There were no drug-related serious adverse events for any of the comparators in the trial and patients in the Rhopressa™ arm reported ocular adverse events similar to ocular adverse events observed in the Phase 3 registration trials for Rhopressa™. We expect to report topline 12-month safety data for Mercury 1 in the third quarter of 2017.
Our second Phase 3 registration trial, named “Mercury 2,” is a 90-day efficacy and safety trial. Mercury 2 commenced in March 2016 and we expect to report topline 90-day efficacy results for Mercury 2 in the second quarter of 2017. We estimate total enrollment of approximately 690 patients in this three-arm 90-day study, with all three arms dosed once daily in the evening. The trial is designed to evaluate patients with maximum baseline IOPs ranging from above 20 mmHg to below 36 mmHg. If both Mercury 1 and Mercury 2 are successful, we expect to submit an NDA for Roclatan™ in late 2017 or early 2018.
We also plan to initiate a third Phase 3 registration trial for Roclatan™, named “Mercury 3,” in mid-2017. Mercury 3 will be designed to compare Roclatan™ to Ganfort®, a fixed-dose combination product of bimatoprost and timolol marketed in Europe, which if successful, should improve our commercialization prospects in that region.
Pipeline Opportunities

AR-13154

One of our owned preclinical molecules, AR-13154, has demonstrated the potential for the treatment of wet AMD. This preclinical small molecule inhibits Rho kinase and Protein kinase C and has shown lesion size decreases in a preclinical model of wet AMD at levels similar to current market-leading products. Additionally, in a preclinical proliferative diabetic retinopathy model, AR-13154 generated meaningful incremental lesion size reduction when used adjunctively with the current market-leading wet AMD anti-VEGF product. Pending additional studies, we may have the potential to provide an entirely new mechanism and pathway to treat this disease. Further, in our preclinical studies, we have seen a promising effect of this molecule on reducing neovascularization in a model of proliferative diabetic retinopathy.

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The graph below depicts the results of a preclinical study designed to show the impact of AR-13154 and Eylea® (aflibercept) on laser-induced choroidal neovascularization, or CNV, in rats.

Data on file; Effectiveness of AR-13154 Monotherapy and Combination Therapy in Animal Models of Wet Age-related Macular Degeneration and Proliferative Diabetic Retinopathy. Cheng-Wen Lin, Jill M. Sturdivant, Mitchell A. deLong and Casey C. Kopczynski

The graph below depicts the impact of AR-13154 when used adjunctively with Eylea® (aflibercept) in a proliferative diabetic retinopathy model.

Data on file; Effectiveness of AR-13154 Monotherapy and Combination Therapy in Animal Models of Wet Age-related Macular Degeneration and Proliferative Diabetic Retinopathy. Cheng-Wen Lin, Jill M. Sturdivant, Mitchell A. deLong and Casey C. Kopczynski

Since AR-13154 is a small molecule with a short half-life, and the aforementioned diseases are located in the back of the eye, a delivery mechanism is needed to deliver the molecule to the back of the eye for a sustained delivery period. We are examining available delivery technologies that might offer this capability. Delivery technologies may also prove useful in delivering other Aerie molecules to the front of the eye, such as Rhopressa™ or Roclatan™, for the purpose of long-term IOP lowering.

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We have not submitted an IND for AR-13154 to the FDA and there can be no assurance that an IND will be submitted.

Our Strategy

Our goal is to become 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 current 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. We resubmitted the NDA for Rhopressa™ on February 28, 2017, using our successful Rocket 2 trial as the pivotal trial and Rocket 1 trial as supportive. We included as supportive data the 90-day efficacy results of Rocket 4 and Mercury 1 with the NDA for Rhopressa™. This is a key step in driving this drug to a commercial stage in the United States. Our Rocket 4 trial, which is ongoing, is designed to provide adequate six-month safety data to support future European regulatory filings, which we expect to submit in the second half of 2018.

Our second product candidate, once-daily, Roclatan™, which is a fixed-dose combination of Rhopressa™ and latanoprost, the most commonly prescribed drug for the treatment of patients with glaucoma, achieved its primary efficacy endpoint of demonstrating superiority of Roclatan™ to each of its components in Mercury 1 in September 2016. We commenced Mercury 2 in March 2016 and we expect to report topline 90-day efficacy results in the second quarter of 2017. If both Mercury 1 and Mercury 2 are successful, we expect to submit an NDA for Roclatan™ in late 2017 or early 2018. We expect to commence Mercury 3 in Europe in mid-2017, which will be designed to compare Roclatan™ to Ganfort®, a fixed-dose combination product of bimatoprost and timolol marketed in Europe, which if successful, should improve our commercialization prospects in that region.

Establish internal sales capabilities to commercialize our product candidates in North America. We own worldwide rights to all indications for our product candidates and we plan to retain commercialization rights in North American markets. Ultimately, if our product candidates are approved, we plan to build a commercial team in the United States 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 North America. Our strategy includes developing our business outside of North America, including obtaining regulatory approval on our own for our current product candidates in Europe and Japan. Regarding our international commercialization strategy, we expect to explore partnership opportunities through collaboration and licensing arrangements in Europe and Japan.

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. and foreign patents and pending U.S. and foreign patent applications related to composition of matter, pharmaceutical compositions, methods of use, and synthetic methods. 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, research collaboration arrangements and in-licensing or acquisitions of additional ophthalmic product candidates, products or technologies. We continue to 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 may enter into research collaboration arrangements, license or acquire additional product candidates and technologies to broaden our presence in ophthalmology, and we continually explore and discuss potential additional opportunities for new ophthalmic products, delivery alternatives and new therapeutic areas with potential partners. Our approach has consistently been to explore opportunities with minimal initial investment allowing us to more fully evaluate the probability of success prior to making a material commitment. We are currently focused on the evaluation of delivery technologies for the delivery of our owned molecules to the front and back of the eye over sustained periods.

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.

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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 mmHg to 14 mmHg to protect the optic nerve from further damage.

There are multiple factors that can contribute to an individual getting open-angle glaucoma, including, but not limited to, age, family history and ethnicity. For example, there generally 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.

In addition to aqueous humor production and drainage through the TM and uveoscleral pathway, EVP plays a significant role in the regulation of IOP. EVP represents the pressure of the blood in the episcleral veins of the eye which are the site of drainage of eye fluid into the bloodstream. Historical studies have shown that EVP accounts for approximately 10 mmHg of IOP, or approximately one-half of IOP in patients with pressures near the normotensive level of 21 mmHg, and approximately one-third of IOP in patients with pressures of 24 mmHg to 30 mmHg. When EVP is lowered, aqueous humor is able to flow more freely from the eye.

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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 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-dose 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 Valeant Pharmaceuticals International, 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 or technologies to treat glaucoma or other diseases of the eye. 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 current product candidates, if approved, are likely to be efficacy and MOAs, 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. They do not target the TM, the diseased tissue in glaucoma. PGAs represent approximately one-half of the U.S. and European prescription volume for the treatment of glaucoma.

Xalatan® (latanoprost), the best-selling PGA, together with Xalacom®, its fixed-dose combination with a beta blocker, which is not available in the United States, had worldwide peak sales of approximately $1.7 billion before its patent expired in 2012, according to publicly reported sales. The adverse effects of PGAs include conjunctival hyperemia, or eye redness, irreversible change in iris color, discoloration of the skin around the eyes, and droopiness of eyelids caused by the loss of orbital fat. 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 monotherapy and as an adjunctive 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.

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- 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 their 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, the requirement for two to three doses per day, and the fact that they do not target the diseased tissue in glaucoma, beta blocker, carbonic anhydrase inhibitor and alpha agonist products account for up to one-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. Fixed-dose combination glaucoma products are also 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-dose combinations of PGAs with other glaucoma drugs currently available in the United States.

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.

New MOAs

Brand	MOA / Dosing	Trial Stage
Rhopressa™ (Aerie AR-13324)	ROCK/NET inhibitor (qd)	Submitted NDA
Roclatan™ (Aerie PG324)	ROCK/NET inhibitor + PGA (qd)	Phase 3
Trabodenoson/Trabodenoson Fixed-Dose Combination (Inotek)	Adenosine-A1 agonist (bid or qd)/Adenosine-A1 agonist + PGA	Phase 2/3
SYL040012 (Sylentis)	RNAi beta blocker (qd)	Phase 2

New PGAs[1]

Brand	MOA / Dosing	Trial Stage
Vyzulta™ (Valeant)	NO donating latanoprost (qd)	Filed NDA
DE-117 (Santen)	EP2 agonist (qd)	Phase 2
DE-126 (Santen)	FP/EP3 agonist (qd)	Phase 2

[1]Not usable as add-on therapy to current PGAs.

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. In July 2015, Bausch + Lomb Inc., a wholly owned subsidiary of Valeant Pharmaceuticals International, Inc., filed an NDA for a nitric oxide-donating latanoprost, which is currently under review by the FDA for the treatment of open angle glaucoma and ocular hypertension. Early-stage companies are also developing treatments for glaucoma and other diseases of the eye and may prove to be significant competitors, such as, despite its recent setbacks, Inotek Pharmaceuticals, which is developing an adenosine receptor agonist. We expect that our competitors will continue to develop new treatments for glaucoma and other diseases of the eye, 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.

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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, in the case of glaucoma treatment, 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, the active ingredient in Rhopressa™, 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, Rhopressa™ and Roclatan™ 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 to support our clinical trials. Latanoprost, used in the manufacture of Roclatan™, 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.

With respect to commercial production of our potential products in the future, we plan on outsourcing the production of the active pharmaceutical ingredients and are currently working to establish contractual relationships for such production with our vendors. We currently manage any production on a purchase order basis. The commercial production of our final drug product manufacturing is expected to be supported by a combination of internal and outsourced manufacturing. We have entered into a contractual relationship for the final drug product manufacturing for commercialization and, in January 2017, we entered into a lease agreement for a new manufacturing plant in Athlone, Ireland. The building shell was constructed by the Industrial Development Agency of Ireland and we are in the early stages of building out the plant. If we obtain regulatory approval, the manufacturing plant is expected to produce commercial supplies of our current product candidates, with commercial product supply of Rhopressa™ from the plant expected to be available by 2020. The build-out of this manufacturing plant will require substantial funds and we will need to hire and train significant numbers of qualified employees to staff this facility.

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 provides 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.

Research and Development Expenses

A significant portion of our operating expenses relates to research and development. Our research and development expenses totaled $52.4 million, $44.5 million, and $29.9 million for the years ended December 31, 2016, 2015, and 2014, respectively.

Intellectual Property

We have obtained patent protection for our primary product candidates, Rhopressa™ and Roclatan™ (patent protection for Roclatan™ arises from the patent protection we have secured for Rhopressa™), in the United States and certain foreign jurisdictions and are seeking patent protection in a number of other 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.”

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Our intellectual property consists of issued patents, and pending patent applications for compositions of matter, pharmaceutical formulations, methods of use, and synthetic methods. We have patent protection for our primary product candidates, Rhopressa™ and Roclatan™, in the United States through at least 2030. Additionally, we hold patents for composition of matter and method of use in certain foreign jurisdictions for our primary product candidates. We also hold 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 December 31, 2016, we had 70 United States or foreign issued patents that cover various aspects of our current and previously discontinued product candidates and our other proprietary technology and 25 U.S. patent applications or foreign 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 and our other proprietary technology.

Aerie® is a registered trademark of ours and we have applications pending from the U.S. Patent and Trademark Office, or USPTO, for the registration of our trademarks Rhopressa™ and Roclatan™.

In 2015, we revised our corporate structure to align with our business strategy outside of North America by establishing Aerie Pharmaceuticals Limited, a wholly-owned subsidiary ("Aerie Limited"), and Aerie Pharmaceuticals Ireland Limited, a wholly owned subsidiary ("Aerie Ireland Limited"). We assigned the beneficial rights to our non-U.S. and non-Canadian intellectual property for our lead product candidates to Aerie Limited (the "IP Assignment"). As part of the IP Assignment, we and Aerie Limited entered into a research and development cost sharing agreement pursuant to which we and Aerie Limited will share the costs of the development of intellectual property and Aerie Limited and Aerie Ireland Limited entered into a license arrangement pursuant to which Aerie Ireland Limited will develop and commercialize the beneficial rights of the intellectual property assigned as part of the IP Assignment. In 2016, we assigned the beneficial rights to certain of our intellectual property in the United States and Canada to Aerie Distribution, Inc., a wholly owned subsidiary ("Aerie Distribution"), and amended and restated the research and development cost sharing agreement to transfer our rights and obligations under the agreement to Aerie Distribution.

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. 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 investigational new drug (“IND”) application, which allows clinical trials to begin unless FDA objects within 30 days;

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- 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 raises concerns or questions about the conduct of the clinical trial within the 30-day time period. 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 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 registration 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 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.

Pursuant to the 21st Century Cares Act, which was enacted on December 13, 2016, the manufacturer of an investigational drug for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug. This requirement applies on the later of 60 calendar days after the date of enactment or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug.

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.

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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 in certain circumstances for up to two years after the date of completion of the trial. 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 $2,000,000 for fiscal year 2017) 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 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 files them. It may request additional information rather than accept an 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 files it. The FDA has 60 days from its receipt of an NDA to conduct an initial review to determine whether the application will be filed based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. If the NDA submission is filed, 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.

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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 a REMS, from manufacturers to ensure that the benefits of a drug outweigh its risks. A sponsor may also voluntarily propose a 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 Prescription Drug User Fee Act ("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 product candidates, 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

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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 with claims covering the applicant's product or method of using the 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 dosage form as the listed drug and has been shown to be bioequivalent 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 labeling 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 filed 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, or NCE. A drug is entitled to NCE exclusivity if it contains a drug substance no active moiety of which has been previously approved by the FDA. This means that, in the case of a fixed-dose combination product, the FDA makes the NCE exclusivity determination for each drug substance in the drug product and not for the drug product as a whole. 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 for the original conditions of use, such as the originally approved indication. 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. Similarly, the Drug Supply Chain Security Act, or DSCSA, regulates the distribution of finished dosage form prescription pharmaceutical drugs, requiring passage of certain transaction information for each prescription drug at the saleable unit level through the distribution system. The DSCSA also imposes obligations on drug manufacturers related to suspect product identification/removal, verification, reporting, dealing only with authorized trading partners, and other elements. The PDMA, DSCSA, and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

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 facilities and in accordance with cGMP. 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. We currently 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. 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 $95,000 per product and $510,000 per establishment for fiscal year 2017. While, these fees are typically increased annually, they decreased from fiscal year 2016 to fiscal year 2017.

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 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.

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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.

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 potential 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

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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 $10,000 and $25,000 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 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

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rebate on most branded prescription drugs and biologic agents to 23.1% of Average Manufacturer Price ("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, beginning in 2011, expanding the population potentially eligible for Medicaid drug benefits. The Centers for Medicare & Medicaid Services, or CMS, expanded Medicaid rebate liability to the territories of the United States as well, effective April 1, 2017. 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, beginning in April 2016, 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").
- 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.
- PPACA requires 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 were required to track this information beginning in 2013, and the first reports were due in 2014. The information reported each year is made publicly available on a searchable website.
- 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 has the 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 and impact of PPACA are yet to be determined, and at this time, it remains unclear the full effect that PPACA would have on our business. In addition, recently, President Donald Trump has made statements that suggest he plans to seek repeal of all or portions of PPACA, and has stated that he will ask Congress to replace PPACA with new legislation. There is uncertainty with respect to the impact these

changes, if any, may have, and any changes likely will take time to unfold.

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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 NCA 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 for Medicinal Products for Human Use, or CHMP, a body of 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.

In addition to regulations in the United States and the EU, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our potential products. Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. In addition, the requirements governing the conduct of clinical trials, commercial sales, product licensing, pricing and reimbursement vary greatly from country to country.

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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. In addition, our international operations and relationships with partners, collaborators, contract research organizations, vendors and other agents are subject to anti-corruption and anti-bribery laws and regulations, including the U.S. Foreign Corrupt Practices Act ("FCPA"), which prohibits U.S. companies and their representatives from engaging in bribery or other prohibited payments to foreign officials for the purpose of obtaining or retaining business. Failure to comply with the FCPA, or similar applicable laws and regulations in other countries, could expose us and our personnel to civil and criminal sanctions. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

We had 95 full-time employees as of December 31, 2016. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Corporate and Available Information

Our principal executive offices are located at 2030 Main Street, Suite 1500, Irvine, California 92614 and our telephone number is (949) 526-8700. We were incorporated in Delaware in June 2005. Our internet address is www.aeriepharma.com. We make available on our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Our SEC reports can be accessed through the Investors section of our website. Further, a copy of this Annual Report on Form 10-K is located at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D. C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov. The information found on our website is not incorporated by reference into this report or any other report we file with or furnish to the SEC.

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ITEM 1A. RISK FACTORS

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.

Risks Related to Development, Regulatory Approval and Commercialization

We depend substantially on the success of our product candidates, particularly Rhopressa™ and Roclatan™, which have not obtained regulatory approval. 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 and other diseases of the eye, particularly Rhopressa™ and Roclatan™, which are in the late stages of 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 adequate internal manufacturing capacity or 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 could 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.

Phase 3 registration trials for Rhopressa™ commenced in July 2014 and in April 2015 we completed Rocket 1. The Rocket 1 trial did not meet its primary efficacy endpoint of demonstrating non-inferiority of IOP lowering for once-daily Rhopressa™ compared to twice-daily timolol, but did achieve its pre-specified secondary endpoint. We evaluated the data and results from Rocket 1 and obtained agreement from the FDA to change the IOP range used for the primary endpoint of Rocket 2 to a level where Rocket 1 would have been successful.

In September 2015, the Rocket 2 trial achieved its primary efficacy endpoint of demonstrating non-inferiority of Rhopressa™ compared to timolol. In February 2016, 12-month safety data from Rocket 2 confirmed a positive safety profile for the drug and demonstrated a consistent IOP lowering effect throughout the 12-month period at the specified timepoint.

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We are also conducting Rocket 3 in Canada, which is designed as a supplementary 12-month safety-only trial and Rocket 4 in the U.S., which is designed to generate adequate six-month safety data for European regulatory filings, expected to be submitted in the second half of 2018. In October 2016, we announced the 90-day efficacy results from Rocket 4 where Rhopressa™ achieved its primary efficacy endpoint of demonstrating non-inferiority of Rhopressa™ compared to timolol for patients with baseline IOPs ranging from above 20 mmHg to below 25 mmHg, and also at a pre-specified secondary range from above 20 mmHg to below 28 mmHg. We included the Rocket 4 results with the Rhopressa™ NDA as supportive data.

Phase 3 registration trials for Roclatan™ commenced in September 2015. In September 2016, we announced that Mercury 1 achieved its primary efficacy endpoint of demonstrating superiority of Roclatan™ to each of its components, including Rhopressa™ and market-leading PGA, latanoprost. We included the Mercury 1 90-day efficacy results with the Rhopressa™ NDA as supportive data.

Mercury 2 commenced in March 2016 and we expect to report topline 90-day efficacy results in the second quarter of 2017. We also plan to initiate Mercury 3 in mid-2017. Mercury 3 will be designed to compare Roclatan™ to Ganfort®, a fixed-dose combination product of bimatoprost and timolol marketed in Europe.

We cannot predict whether ongoing 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.

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.

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 file the NDA or refuse to file the NDA. In the United States, we have not had an NDA accepted for review 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. We resubmitted our NDA with the FDA for Rhopressa™ on February 28, 2017. Our initial submission, announced in September 2016, was withdrawn as a result of a contract manufacturer of our drug product not being prepared for pre-approval inspection by the FDA. Although we believe our NDA for Rhopressa™ contains substantial evidence of effectiveness for the product, we cannot guarantee that the NDA will be filed or subsequently approved by the FDA. In addition, if both Mercury 1 and Mercury 2 are successful, we expect to submit an NDA for Roclatan™ in late 2017 or early 2018, which may be prior to obtaining approval for Rhopressa™.

As with the Rhopressa™ NDA, we cannot be certain the Roclatan™ NDA will be filed or subsequently approved by the FDA. In addition, we may be required to supplement the Rhopressa™ NDA with additional information and/or receive unfavorable feedback from the FDA regarding the likelihood of obtaining FDA approval for Rhopressa™ during or after review of the Rhopressa™ NDA. If based on the FDA review of the Rhopressa™ NDA or for other reasons, we delay or abandon the advancement of FDA approval for Rhopressa™, in certain circumstances we may similarly delay or determine not to submit an NDA for or seek FDA approval of Roclatan™, which combines Rhopressa™ with latanoprost.

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

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claims, will be subject to additional review and approval by the FDA and other regulatory authorities. 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 current and potential future 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 current and potential future product candidates on schedule, if at all. If regulatory authorities require additional time or studies to assess the safety or efficacy of our product candidates, we may require funding beyond the amounts currently on our balance sheet. In addition, in the event of any unforeseen costs or other business decisions, 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;
- 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 the effectiveness or safety of product candidates during clinical trials;
- any determination that a clinical trial or product candidate 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;
- the failure of a third party to comply with applicable FDA and other U.S. and non-U.S. regulatory requirements, including site inspections and inspection readiness;
- 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.

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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.

Failure can occur at any stage of clinical development. If the clinical trials for our current and potential future 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 3 registration trials that may 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 current and potential future product candidates.

Flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced or after data results have been obtained. We have limited experience in designing clinical trials and may be unable to design and execute clinical trials 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 had an NDA filed by the FDA 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, analyses and entry criteria, 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 ongoing clinical trials for our primary product candidates, Rhopressa™ and Roclatan™, may not produce the results that we expect and remain subject to the risks associated with clinical drug development as indicated above.

Other companies have previously pursued ROCK inhibitors for ophthalmic use but to date no ROCK inhibitors have been approved in the United States. In 2013, one of our ROCK inhibitors, AR-12286, and its fixed-dose combination

product, PG286, were discontinued in the clinical stage of development due to an inability to maintain efficacy over time.

In April 2015, we announced that Rocket 1 did not meet its primary efficacy endpoint of demonstrating non-inferiority of IOP lowering for once-daily Rhopressa™ compared to twice-daily timolol, but did achieve its pre-specified secondary endpoint. We evaluated the data and results from Rocket 1 and obtained agreement from the FDA to change the IOP range used for the primary endpoint of Rocket 2 to a level where Rocket 1 would have been successful.

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In September 2015, the Rocket 2 trial achieved its primary efficacy endpoint of demonstrating non-inferiority of Rhopressa™ compared to timolol. In addition to successfully achieving non-inferiority to timolol at this endpoint range, the 12-month safety data from Rocket 2 confirmed a positive safety profile for the drug and demonstrated a consistent IOP lowering effect throughout the 12-month period at the specified timepoint.

Our clinical trials are designed to test the use of Rhopressa™ and Roclatan™ as a monotherapy, rather than as an adjunctive therapy. Accordingly, the efficacy of our primary product candidates may not be similar or correspond directly to their efficacy when used as an adjunctive therapy, which we expect will be a primary use of Rhopressa™.

In February 2014, we reported the results of a preclinical animal study sponsored by Aerie, whereby the administration of Rhopressa™ eye drops demonstrated statistically significant reductions in EVP and IOP in rabbits following the third daily dose. Based on the results of this preclinical study, together with the consistent IOP-lowering effect of Rhopressa™ demonstrated in our clinical trials, we believe the reduction of EVP is an additional MOA of Rhopressa™ and Roclatan™. However, like the other differentiated MOAs of our product candidates, increasing outflow through the TM and decreasing fluid production in the eye, our product candidates' effect on EVP has not been studied in humans and neither our ongoing, nor our planned, Phase 3 registration trials for Rhopressa™ or Roclatan™ have been or will be designed to demonstrate reduction of EVP or other MOAs of our product candidates. If we are not able to demonstrate to the satisfaction of the FDA and relevant non-U.S. regulators the reduction of EVP, or any of the other differentiated MOAs of our product candidates, even if we otherwise obtain regulatory approval for Rhopressa™ and Roclatan™, it could limit the types of claims we will be able to make in our marketing and labeling of our product candidates.

We believe Rhopressa™, if approved, will compete against non-PGA products as a preferred adjunctive therapy to PGAs. In addition, if approved, we believe that Rhopressa ™ may also become a preferred therapy in several populations including where patients have low to moderately elevated IOPs at the time of diagnosis. No patients with low-tension glaucoma have been or will be included in our clinical trials, and our expectations with respect to subjects with low IOP are based to a large extent on extrapolation of results for subjects with moderately elevated IOP. Even if our product candidates were to obtain regulatory approval, if we are unable to support claims about our product candidates to the satisfaction of the FDA and relevant non-U.S. regulators, including claims with respect to the efficacy of Rhopressa™ as an adjunctive therapy or for patients with low IOP, it could limit the types of claims we will be able to make in our marketing and product labeling of these product candidates.

In addition to the circumstances noted above, we may experience numerous unforeseen events that could cause our clinical trials to be unsuccessful, delayed, suspended or terminated, or which could delay or prevent our ability to receive regulatory approval or commercialize our current and potential future 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 current and potential future product candidates, our commercial prospects will be adversely impacted and our ability to generate product revenues may be delayed or eliminated.

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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 Rhopressa™ has been mild conjunctival hyperemia, or eye redness. In February 2016, we reported 12-month safety data from Rocket 2, in which some patients also experienced conjunctival hemorrhages, or petechaie, corneal verticillata, blurry vision, and decreased visual acuity as adverse events. Roclatan™ combines Rhopressa™ with latanoprost. To date, the main tolerability finding of Roclatan™ has also been mild conjunctival hyperemia, which was reported in approximately 50% of patients and was scored as mild for approximately 80% of affected patients in the 90-day safety data from Mercury 1. The main adverse effects of latanoprost include conjunctival hyperemia, irreversible change in iris color, discoloration of the skin around the eyes and droopiness of eyelids caused by the loss of orbital fat.

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 receive 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 boxed warning or a contraindication, or other safety labeling changes;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or a REMS;
- 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 revenues from its sale.

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

We have no experience selling, marketing or distributing our product candidates, and 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 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. If our product candidates are approved outside of the United States for commercial sale and if we self-commercialize our product candidates in these other countries, we will need to establish similar functions or outsource these functions to third parties. 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;
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- 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

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- 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 have international operations. We intend to explore the licensing of commercialization rights or other forms of collaboration outside of North America and to develop internal manufacturing capabilities in Ireland, both of which will expose us to additional risks of conducting business in international markets.

Markets outside of North America are an important component of our growth strategy. As part of this strategy, in March 2015 and April 2015, we formed Aerie Limited and Aerie Ireland Limited, respectively. If we fail to commercialize, 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. Additionally, in January 2017, we entered into a lease agreement for a new manufacturing plant in Ireland. If we fail to develop internal manufacturing capabilities we may be forced to continue to rely on third-party manufacturers, which could adversely affect our results of operations and financial condition. Moreover, international operations and 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 or expand collaboration or licensing arrangements with third parties in connection with our international sales, marketing, manufacturing 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 or changes in governmental regulations and laws;
- differing regulatory requirements for drug approvals, manufacturing 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 other regulatory requirements;
- divergent environmental laws and regulations;
- 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 (including tax reform proposals being considered by the new U.S. presidential administration and being considered in the U.S. Congress that create uncertainty with respect to the future tax impact on our business operations and profitability);
- 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;
- 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 business, results of operations, financial condition or ability to attain or sustain revenue from international markets.

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We have no experience developing manufacturing facilities or manufacturing our product candidates, and we cannot assure you that we will be able to develop our manufacturing plant or manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We have entered into a lease agreement for a new manufacturing plant in Athlone, Ireland. The building shell was constructed by the Industrial Development Agency of Ireland and we are in the early stages of building out the plant for the future commercial production of our current product candidates. We have no experience in developing manufacturing facilities or manufacturing drug products. The build-out of this manufacturing plant will require substantial additional funds and we will need to hire and train significant numbers of qualified employees to staff this facility. There can be no assurance that we will develop a manufacturing plant that is adequate to produce materials for commercial use on our expected timing or at all.

The development of manufacturing facilities and the manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. The equipment and facilities employed in the manufacture of pharmaceuticals are subject to stringent qualification requirements by regulatory agencies, including validation of facility, equipment, systems, processes and analytics. We may be subject to lengthy delays and expense in conducting validation studies, if we can meet the requirements at all. Although we expect to complete internal construction of the plant to meet these qualification requirements, there can be no assurance that we will obtain certification from the FDA and other regulatory authorities to allow the plant to manufacture Rhopressa™ and Roclatan™ for export to the United States and other markets. If we are unable to obtain such certification in a timely manner, our ability to successfully manufacture and commercialize our potential products may be harmed.

In addition, we will be subject to customary risks associated with the construction of manufacturing plants, including, design defects, construction cost overruns (including labor and materials) and other factors that may delay build-out of the manufacturing plant. Our manufacturing operations and those of our third-party suppliers are subject to environmental, health and safety laws and regulations concerning, among other things, the use, storage, generation, handling, transportation and disposal of hazardous substances or wastes, the cleanup of hazardous substance releases, exposure to hazardous substances and emissions or discharges into the air or water. Violations of these laws and regulations can result in significant business interruptions and/or civil and criminal penalties. New laws and regulations, violations of or amendments to existing laws or regulations, or stricter enforcement of existing requirements, could require us to incur material costs, subject us to new or increased liabilities, and cause disruptions to our manufacturing activities that could be material. If the cost of funding the build-out of our manufacturing plant exceeds budgeted amounts and/or the time period for construction is longer than initially anticipated, our business, results of operations and financial condition could be materially adversely affected. Similarly, if we cannot access the capital we need to fund our operations, we may need to postpone or cancel the construction of the manufacturing plant or other components of our business strategy, which could impair our ability to compete effectively and harm our business, financial condition and results of operations.

Manufacturers of pharmaceutical products often encounter difficulties in production, especially in scaling up initial production. These problems include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced regulations. If we are unable to obtain certification from the FDA and other regulatory authorities or effectively produce commercial supplies of our product candidates, we will be required to rely on a third-party manufacturer to meet our commercial manufacturing needs, which may materially adversely affect our business, results of operations and financial condition. See “-Risks Related to Our Reliance on Third Parties-We currently 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 until such a time when we can develop internal manufacturing capabilities, if at all.”

Any of these risks could entail higher costs, cause us to delay production and may result in our being unable to effectively support commercialization of our potential products. Furthermore, if we obtain regulatory approval and fail to deliver the required commercial quantities of product on a timely basis, and at commercially reasonable prices and acceptable quality, we would likely be unable to meet demand, if any, for our potential products and we would lose potential revenues.

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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 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 patients with glaucoma or other diseases of the eye. 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. In July 2015, Bausch + Lomb Inc., a wholly owned subsidiary of Valeant Pharmaceuticals International, Inc., filed an NDA for a nitric oxide-donating latanoprost, which is currently under review by the FDA for the treatment of open angle glaucoma and ocular hypertension. Additionally, early-stage companies are also developing treatments for glaucoma and other diseases of the eye and may prove to be significant competitors, including Inotek Pharmaceuticals, which is developing an adenosine receptor agonist. We expect that our competitors will continue to develop new treatments for glaucoma and other diseases of the eye, 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 or other diseases of the eye.

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. 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 currently dominated by generic drugs, such as latanoprost and timolol, in the case of glaucoma treatment, 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.

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;
- develop effective manufacturing capabilities and build an effective selling and marketing infrastructure;
- demonstrate the advantages of our product candidates compared to alternative therapies, including currently marketed PGA and non-PGA products;
- 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 potential 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 and other diseases of the eye. Some of these drugs are branded and subject to patent protection, but most others, including latanoprost and many beta blockers, in the case of glaucoma treatment, 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

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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 possibility that third-party payors will not give our products favorable positions on their formularies or will place restrictions on the use of our products, including through use of step therapy or prior authorization programs;
- 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 and MOAs for our product candidates;
- relative convenience and ease of administration;
- the strength of our selling, marketing and distribution capabilities;
- the quality of our relationships with eye-care professionals, patient advocacy groups, third-party payors and the medical community;
- sufficient third-party coverage or reimbursement; and
- potential product liability claims.

In addition, it is possible that we may find it necessary or desirable to provide rebates on our products to customers or third party payors or to implement patient assistance programs, including co-pay assistance programs, which could affect our profitability.

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 prove to be inaccurate and the actual market for our potential products is smaller than we expect or if we fail to achieve market acceptance of our potential products in the United States and abroad, our potential product revenue may be limited, and it may be more difficult for us to achieve or maintain profitability.

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 for glaucoma or other diseases of the eye. 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

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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.

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

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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.

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 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 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 are covered in any therapeutic class under the 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 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 expanded Medicaid rebates to the utilization that occurs in the territories of the United States, such as Puerto Rico and the Virgin Islands, effective April 1, 2020. 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 and teaching hospitals, and the first reports were due in 2014 and the reported information was made publicly available on a searchable website 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. In addition, recently, President Donald

Trump has made statements that suggest he plans to seek to repeal of all or portions of PPACA, and has stated that he will ask Congress to replace PPACA with new legislation. There is uncertainty with respect to the impact these changes, if any, may have, and any changes likely will take time to unfold.

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

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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.

If we face allegations of noncompliance with the law and encounter sanctions, our reputation, revenues and liquidity may suffer, and our potential 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 potential 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 manufacturing facilities are required to comply with extensive FDA and EMA requirements and the requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to cGMP requirements. As such, if our product candidates receive approval, we and our 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, uses or claims for which they are not approved, even though physicians may prescribe them for those uses.

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 product candidates.

We continue to explore other therapeutic opportunities in ophthalmology through internal research programs and from time to time we may explore such opportunities through research collaboration arrangements, and may seek to commercialize a portfolio of new ophthalmic drugs or drug delivery technologies in addition to our product candidates that we are currently developing. All of our preclinical studies to identify potential new indications for our current product candidates and potential future product candidates will require additional research and development and, in some cases, significant preclinical, clinical and other testing prior to seeking regulatory approval to market such new indications and/or product candidates. Accordingly, these additional indications and product candidates will not be commercially available for a number of years, if at all.

Research programs, including through collaboration arrangements, to pursue the development of our product candidates for additional indications and to identify new product candidates, drug delivery technologies 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 additional 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 additional indications and/or product candidates;
- potential additional indications may, after further study, fail to demonstrate efficacy sufficient to warrant further clinical development;
- potential product candidates may, after further study, be shown to be ineffective or 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 or drug delivery technologies through internal research programs than we possess, thereby limiting our ability to diversify and expand our product portfolio.

The decision whether to pursue, and the timing of, any additional preclinical research programs is subject to a number factors and we may suspend or discontinue research programs at any time. For example, in 2015, we decided to no longer actively pursue further development of AR-13533, a second generation ROCK/NET inhibitor, for strategic business purposes.

In addition, 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 any uses for our existing proprietary compounds beyond glaucoma or to develop suitable potential product candidates or drug delivery technologies through internal research programs or research collaboration arrangements, which could materially adversely affect our future growth and prospects.

Our current 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 current 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 MOAs. 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 current 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 clinical-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 product candidates 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;
- manufacture or 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 for a number of reasons, including 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 product candidates.

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.

We have incurred net losses since inception and anticipate that we will continue to incur net losses until such a time when our product candidates are commercially successful, if at all.

We have incurred losses in each year since our inception in June 2005. Our net losses were $99.1 million, $74.4 million and $48.1 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $316.6 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 the majority 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 equity securities and issuance of convertible debt, including the completion of our IPO in October 2013, the issuance of the 2014 Convertible Notes in September 2014 and the issuance and sale of common stock pursuant to our registration statements on Form S-3 and former “at-the-market” sales agreements. 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 3 registration trials. In addition, if we obtain regulatory approval for our product candidates, we expect to incur increased manufacturing, sales and marketing expenses. As a result, we expect to continue to incur significant and increasing operating losses and negative cash flows until such a time when our product candidates are commercially successful, if at all. These losses have had and will continue to have a material adverse effect on our stockholders’ equity, financial position, cash flows and working capital.

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We may 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 and construction of our new manufacturing plant.

Our operations have consumed substantial amounts of cash since inception. In October 2013, we received net proceeds from our IPO of approximately $68.3 million, after deducting underwriting discounts and commissions and expenses. Since our IPO, we have raised additional net proceeds of approximately $122.9 million from the issuance of the 2014 Convertible Notes and approximately $217.6 million through the issuance and sale of common stock under our shelf registration statements on Form S-3 and former "at-the-market" sales agreements. We may need to obtain additional financing to fund our future operations, including construction of our new manufacturing plant. Additionally, we may 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 or drug delivery technologies. Moreover, our fixed expenses, such as rent and other contractual commitments, are substantial and are expected to increase in the future, and we also expect to incur increased expenses as we expand our employment base.

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;
- the time and cost necessary to establish internal manufacturing capabilities or arrangements with third-party manufacturers;
- 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 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.

We believe that our existing cash and cash equivalents and investments will be sufficient to complete all currently known non-clinical and clinical requirements for our development programs advancing Rhopressa™ and Roclatan™, approval by the FDA and product commercialization, pending successful outcome of the trials. We also intend to use these funds for general corporate purposes and for strategic growth opportunities, including the execution of clinical trials in Japan, the commencement of construction of our manufacturing plant in Ireland and the continuation of preclinical activity in support of our product pipeline.

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 or manufacturing 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.

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

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more rapidly than we currently anticipate. Our inability to obtain additional funding when we need it could seriously harm our business.

Our substantial leverage and related obligations could adversely affect our financial condition and restrict our operating flexibility.

We have substantial debt and related obligations. As of December 31, 2016, our total indebtedness consisted of our $125.0 million aggregate principal amount of 2014 Convertible Notes which bear interest at a rate of 1.75% per annum and mature on the seventh anniversary from the date of issuance, unless earlier converted. Our substantial level of debt and related obligations, including interest payments, covenants and restrictions, could have important consequences, including the following:

- impairing our ability to successfully complete the development of our product candidates, which would prevent us from generating a source of revenue and becoming profitable;
- making it more difficult for us to satisfy our obligations with respect to our indebtedness, which could result in an event of default under the agreement governing the 2014 Convertible Notes;
- limiting our ability to obtain additional financing on satisfactory terms to fund our working capital requirements, capital expenditures, potential acquisitions, debt obligations and other general corporate requirements;
- increasing our vulnerability to general economic downturns, competition and industry conditions, which could place us at a competitive disadvantage compared to our competitors that are less leveraged and therefore we may be unable to take advantage of opportunities that our leverage prevents us from exploiting; and
- imposing additional restrictions on the manner in which we conduct our business, including restrictions on our ability to pay dividends, incur additional debt and sell assets.

The occurrence of any one of these events could have an adverse effect on our business, financial condition, operating results or cash flows and ability to satisfy our obligations under our indebtedness.

Although the agreement governing the 2014 Convertible Notes contains restrictions on the incurrence of additional indebtedness, these restrictions are subject to a number of significant qualifications and exceptions, and any indebtedness incurred in compliance with these restrictions could be substantial. In addition, the agreement governing the 2014 Convertible Notes allows us to incur a significant amount of indebtedness in connection with acquisitions and a significant amount of purchase money debt. If new debt is added to current debt levels, the related risks that we and noteholders face would be increased.

The terms of the agreement governing the 2014 Convertible Notes may restrict our current and future operations, particularly our ability to respond to changes in our business or to take certain actions.

The agreement governing the 2014 Convertible Notes contains, and the terms of any future indebtedness of ours would likely contain, a number of restrictive covenants that impose significant operating restrictions, including restrictions on our ability to engage in acts that may be in our best long-term interests. The agreement governing the 2014 Convertible Notes includes covenants that, among other things, restrict or otherwise limit our ability to:

- incur additional indebtedness and create liens;
- pay dividends on capital stock and make other restricted payments;
- enter into any merger, partnership, joint venture, syndicate, pool, profit-sharing or royalty agreement, or engage in any transactions with our affiliates;
- sell or transfer assets;
- merge; and
- issue equity securities senior to our common stock or convertible or exercisable for equity securities senior to our common stock.

If not cured, as applicable, a breach of any of these provisions could result in a default under the agreement governing the 2014 Convertible Notes that would allow noteholders to declare the outstanding debt immediately due and payable. In addition, the 2014 Convertible Notes are secured by substantially all of our existing and hereafter created or acquired assets, including our intellectual property, accounts receivable, equipment, general intangibles, inventory and investment property, and all of the

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proceeds and products of the foregoing. If we are unable to pay those amounts because we do not have sufficient cash on hand or are unable to obtain alternative financing on acceptable terms, the noteholders could initiate a bankruptcy proceeding or proceed against any assets that serve as collateral to secure the 2014 Convertible Notes.

These restrictions could limit our ability to obtain future financings, make needed capital expenditures, withstand future downturns in the economy or otherwise conduct necessary corporate activities. We may also be prevented from taking advantage of business opportunities that arise because of limitations imposed on us by the restrictive covenants under the 2014 Convertible Notes.

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

In order to raise additional funds to support our operations, business strategies and growth, 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 relatively short operating history may make it difficult for investors to evaluate the success of our business to date and to assess our future viability.

We are a clinical-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 program, obtain regulatory approval, develop a manufacturing plant, 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 and manufacturing activities. We may not be successful in such a transition.

Determining our income tax rate is complex and subject to uncertainty.

The computation of income tax provisions is complex, as it is based on the laws of federal, state, local and non-U.S. taxing jurisdictions and requires significant judgment on the application of complicated rules governing accounting for tax provisions under U.S. GAAP. Our provision for income tax can be materially impacted, for example, by the geographical mix of our profits and losses, changes in our business, such as internal restructuring and acquisitions, changes in tax laws and accounting guidance and other regulatory, legislative or judicial developments, transfer pricing policies, tax audit determinations, changes in our uncertain tax positions, changes in our intent and capacity to permanently reinvest foreign earnings, changes to our transfer pricing practices, tax deductions attributed to equity compensation and changes in our need for a valuation allowance for deferred tax assets. In addition, relevant taxing authorities may disagree with our determinations as to the income and expenses attributable to specific jurisdictions. If such a disagreement were to occur, and our position was not sustained, we could be required to pay additional taxes, interest and penalties, which could result in one-time tax charges, higher effective tax rates and reduced cash flows than otherwise would be expected. For these reasons, our actual income taxes may be materially different than our provision for income tax.

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

If we experience an “ownership change” for purposes of Section 382 of the Internal Revenue Code of 1986, as amended (Section 382), or similar state provisions, 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. As of December 31, 2016, we had federal and state net operating losses of approximately $104.1 million and $122.5 million, respectively, which begin to expire at various dates beginning in 2024, if not utilized. Certain transactions occurred in 2015 and prior years that resulted in ownership changes as defined under Section 382 and similar state provisions, which will limit the future use of certain federal

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and state net operating loss carry-forwards. Those federal and state net operating losses that are not limited are included as deferred tax assets and have been fully offset by a valuation allowance as of December 31, 2016.

The enactment of legislation implementing changes in the U.S. taxation of international business activities or the adoption of other tax reform policies could materially impact our financial position and results of operations.

Recent changes to U.S. tax laws, including limitations on the ability of taxpayers to claim and utilize foreign tax credits, as well as changes to U.S. tax laws that may be enacted in the future, could impact the tax treatment of our potential future foreign earnings. In particular, the tax reform proposals being considered by the new U.S. presidential administration and being considered in the U.S. Congress create uncertainty with respect to the future tax impact on our business operations and potential profitability. For example, certain of the proposals may result in changes to the taxation of cross-border transactions and certain business tax credits or deductions. Other proposals could limit or eliminate the deduction for interest expense. It is unclear whether, when, how and to what extent any of these (or other proposals) will be adopted. Further, due to the expansion of our international business activities, any changes in the U.S. taxation of such activities may increase our worldwide effective tax rate and adversely affect our financial position and results of operations.

Our international operations subject us to potentially adverse tax consequences.

We generally conduct our international operations through wholly-owned subsidiaries and report our taxable income, if any, in various jurisdictions worldwide based upon our business operations in those jurisdictions. Our intercompany relationships are subject to complex transfer pricing regulations administered by taxing authorities in various jurisdictions. The relevant taxing authorities may disagree with our determinations as to the income and expenses attributable to specific jurisdictions. If such a disagreement were to occur, and our position was not sustained, we could be required to pay additional taxes, interest and penalties, which could result in one-time tax charges, higher effective tax rates and reduced cash flows.

Risks Related to Our Reliance on Third Parties

We currently 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 until such a time when we can develop internal manufacturing capabilities, if at all.

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 currently lack the resources and the capabilities to manufacture our product candidates and potential products on a clinical or commercial scale. 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 support our clinical trials. 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.

With respect to production of our potential commercial products in the future, if and when our product candidates are approved for marketing by the applicable regulatory authorities, we plan to outsource the production of the active pharmaceutical ingredients and final product manufacturing until such a time when we can develop internal manufacturing capabilities, if at all. We are working to establish contractual relationships for the commercial production of the active pharmaceutical ingredients with our vendors and currently manage any such production on a purchase order basis. This process is difficult and time consuming and we can give no assurance that we will enter any future commercial supply agreements with any manufacturers on favorable terms or at all.

We have entered into a contractual relationship for the final commercial drug product manufacturing and in January 2017, we entered into a lease agreement for a new manufacturing plant in Athlone, Ireland. If approved, commercial product supply of Rhopressa™ from the plant is expected to be available by 2020. However, there can be no assurance that we will be able to develop the manufacturing capabilities required to produce our final drug product on a commercial scale or in accordance with manufacturing regulations. See “-Risks Related to Development, Regulatory

Approval and Commercialization-We have no experience manufacturing our product candidates, and we cannot assure you that we will be able to manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable." If our manufacturing operations fail to achieve regulatory approval or to effectively produce commercial supplies of our product candidates, or until such time we are capable of developing internal manufacturing capabilities, we will be required to rely solely on third-party manufacturers to meet our commercial manufacturing needs, which may materially adversely affect our business, results of operations or financial condition.

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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;
- delays in obtaining regulatory approval for our product candidates, if our third-party manufacturers fail to satisfy or comply with regulatory requirements;
- 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.

For example, in October 2016, we were required to withdraw the initial submission of our NDA filing for Rhopressa™ due to a contract manufacturer of our drug product not being prepared for pre-approval inspection by the FDA. We resubmitted the Rhopressa™ NDA on February 28, 2017 upon receiving confirmation from the contract manufacturer that it is prepared for FDA inspection. Although we have been advised that the contract manufacturer is prepared for FDA inspection, there can be no assurance that the contract manufacturer's facility will meet FDA standards.

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

Before we or a third party can begin commercial manufacture of our product candidates and potential products, we or the third party must obtain regulatory approval of our or their manufacturing facilities, processes and quality systems. If our third party manufacturers do not have a cGMP compliance status acceptable to the FDA, approval of any NDA that includes those third party manufacturers will be delayed.

Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, we or any potential third-party manufacturer may be unable to initially pass federal, state or international regulatory inspections in a cost effective manner. We or certain of our contract manufacturers may fail to satisfy or comply with manufacturing regulations. If we or our contract manufacturers are not approved by the FDA, regulatory approval of our product candidates and/or commercial supply of active pharmaceutical ingredients will be significantly delayed and may result in significant additional costs.

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. We or our contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. In addition, 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 we or a third-party manufacturer with whom we contract is unable to comply with manufacturing regulations, we may 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-

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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 continually explore and discuss additional opportunities for new ophthalmic products, delivery alternatives and new therapeutic areas with potential partners. We may seek collaboration arrangements with pharmaceutical or biotechnology companies or universities for the development or commercialization of our current and potential future product candidates. 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, implement and maintain collaborations or other alternative arrangements and the terms of such arrangements may not be favorable to us. If and when we collaborate with a third party for development and commercialization of a product candidate and/or technology, we can expect to relinquish some or all of the control over the future success of that product candidate and/or technology 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. Accordingly, there can be no assurance that any collaboration or licensing arrangement or similar strategic transaction we enter into will result in the benefits that we anticipate.

Disagreements between parties to a collaboration arrangement regarding research, clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate or technology 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. In addition, collaborators may not pursue development and commercialization of our preclinical molecules or product candidates or may elect not to continue or renew development or commercialization programs based on our results, changes in their strategic focus due to the acquisition of competitive products or technologies, availability of funding, or other external factors, such as a business combination that diverts resources or creates competing priorities. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. For example, in 2016, we terminated our collaboration and licensing arrangements with GrayBug, Inc. for drug delivery technology and elected not to extend our collaboration agreement with Ramot at Tel Aviv University, Ltd. for a preclinical anti-beta amyloid molecule. Any such termination or expiration may 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 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 GCP 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.

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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. 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 potential 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 potential 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 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, pharmaceutical formulations, methods of use, and synthetic methods. As of December 31, 2016, we own 21 patents and have 12 pending patent applications in the United States and certain foreign jurisdictions for our primary product candidates Rhopressa™ and Roclatan™. Patent protection for Roclatan™ arises from the U.S. patents that cover Rhopressa™. The patents cover composition of matter and method of use. We own 49 patents and have 13 pending patent applications in the United States and certain foreign jurisdictions relating to our previously discontinued product candidates and other proprietary technology. See "Business—Intellectual Property" included elsewhere in this report 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:

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- 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 market for our Rhopressa™ and Roclatan™ product candidates;
- we do not at this time own or control issued foreign patents outside of Australia, Canada, and 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;
- 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 ANDAs 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 December 31, 2016, we own 70 patents and have 25 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 report for further information about our issued patents and patent applications. Our issued patents include 21 patents for composition of matter and method of use covering our lead product candidate, Rhopressa™ in the United States and certain foreign jurisdictions. These patents also cover our other primary product candidate Roclatan™ to the extent

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that Rhopressa™ forms a part of Roclatan™. The remainder of our portfolio is made up of patents covering previously discontinued product candidates and other proprietary technology and pending patent applications that have not yet been issued by the USPTO, or any other jurisdiction that covers 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.

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. It may be difficult for us to stop the infringement of our patents or the misappropriation of these intellectual property rights in any foreign jurisdictions. 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 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

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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 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

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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.

We assigned the trade names Rhopressa™ and Roclatan™ to our lead product candidates in 2014, with trademark applications for registration pending from the USPTO. These and any other names 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.

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.

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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 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.

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

We are currently a small company with 95 full-time employees as of December 31, 2016. In order to commercialize and manufacture 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. Our management, personnel and systems currently in place may not be adequate to support our 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 development of our manufacturing plant and the manufacturing of product candidates and potential products for clinical and commercial use;
- integrate current and additional management, administrative, financial, manufacturing and sales and marketing personnel;
- develop a marketing and sales infrastructure;
- hire new personnel necessary to effectively commercialize and manufacture our product candidates;
- continue to develop and maintain 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.

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 adopted a code of conduct, but it is not always possible to

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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.

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 and when our product candidates are approved, 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 potential products. Similarly, these macroeconomic factors could affect the ability of our potential future contract manufacturers, sole-source or single-source suppliers, collaboration partners or licensees to remain in business or otherwise develop, manufacture or supply product. Failure by any of them to remain in business could affect our ability to manufacture potential products.

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

We may attempt to acquire or license 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 or licenses. However, if we do undertake any acquisitions or licenses, the process of integrating an acquired or licensed business, technology, service, product or product candidate into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management’s attention from our core 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 or licenses could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions or licenses could also result in the incurrence of debt, actual or contingent liabilities or the amortization of expenses related to intangible assets, any of which could adversely affect our operating results.

We have limited experience identifying, negotiating and implementing acquisitions or licenses of additional businesses, technologies, services, products or product candidates, which is a lengthy and complex process. The market for acquiring or licensing businesses, technologies, services, products or product candidates is intensely competitive, and other companies, including some with substantially greater financial, marketing and sales resources, may also pursue strategies to acquire or license businesses, technologies, products or product candidates that we may consider attractive. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us.

We have limited resources to identify and execute the acquisition or licensing of additional businesses, technologies, services, products, or product candidates and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire or license the rights to additional businesses, technologies, services, products or product candidates on terms that we find acceptable, or at all. In particular, any product candidate that we acquire or license may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities.

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Business interruptions could delay the development of our potential products and our manufacturing acitivies, and could disrupt our potential sales.

Our principal executive offices are located in Irvine, California, our clinical and finance operations are located in Bedminster, New Jersey and our research and development facility is located in Durham, North Carolina. We also have offices in Malta and Ireland and recently signed a lease for a new manufacturing plant in Ireland. We are vulnerable to natural disasters, such as severe storms and other events that could disrupt our operations. We carry limited 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, manufacturing activities and/or potential commercialization efforts. 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 or commercialization of our current and potential future product candidates could be delayed.

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

As a public company, we are subject to the periodic reporting requirements of 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 SEC. We 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.

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;

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- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- 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.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been, and may continue to be, highly volatile.

Our stock price has been volatile and is likely to continue to be volatile. The following factors, in addition to other factors described in this "Risk Factors" section, may have a significant impact on the market price of our common stock:

- the results of our testing and clinical trials, including the results of our Phase 3 registration trials for Rhopressa™ and Roclatan™;
- 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 relationships with manufacturers, suppliers, licensees or collaboration partners;
- the results of our efforts to develop, acquire or license additional product candidates or technologies;
- 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;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our quarterly or annual operating results;

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- 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 capital 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, any decline in the financial markets and related factors beyond our control may cause our stock price to decline rapidly and unexpectedly.

We previously had been named a defendant in a purported securities class action lawsuit. This, and any additional securities litigation, could result in substantial damages and may divert management's time and attention from our business.

A putative securities class action lawsuit captioned Kelley et al. v. Aerie Pharmaceuticals, Inc., et al., Case No. 3:15-cv-03007, was filed against us and certain of our officers and directors in the United States District Court for the District of New Jersey on April 29, 2015. An amended complaint was filed on September 28, 2015 on behalf of a purported class of persons and entities who purchased or otherwise acquired our publicly traded securities between June 25, 2014 and April 23, 2015. The amended complaint asserted claims under the Securities Exchange Act of 1934, as amended, and alleged that the defendants made materially false and misleading statements or omitted allegedly material information during that period related to, among other things, the prospects of our initial Phase 3 registration trial of Rhopressa™, named "Rocket 1," and Rhopressa™. On November 30, 2015, the defendants filed a motion to dismiss the amended complaint. On June 20, 2016, the United States District Court for the District of New Jersey granted the defendants' motion to dismiss the amended complaint. The time for a motion for reconsideration and/or appeal has expired. The matter has now concluded.

If our stock price experiences volatility, we may be the subject of additional securities 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. Monitoring and defending against legal actions is time-consuming for our management and detracts from our ability to fully focus on our business activities. Any adverse determination in litigation could also subject us to significant liabilities.

Certain of our existing stockholders, executive officers and directors own a significant percentage of our common stock and may be able to influence or control matters submitted to our stockholders for approval.

Our officers and directors, and stockholders who own more than 5% of our outstanding common stock, beneficially own approximately 51.7% of our common stock as of December 31, 2016. 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 ownership concentration. Some or all of our stockholders may be able to influence or determine 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 other stockholders may feel are in their best interest, and certain of our existing stockholders 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.

Additionally, under certain circumstances, our amended and restated certificate of incorporation renounces any interest or expectancy that we have in, or in being offered an opportunity to participate in, corporate opportunities that are presented to certain of our existing stockholders or their affiliates and certain other related parties (whether or not

any such person is 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.

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Sales of a substantial number of shares of our common stock in the public market 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. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.
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 may 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 continue to 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 the 2014 Convertible Notes and 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 for the foreseeable future.
The requirements associated with being a public company require significant company resources and management attention.
We are 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 have incurred, and we will continue to 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 Jumpstart Our Business Startups Act of 2012, or 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.
The JOBS Act allows 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:

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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; and

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- 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.

We currently take advantage of some, but not all, of the reduced regulatory and reporting requirements that are 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 is not 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 investors 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.

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) December 31, 2018; (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.

If the market value of our common stock held by non-affiliates continues to exceed $700 million as of June 30, 2017, as of the end of the year ending December 31, 2017, we would cease to be an "emerging growth company." If we cease to be an "emerging growth company," beginning with our annual report on Form 10-K for the year ending December 31, 2017, we will be subject to Section 404(b) of the Sarbanes-Oxley Act, which requires that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting. Compliance with Section 404 will be expensive and time consuming for management and could result in the detection of internal control deficiencies of which we are currently unaware. Moreover, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis, and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal controls over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our common stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our results of operations on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Market or other adverse consequences that would materially harm our business.

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, 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;

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- 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal executive offices are located in Irvine, California, our clinical and finance operations are located in Bedminster, New Jersey and our research and development facility is located in Durham, North Carolina. We also have offices in Malta and Ireland and recently signed a lease for a new manufacturing plant in Athlone, Ireland. Our Irvine, California location consists of approximately 14,500 square feet of office space under a lease that expires in January 2021 and our Bedminster, New Jersey location consists of approximately 16,000 square feet of office space under a lease that expires in August 2020. Our Durham, North Carolina research and development facility consists of approximately 19,500 square feet of laboratory and office space under a lease that expires in January 2022. Our new manufacturing plant in Ireland consists of approximately 30,000 square feet of interior floor space for future build-out and is under lease through at least September of 2027. We may require additional space and facilities as our business expands.

ITEM 3. LEGAL PROCEEDINGS

We may periodically become subject to legal proceedings and claims arising in connection with our business. Except as set forth below, we are not a party to any known litigation, are not aware of any unasserted claims and do not have contingency reserves established for any litigation liabilities.

A putative securities class action lawsuit captioned Kelley et al. v. Aerie Pharmaceuticals, Inc., et al., Case No. 3:15-cv-03007, was filed against us and certain of our officers and directors in the United States District Court for the District of New Jersey on April 29, 2015. An amended complaint was filed on September 28, 2015 on behalf of a purported class of persons and entities who purchased or otherwise acquired our publicly traded securities between June 25, 2014 and April 23, 2015. The amended complaint asserted claims under the Securities Exchange Act of 1934, as amended, and alleged that the defendants made materially false and misleading statements or omitted allegedly material information during that period related to, among other things, the prospects of our initial Phase 3 registration trial of Rhopressa™, named “Rocket 1,” and Rhopressa™. On November 30, 2015, the defendants filed a motion to dismiss the amended complaint. On June 20, 2016, the United States District Court for the District of New Jersey granted the defendants’ motion to dismiss the amended complaint. The time for a motion for reconsideration and/or appeal has expired. The matter has now concluded.

ITEM 4. MINE SAFETY DISCLOSURES

None.

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PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is traded on the NASDAQ Global Market under the symbol "AERI." On February 28, 2017, the closing price for our common stock as reported on the NASDAQ Global Market was $47.35. The following table sets forth the high and low intraday sale prices per share of our common stock for the periods indicated as reported by the NASDAQ Global Market.

	High	Low
2016		
Fourth Quarter	$43.40	$32.05
Third Quarter	41.72	16.61
Second Quarter	19.99	11.89
First Quarter	24.08	10.82
2015		
Fourth Quarter	$28.21	$16.52
Third Quarter	33.25	14.29
Second Quarter	35.89	8.84
First Quarter	32.07	22.36

Stockholders

As of February 28, 2017, we had 33,626,226 shares of common stock outstanding held by approximately 5 stockholders of record. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in "street" name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since October 25, 2013, which is the date our common stock first began trading on the NASDAQ Global Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on October 25, 2013, in our common stock and in each index. It also assumes reinvestment of dividends, if any. Historical stockholder return shown is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

*This performance graph shall not be deemed “soliciting material” or be deemed “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Dividend Policy

We have not declared or paid any cash dividends on our capital stock in the last two fiscal years. 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 our current and 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 for at least the foreseeable future.

Purchase of Equity Securities

We did not purchase any of our equity securities during the period covered by this report.

Recent Sales of Unregistered Securities

None.

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Use of Proceeds from Registered Securities

On November 3, 2014, we filed a shelf registration statement on Form S-3 (the "2014 Registration Statement") that permitted the offering, issuance and sale by us of up to a maximum aggregate offering price of $150.0 million of our common stock and permits sales of common stock by certain selling stockholders.

From November 10, 2014 through December 31, 2016, we issued and sold 5,933,712 shares of common stock under our former "at-the-market" sales agreements, of which 4,179,156 shares were issued and sold during the year ended December 31, 2016, and received net proceeds of approximately $146.6 million, of which $96.2 million were received during the year ended December 31, 2016, in each case, after deducting commissions at a rate of up to 3% of the gross sales price per share sold and other fees and expenses. Sales under the "at-the-market" sales agreement were made pursuant to the 2014 Registration Statement. As of December 31, 2016, no shares remain available for issuance under the "at-the-market" sales agreements or the 2014 Registration Statement.

Any remaining net proceeds from these sales are held as cash deposits and in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

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ITEM 6. SELECTED FINANCIAL DATA

	125,057
Interest expense, net	
	(509,103)
	(461,145)
OTHER INCOME (EXPENSE)	
	(684,121)
	1,178,734
NET LOSS	
$	(3,417,205)
$	(3,362,853)
PER COMMON SHARE DATA	
NET LOSS PER SHARE:	
BASIC and DILUTED	
$	(0.01)
$	(0.01)
WEIGHTED AVERAGE SHARES:	
BASIC and DILUTED	
	632,009,690

420,841,556

See accompanying notes to consolidated financial statements

WORLD SURVEILLANCE GROUP INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT
FOR THE YEARS ENDED DECEMBER 31, 2013 AND 2012

	COMMON STOCK		ADDITIONAL PAID-IN
Description	SHARES	AMOUNT	CAPITAL
BALANCE, DECEMBER 31, 2011	426,884,160	$ 4,269	$ 131,426,211
Shares issued for convertible debt conversion	81,785,908	818	1,692,053
Shares issued for services	13,140,325	131	458,848
Shares issued for legal settlements	16,715,543	167	269,158
Shares issued for directors' compensation	12,700,000	127	586,793
Shares issued for compensation and accrued salaries	12,978,261	130	396,170
Fair value of vested restricted shares issued for compensation	5,000,000	50	58,929
Vested restricted shares previously issued as performance-based compensation	0	0	342,370
Common and restricted shares rescinded and exchanged for fully-vested options	(22,316,667)	(223)	223
Fair value of vested options issued as share-based compensation	0	0	598,439
Net loss	0	0	0
BALANCE, DECEMBER 31, 2012	546,887,530	$ 5,469	$ 135,829,194
Shares issued as inducement for loans	2,000,000	20	34,380
Shares issued for cash	6,000,000	60	119,940
Shares issued for legal settlements	24,741,372	247	338,879
Shares issued for services	24,972,500	250	367,000
Shares issued for LTAS acquisition	25,000,000	250	672,250
Shares issued for LTAS selling shareholder debt	20,000,000	200	191,800
Shares issued for directors' fees	900,000	9	13,881
Shares issued for accrued salaries	7,692,308	77	99,923
Shares issued for convertible debt	2,933,333	29	76,310
Fair value of vested restricted shares issued as retention bonuses	20,000,000	200	85,768
Fair value of vested options issued as share-based compensation and director's fees	0	0	339,697
Common and restricted shares rescinded and exchanged for fully-vested options	(12,000,000)	(120)	216,120
	0	0	524,624

Fair value of vested options issued for salary conversions					
Net loss	0		0		0
BALANCE, DECEMBER 31, 2013	669,127,043	$	6,691	$	138,909,766

(continued)

See accompanying notes to consolidated financial statements

WORLD SURVEILLANCE GROUP INC. AND SUBSIDIARIES (continued)
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT
FOR THE YEARS ENDED DECEMBER 31, 2013 AND 2012

Description	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' DEFICIT
BALANCE, DECEMBER 31, 2011	(145,632,499)	(14,202,019)
Shares issued for convertible debt conversion	0	1,692,871
Shares issued for services	0	458,979
Shares issued for legal settlements	0	269,325
Shares issued for directors' compensation	0	586,920
Shares issued for compensation and accrued salaries	0	396,300
Fair value of vested restricted shares issued for compensation	0	58,979
Fair value of vested restricted shares previously issued as performance-based compensation	0	342,370
Common and restricted shares rescinded and exchanged for fully-vested options	0	0
Fair value of vested options issued as share-based compensation	0	598,439
Net loss	(3,362,853)	(3,362,853)
BALANCE, DECEMBER 31, 2012	$ (148,995,352)	$ (13,160,689)
Shares issued as inducement for loans	0	34,400
Shares issued for cash	0	120,000
Shares issued for legal settlements	0	339,126
Shares issued for services	0	367,250
Shares issued for LTAS acquisition	0	672,500
Shares issued for LTAS selling shareholder debt	0	192,000
Shares issued for directors' fees	0	13,890
Shares issued for accrued salaries	0	100,000
Shares issued for convertible debt	0	76,339
Fair value of vested restricted shares issued as retention bonuses	0	85,968
Fair value of vested options issued as share-based compensation and director's fees	0	339,697
Common and restricted shares rescinded and exchanged for fully-vested options	0	216,000
Fair value of vested options issued for salary conversions	0	524,624
Net loss	(3,417,205)	(3,417,205)
BALANCE, DECEMBER 31, 2013	$ (152,412,557)	$ (13,496,100)

See accompanying notes to consolidated financial statements

WORLD SURVEILLANCE GROUP INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS
FOR THE YEARS ENDED DECEMBER 31,

	2013	2012
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$ (3,417,205)	$ (3,362,853)
Adjustments to reconcile net loss to net cash used by operating activities:		
Depreciation and amortization	184,915	183,000
Fair value of share-based compensation	664,596	1,879,813
Change in fair value of derivative liabilities	(363)	(125,057)
Net gain on release of restricted assets and derecognition of liabilities of discontinued operations	0	(544,201)
Gain on derecognition of legacy payables	0	(1,787,324)
Loss on conversion of convertible debt	233,382	1,304,712
Gain on settlement of LTAS selling shareholder debt	(58,000)	0
Loan interest capitalized to debt	432,703	420,078
Shares issued as inducement to loans	34,400	0
Amortization of deferred financing costs	20,676	18,952
Change in operating assets and liabilities:		
Accounts receivables	120,447	(8,977)
Accounts receivable from related party	(11,613)	(27,334)
Inventories	154,387	4,500
Prepaid expenses	8,974	56,015
Deposits	50,000	(50,000)
Accounts payable	186,333	535,051
Accounts payable due related party	(57,003)	0
Accrued liabilities	1,100,065	804,622
Deferred revenues	(5,850)	(197,160)
NET CASH USED IN OPERATING ACTIVITIES	(359,156)	(896,163)
CASH FLOWS FROM INVESTING ACTIVITIES		
Acquisition, net of cash acquired	158,545	0
NET CASH PROVIDED BY INVESTING ACTIVITIES	158,545	0
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from sale of common stock	120,000	0
Notes payable	150,000	0
Proceeds from convertible debt, net of deferred financing costs	0	354,974
Proceeds from purchases under the Equity Investment Agreement	0	585,000
NET CASH PROVIDED BY FINANCING ACTIVITIES	270,000	939,974
NET CHANGE IN CASH	69,389	43,811
CASH – BEGINNING OF YEAR	49,343	5,532
CASH – END OF YEAR	$ 118,732	$ 49,343
SUPPLEMENTAL DISCLOSURES		
Cash paid during the period for:		
Interest	$ 0	$ 0
NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Reclassification of long-term convertible notes payable to current notes payable	267,000	0

Common stock issued for LTAS acquisition	672,500	0
Common stock issued for settlement of LTAS selling shareholder debt	192,000	0
Common stock issued in exchange for convertible debt	76,339	1,692,871
Common stock issued as payments for services	367,250	458,979
Common stock issued for accrued settlements	339,126	269,325
Common stock issued as payments for accrued salaries and directors' fees	100,000	103,200
Fair value of vested options issued for accrued salary conversions	524,624	0

See accompanying notes to consolidated financial statements

WORLD SURVEILLANCE GROUP INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
YEARS ENDED DECEMBER 31, 2013 AND 2012

NOTE 1. SUMMARY OF SIGNIFICANT ACCOUNTING PRINCIPLES

DESCRIPTION OF BUSINESS

World Surveillance Group Inc. (the "Company") designs, develops, markets, and sells, autonomous lighter-than-air (LTA) aerostats and unmanned aerial systems (UAS) capable of carrying payloads that provide semi-persistent intelligence, surveillance and reconnaissance (ISR), security and/or wireless communications from air to ground solutions at low and mid altitudes. The Company's business focuses primarily on the design and development of innovative aerostats and UAS that provide situational awareness and other communications capabilities via the integration of wireless capabilities and customer payloads. The Company's aerostats and airships, when integrated with cameras, electronics systems and other high technology payloads, are designed for use by government-related and commercial entities that require real-time ISR or communications support for military, homeland defense, border control, drug interdiction, natural disaster relief, maritime and environmental missions.

The Company's wholly owned subsidiary Global Telesat Corp. (GTC), provides mobile voice and data communications services globally via satellite to the U.S. government, defense industry and commercial users. GTC specializes in services related to the Globalstar satellite constellation, including satellite telecommunications voice airtime, tracking devices and services, and ground station construction. GTC has an e-commerce mobile satellite solutions portal and is an authorized reseller of satellite telecommunications equipment and services offered by other leading satellite network providers such as Inmarsat, Iridium, Globalstar and Thuraya. GTC also has a new subscription based online tracking portal called GTCTrack, designed to attract new satellite and GSM tracking customers by offering an easy-to-use interface and compatibility with a wide range of devices. GTC's equipment is installed in various ground stations across Africa, Asia, Australia, Europe and South America.

The Company's wholly owned subsidiary Lighter Than Air Systems Corp. (LTAS), provides critical aerial and land-based surveillance and communications solutions to government and commercial customers. LTAS systems are designed and developed in-house utilizing proprietary technologies and processes that result in compact, rapidly deployable aerostat solutions and mast-based ISR systems. The LTAS systems have been proven to fulfill critical requirements of the military and law enforcement in the U.S. and internationally.

PRINCIPLES OF CONSOLIDATION AND BASIS OF PRESENTATION

The accompanying consolidated financial statements of World Surveillance Group Inc. and its subsidiaries were prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") and include the assets, liabilities, revenues and expenses of all majority-owned subsidiaries over which the Company exercises control and, where applicable entities for which the Company has a controlling financial interest or is the primary beneficiary.

All material intercompany accounts and transactions are eliminated in consolidation.

The preparation of financial statements in accordance with U.S. GAAP requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. The

Company's consolidated financial statements include amounts that are based on management's best estimates and judgments. Actual results could differ from those estimates.

RECLASSIFICATIONS

Certain 2012 amounts have been reclassified to conform to the 2013 presentation.

GOING CONCERN

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. However, as reflected in the accompanying consolidated financial statements, the Company incurred a loss from operations of $2,733,084 and negative cash flows from operations of $359,156 for the year ended December 31, 2013. The Company had a working capital deficit of $16,598,286 and total stockholders' deficit of $13,496,100 at December 31, 2013. The Company had an accumulated deficit of $152,412,557 at December 31, 2013. These factors raise substantial doubt about the Company's ability to continue as a going concern. The Company's ability to continue as a going concern is dependent upon its ability to raise additional funds either through investments or by generating revenue from the sale of the Company's products to continue its business operations and implement its strategic plan, which includes, among other things, continued development of its aerostats and UAS, the pursuit or continued development of strategic relationships and expansion of the Company's subsidiaries' businesses. The Company's business plan, which if successfully implemented, will allow it to sell its products for a profit, which in turn will reduce the Company's dependence on raising additional funds from outside sources. The consolidated financial statements do not include any adjustments that might be necessary if the Company is unable to continue as a going concern. The Company anticipates a net loss to continue for at least the next several quarters if not for all of the year 2014.

Additional cash will be needed to support our ongoing operations until such time that operations provide sufficient cash flow to cover expenditures. We are currently pursuing both short and long-term financing options from private investors as well as through institutional investors. We are also working to commercialize our aerostats, Argus One airship, and subsidiaries' products to begin generating revenues from customers. We are already generating revenue from our aerostats, mast-based products and GTC products. The costs associated with our strategic plan are variable and contingent on our ability to raise capital or begin generating revenue from customer contracts, but we expect to need funding of approximately $3 million over the next 12 months. We are currently in litigation with La Jolla Cove Investors and do not expect any future financing under those agreements. We continue to have discussions with various entities relating to funding, but there can be no assurance that such funding will be received in the amounts required, on a timely basis, or at all. While we believe we will be able to continue to raise capital from various funding sources in such amounts sufficient to sustain operations at our current levels through at least December 31, 2014, if we are not able to do so and if we are not able to generate revenue through the sale of our products, we would likely need to modify our strategy or cut back or terminate some of our operations. If we are able to raise additional funds through the issuance of equity securities, substantial dilution to existing shareholders may result. However, if our plans are not achieved and/or if significant unanticipated events occur or if we are unable to obtain the necessary additional funding on favorable terms or at all, we will likely have to modify our business plan and reduce, delay or discontinue some or all of our operations to continue as a going concern or seek a buyer for all or a portion of our assets. As of the date hereof, we continue to raise capital to sustain our current operations.

REVENUE RECOGNITION

The Company recognizes revenue when all four of the following criteria are met: 1) persuasive evidence of an arrangement exists; 2) delivery has occurred and title has transferred or services have been rendered; 3) our price to the buyer is fixed or determinable; and 4) collectability is reasonably assured. The Company records unearned contract revenues and subscription fees as deferred revenues and their associated costs of sales as prepaid expenses. Deferred revenue from contracts and their related costs are recognized upon completion and fulfillment of the contractual obligation using the completed contract method. During 2012, the Company recognized $200,000 in contract revenue, previous recorded as deferred revenue. Deferred revenues from subscription fees and their related costs are amortized over the subscription term.

INCOME TAXES

The Company accounts for income taxes using the asset and liability approach. Under this approach, deferred income taxes are recognized based on the tax effects of temporary differences between the financial statement and tax bases of assets and liabilities, as measured by current enacted tax rates. Valuation allowances are recorded to reduce the deferred tax assets to an amount that will more likely than not be realized.

U.S. GAAP requires that, in applying the liability method, the financial statement effects of an uncertain tax position be recognized based on the outcome that is more likely than not to occur. Under this criterion the most likely resolution of an uncertain tax position should be analyzed based on technical merits and on the outcome that will likely be sustained under examination. There were no adjustments related to uncertain tax positions recognized during the years ended December 31, 2013 and 2012, respectively.

DISCLOSURES ABOUT FAIR VALUE OF FINANCIAL INSTRUMENTS

The Company's financial instruments include cash, accounts payable, notes payable. The carrying values for the current financial assets and liabilities approximate fair value due to their short maturity.

BASIC AND DILUTED NET LOSS PER COMMON SHARE

Basic and diluted net loss per common share has been computed by dividing the net loss by the weighted average number of shares of common stock outstanding during each period. Whenever losses are reported, the weighted average number of common shares outstanding excludes common stock equivalents because their inclusion would result in a diluted loss per share less than the basic loss per share and therefore would be anti-dilutive. Whenever net income is reported, the weighted average number of common shares outstanding will include common stock equivalents that are in-the-money. If all outstanding options, warrants and convertible shares were converted or exercised as of December 31, 2013, the shares outstanding would be 802,338,749.

PROPERTY AND EQUIPMENT

Property and equipment are carried at historical cost less accumulated depreciation. Depreciation is based on the estimated service lives of the depreciable assets and is calculated using the straight-line method. Expenditures that increase the value or productive capacity of assets are capitalized. Fully depreciated assets are retained in the property and equipment, and accumulated depreciation accounts until they are removed from service. When property and equipment are retired, sold or otherwise disposed of, the asset’s carrying amount and related accumulated depreciation are removed from the accounts and any gain or loss is included in operations. Repairs and maintenance are expensed as incurred.

The estimated useful lives of property and equipment are generally as follows:

·	Appliqués and ground stations	15 – 25 years
·	Machinery and equipment	3 – 12 years
·	Office furniture and fixtures	3 – 10 years
·	Computer hardware and software	3 – 7 years
·	Transportation vehicles	3 – 6 years

LONG LIVED ASSETS

The Company evaluates the fair value of long-lived assets on an annual basis or whenever events or changes in circumstances indicate that its carrying amounts may not be recoverable. Accordingly, any impairment of value is recognized when the carrying amount of a long-lived asset exceeds its fair value. The Company's evaluations have not indicated any impairment of fair values.

SHARE-BASED COMPENSATION

The Company offers share-based compensation programs to its officers, directors and employees that consist of employee stock options, common stock and restricted stock awards. Common stock and restricted stock awards are issued at the closing price of the Company's common stock on the date of grant. The Company recognizes compensation expense ratably over the vesting periods for restricted stock awards using the grant date fair value of the stock awarded. The Black-Scholes option pricing model is used to value stock options, and compensation expense is recognized ratably over the requisite service vesting period. Stock options typically have contractual terms of three to seven years. Share-based compensation for employees and non-employees is reflected in the appropriate functional expense category, primarily general and administrative, and research and development. Share-based compensation incurred during the years ended December 31, 2013 and 2012 was $991,893 and $1,983,008, respectively.

NOTE 2. DISCONTINUED OPERATIONS

In 2007, the Company discontinued operations of its telecom and wireless segments and reported the effects as discontinued operations.
During the quarter ended June 30, 2012, the Company conducted a detailed analysis of certain of its accounts payable and accrued liabilities including (i) liabilities from discontinued operations of $1,365,929, and (ii) legacy payables and accrued liabilities of $1,787,324. Accounts payable includes an amount for legal judgments that were excluded from the potential write-off. The remaining analyzed liabilities from discontinued operations and legacy payables and accrued liabilities are no longer enforceable debts of the Company due to the passage of the applicable statutes of limitation and were written-off the books of the Company. These liabilities along with the assets of discontinued operations of $6,406 have resulted in an aggregate gain of $2,331,525, comprised of the gain on the release of restricted assets and derecognition of liabilities of discontinued operations of $544,201 and the gain on the derecognition of legacy payables of $1,787,324.

NOTE 3. ACQUISITIONS

On March 28, 2013, the Company consummated a Stock Purchase Agreement (the "Agreement") by and among the Company, Lighter Than Air Systems Corp. ("LTAS"), Felicia Hess (the "Shareholder") and Kevin Hess ("KHess") pursuant to which the Company acquired 100% of the outstanding shares of capital stock of LTAS, thereby making LTAS a wholly-owned subsidiary of the Company.

The purchase price paid by the Company for LTAS consisted of $250,000 in cash payable on or before the date that is 30 days after the closing of the acquisition (the "Closing"), 25,000,000 shares of the Company's common stock valued at the acquisition date based on the market price of $0.0269 per share, and an earn-out based on varying percentages of the gross revenues based on the level of revenue from contracts with an identified group of potential customers. No value was ascribed to the earn-out because future revenues, if any, cannot be reliably predicted. Pursuant to the Agreement and an Escrow Agreement, 7,500,000 shares of common stock out of the 25,000,000 shares issued by the Company have been placed in escrow for one year to satisfy possible indemnification claims of the Company. Felicia Hess, the President of LTAS, has entered into an employment agreement to continue in her role as President of LTAS. The Agreement also includes restrictions on the sale of the Company's securities issued as the purchase price by the Shareholder for a one-year period following the Closing.

The Shareholder has the right pursuant to the Agreement to nominate one member of the Company's Board of Directors, and as a result, the size of the Company's Board of Directors has been increased and Felicia Hess has been appointed as a Class I director as of March 28, 2013. Since Ms. Hess would not be an "independent" director pursuant to the rules of the Securities and Exchange Commission, it is not expected that she will be appointed to any committees.

In connection with the Closing, LTAS, the Shareholder and the Company also entered into an Option Agreement dated March 28, 2013 pursuant to which the Shareholder was granted an exclusive option to purchase the shares of LTAS held by WSGI on the occurrence of (i) a WSGI bankruptcy event, or (ii) a decrease in the daily volume of WSGI's common stock to below 50,000 shares for 30 consecutive days, occurring within 18 months of the Closing at a purchase price equal to the fair market value of the LTAS stock at the time of such triggering event, as determined by an independent valuation firm.

The common stock of the Company issued as purchase price pursuant to the Agreement was issued as restricted securities under an exemption provided by Section 4(2) of the Securities Act of 1933, as amended. The Agreement, however, provides the Shareholder with certain piggyback registration rights.

LTAS provides critical aerial and land-based surveillance and communications solutions to government and commercial customers. LTAS systems are designed and developed in-house utilizing proprietary technologies and processes that result in compact, rapidly deployable aerostat solutions and mast-based ISR systems. The LTAS systems have been proven to fulfill critical requirements of the military and law enforcement in the U.S. and internationally.

On December 31, 2013, the Company entered into a First Amendment to Agreement (the "First Amendment") by and among the Company, Lighter Than Air Systems Corp. ("LTAS"), Felicia Hess (the "Shareholder") and Kevin Hess ("KHess"), which amended and restated various terms and conditions of the Agreement and revised the purchase price from 25 million shares plus $250,000 cash payment to 45 million shares and no cash payment due the selling shareholder and deleted the earn-out payment provisions in their entirety.

The Company's Consolidated Balance Sheet at December 31, 2013 includes the accounts of LTAS amended and restated pursuant to the First Amendment to the Agreement. The operating results of LTAS since the acquisition date of March 28, 2013 are reflected in the Company's Consolidated Statements of Operations.

The following table summarizes the original allocation of the LTAS acquisition purchase price, which has been accounted at the fair values of the assets acquired and liabilities assumed under the acquisition method of accounting adjusted pursuant to the First Amendment to the Agreement:

	Original Allocation	Allocation Adjustments	Amended Allocation
Current assets	$ 703,220	$ 7,195	$ 710,415
Property and equipment	1,357	2,556	3,913
Goodwill	479,585	328,239	807,824
Due to selling shareholder	0	(350,000)	(350,000)
Current liabilities assumed	(261,662)	12,010	(249,652)
Total Purchase Price	$ 922,500	$ 0	$ 922,500

NOTE 4. RELATED PARTY TRANSACTIONS

The accounts receivable from related party at December 31, 2013 and 2012, includes trade receivables from Global Telesat Communications, Ltd. ("GTCL") of $59,833 and $48,220, respectively. GTCL is a related party based in the United Kingdom and controlled by a current officer of GTC. Total sales to GTCL for the years ended December 31, 2013 and 2012 were $478,582 and $632,992, respectively, and account for 75% and 71% of GTC's total sales for the respective periods. GTC began charging a 10% handling fee on all orders from GTCL in 2012.

The accounts payable due to related party at December 31, 2013, includes allocated rent charges, aerostat envelopes, and labor charges due Aerial Products Corp ("APC") of $50,691. APC is a related party, controlled by a current employee of the Company. APC shares the manufacturing facilities with LTAS and provides aerostat envelopes and manufacturing labor to LTAS. Total charges from APC to LTAS during the period ended December 31, 2013 were $28,589.

NOTE 5. PROPERTY AND EQUIPMENT

Property and equipment consisted of the following:

	December 31, 2013	December 31, 2012
Appliqués	$ 2,755,732	$ 2,755,732
Office furniture and fixtures	13,4654	6,904
	2,769,197	2,762,636
Less: accumulated depreciation	(497,233)	(309,670)
	$ 2,271,964	$ 2,452,966

NOTE 6. OTHER ACCRUED LIABILITIES

Accrued liabilities consisted of the following:

	December 31, 2013	December 31, 2012
Payroll liabilities	$ 1,908,171	$ 1,494,883
Professional fees	10,000	10,000
Accrued legal claims payable	354,684	334,540
Accrued cash true-up from conversion	353,873	176,831
Accrued interest on debenture	31,133	18,243
GTC acquisition payable	75,000	75,000
Other	80,092	22,588
OTHER ACCRUED LIABILITIES	$ 2,812,953	$ 2,132,085

NOTE 7. NOTES PAYABLE

Notes payable is comprised of the following:

	December 31, 2013	December 31, 2012
Unsecured promissory notes	$ 5,997,030	$ 5,997,030
Unsecured short-term promissory notes	150,000	0
Convertible debenture	267,000	0
Accrued interest	3,087,053	2,654,350
NOTES PAYABLE	$ 9,501,083	$ 8,651,380

At December 31, 2013 and 2012, notes payable included two unsecured promissory notes aggregating $5,997,030 with no stated interest rate or terms of repayment. The Company has accrued interest at 7% per annum on both notes since their inception and includes the notes in current liabilities.

On February 1, 2013, the Company issued a $100,000 75-day unsecured 10% promissory note to an individual investor for funds received. On March 18, 2013, the Company issued a $50,000 60-day unsecured 12% promissory note to the same investor for funds received. The Company issued 2 million common shares to the investor as an inducement for the loans, which were amortized as financing fees. As of December 31, 2013, the Company is in default has not repaid these notes.

On February 2, 2012, the Company closed on a Securities Purchase Agreement with La Jolla Cove Investors, Inc. a California-based institutional investor (the “Investor”) for an aggregate of $5.5 million. The $500,000 initial tranche was funded at the closing in connection with a Convertible Debenture due in February 2015 and an Equity Investment Agreement (the “EIA”). A portion of the Debenture was converted by the Investor into shares of common stock beginning on May 3, 2012.

The Debenture grants the Investor with a right of first refusal on future financings of the Company subject to certain terms and conditions and contains acceleration provisions requiring 120% of the principal amount, accrued and unpaid interest, to become immediately due and payable on certain events of default described therein.

Pursuant to the EIA, the Investor agreed to invest an additional $5.0 million in monthly tranches beginning on May 3, 2012. The Investor also has the right to purchase an additional $5.0 million of the Company’s common stock at an exercise price of $0.21 per share for a period of three years.

The Company incurred customary closing costs including attorney's fees, commissions and closing costs of $62,027, which are recorded as deferred financing costs to be amortized as additional interest expense on a straight-line basis over the 3-year term of the Debenture and EIA.

On July 25, 2013, the Company filed a lawsuit against the Investor in the United States District Court for the Northern District of California relating to the finance documents entered into by the Company and the Investor in January 2012. In the lawsuit, the Company alleges breach of contract and other causes of action. The Company has reclassified the convertible notes payable to current notes payable.

NOTE 8. DERIVATIVE LIABILITIES

The Company accounts for derivative instruments at fair value. Gains and losses from changes in the fair value of derivatives are recognized in interest expense. The Company's derivative instruments consist of stock warrants that contained anti-dilution provisions that were issued with certain debt and equity financings. During 2013, all financial instruments that gave rise to the derivative liabilities have expired.

Warrants

In the past, the Company entered into financing agreements for convertible promissory notes and stock purchase agreements, which included Class A and Class B warrants. Both Class A and Class B warrants contained anti-dilution rights and are considered to be derivative liabilities under U.S. GAAP. During 2010 and 2011, the Company entered into new stock purchase agreements and issued an aggregate of 9,677,167 warrants under the 2010 and 2011 stock purchase agreements. Warrants issued under the 2010 and 2011 stock purchase agreements have no anti-dilution rights and are not considered to be derivative liabilities. All warrants have 3-year terms and are exercisable for a purchase price of $0.21 per share or, in the case of Class B warrants, $0.315 per share.

The following table summarizes certain information about the Company's warrants to purchase common stock.

	Derivative Liabilities			
	Warrants Class A	Warrants Class B	Warrants & Purchase Rights	Weighted Average
Outstanding at December 31, 2012	8,327,462	8,327,462	20,033,021	$0.234
Warrants Granted	0	0	972,381	0.210
Warrants Expired	(8,327,462)	(8,327,462)	(2,377,167)	0.256
Outstanding at December 31, 2013	0	0	18,628,235	$0.210

The warrants outstanding and exercisable at December 31, 2013 and 2012 had no intrinsic value. All warrants were fully exercisable and there was no unamortized cost to be recognized in future.

NOTE 9. SHARE-BASED COMPENSATION

The Company makes share-based compensation awards to its directors, officers, employees and consultants that consist of common stock, restricted stock and stock options. All common stock and restricted stock awards are subject to the securities law restrictions of Rule 144 as promulgated under the Securities Act of 1933, as amended.

Common Stock

The Company recognizes the cost of the common stock issued to directors, officers, and employees as compensation expense at the closing market price on the grant date. All common stock awards are fully vested on the date of grant, therefore no unrecognized compensation expense is associated with these awards. During 2013, the Company issued 7,692,308 common shares totaling $100,000 for salary conversions against accrued salaries; and issued 900,000 common shares for director fees totaling $13,890. Director fees and compensation expenses are included in general and administrative expense.

Restricted Stock

Awards of restricted stock are independent of stock option grants and are generally subject to forfeiture if employment terminates prior to vesting. Prior to vesting, ownership of the restricted stock cannot be transferred. The restricted stock has the same voting rights as the common stock. The Company recognizes fair value of restricted stock awards based upon the stock's closing market price on the grant date as compensation according to the terms of award's vesting schedule; i.e. ratably over the vesting period or upon attainment of specific performance-based goals and objectives. During 2013, the Company awarded 20 million common shares with a vested total of $85,968 as retention bonuses, of which 12 million were rescinded and exchanged for fully-vested stock options on December 31, 2013. Share-based compensation is included in general and administration expense. At December 31, 2013, there remains approximately $118,650 in unrecognized compensation relating to performance-based restricted stock awards.

Stock Options

The Company has issued stock options at exercise prices equal to the Company's common stock market price on the date of grant with contractual terms of three to seven years. Historically, the stock options were fully vested and expensed as compensation on the grant date. During 2010, the Company began issuing stock options with vesting schedules and such stock options are generally subject to forfeiture if employment terminates prior to vesting. On December 31 2013, certain officers and employees rescinded 12 million shares of previously awarded restricted shares for fully-vested stock options on a one-for-one basis valued at $216,000. Also during 2013, the Company issued 40,355,693 stock options in lieu of accrued salaries for $524,624; awarded 14 million options for retention bonuses totaling $285,600; issued 900,000 options for director's fees totaling $23,412 and; had previously issued options vest totaling $30,685. Total share-based compensation attributable to vested option agreements of $339,697 is included in general and administrative. At December 31, 2013, there was approximately $80,700 in unrecognized compensation expense.

The Company uses the Black-Scholes option pricing model to estimate the fair value of stock options. The principal assumptions utilized in valuing stock options include the expected stock price volatility (based on the most recent historical period equal to the expected life of the option); the expected option life (an estimate based on historical experience); the expected dividend yield; and the risk-free interest rate (an estimate based upon on the yields of Treasury constant maturities equal to the expected life of the option).

The following table summarizes the stock option activity for the years ended December 31,

	2013		2012	
	Shares	Weighted average exercise price	Shares	Weighted average exercise price
Outstanding at beginning of year	68,650,000	$ .046	40,916,667	$ .067
Granted	15,300,000	.023	0	.000
Exchanged for salary conversion	40,355,693	.013	22,316,667	.023
Exchanged for rescinded stock	12,000,000	.009	14,000,000	.015
Exercised	0	.000	0	.000
Forfeited / expired / cancelled	(11,722,222)	.086	(8,583,334)	.073
Outstanding at end of year	124,583,471	$ .025	68,650,000	$ .046
Options exercisable at end of year	119,583,471	$ .026	63,358,333	$ .048
Weighted average remaining contractual term	5.60 years		4.55 years	

The following table summarizes information about stock options outstanding and exercisable at December 31, 2013:

	Options Outstanding and Exercisable		
Exercise prices	Number outstanding	Weighted average remaining contractual terms (years)	Weighted Average Exercise price
$.0096	12,000,000	7.00	.0096
$.011	400,000	2.87	.011
$.013	40,355,693	6.73	.013
$.015	11,000,000	5.75	$ .015
$.016	250,000	2.17	.016
$.021	250,000	2.37	.021
$.023	22,316,667	5.87	.023
$.0238	12,000,000	6.58	.0238
$.0275	400,000	2.58	.0275
$.045	4,444,444	.34	.045
$.070	1,500,000	.11	.070
$.075	10,250,000	3.25	.075
$.080	1,500,000	.27	.080
$.090	2,916,667	.27	.090
	119,583,471	5.59	$ .026

The aggregate intrinsic value of the 119,583,471 options outstanding and exercisable at December 31, 2013 was $0. The aggregate intrinsic value for the options is calculated as the difference between the prices of the underlying awards and quoted price of the Company’s common stock for the options that were in-the-money at December 31, 2013.

NOTE 10. INCOME TAXES

The Company has federal and state net operating loss (NOL) carryforwards, which can be used to offset future earnings. Accordingly, no provision for income taxes is recorded in these consolidated financial statements. A deferred tax asset for the future benefits of net operating losses and other differences is offset by a 100% valuation allowance due to the uncertainty of the Company's ability to realize future tax benefits from the losses. These net operating losses will expire in the years 2021 through 2031.

Certain income and expenses are recognized in different periods for tax and financial reporting purposes. The items that give rise to these temporary differences at the Company consist of its NOL carryforwards and the related valuation allowances. The resulting deferred tax assets and liabilities consist of the tax effects (computed at 15%) of the temporary differences and are listed below:

	2013	2013 Changes	2012
Deferred tax assets:			
Net operating loss carry-forwards	$ 18,245,910	$ 496,209	$ 17,749,701
Valuation allowance	(18,245,910)	(496,209)	(17,749,701)
Net deferred tax asset	$ —	$ —	$ —

A reconciliation of income benefit provided at the federal statutory rate of 15% to income tax benefit is as follows:

	2013	2012
Income tax benefit computed at federal statutory rate	$ (496,209)	$ (504,428)
Deferred income taxes	496,209	504,428
	$ —	$ —

At the end of 2013, the Company also had net operating loss carry-forwards of its predecessor, related to its reincorporation and reorganization under the Internal Revenue Code, available to offset future taxable income. These NOL carryforwards total approximately $81,429,083 and expire at various dates through 2022.

The Company operated in multiple tax jurisdictions within the United States of America. Although management does not believe that the Company is currently under examination in any major tax jurisdiction in which it operates other than for the issues with the IRS as described in Note 15, the Company remains subject to examination in all of those tax jurisdictions until the applicable statute of limitations expire. As of December 31, 2013, 2008 and subsequent tax years remain subject to examination by the Internal Revenue Service (“IRS”) and in the Company’s major state tax jurisdictions. The Company does not expect to have a material change to unrecognized tax positions within the next twelve months.

NOTE 11. PER SHARE INFORMATION:

Basic earnings per share ("Basic EPS") of common stock is computed by dividing the net loss by the weighted-average number of shares of common stock outstanding. Diluted earnings per share of common stock ("Diluted EPS") is computed by dividing the net loss by the weighted-average number of shares of common stock, and dilutive common stock equivalents and convertible securities then outstanding. U.S. GAAP requires the presentation of both Basic EPS and Diluted EPS on the face of the Company's Condensed Consolidated Statements of Operations. There were no dilutive common stock equivalents at December 31, 2013 and 2012.

	Years Ended December 31,	
	2013	2012
Numerator:		
Net loss	$(3,417,205)	$(3,362,853)
Denominator:		
Weighted-average common shares outstanding	632,009,690	420,841,556
Net loss per share:		
Basic and diluted	$(0.01)	$(0.01)

NOTE 12. COMMITMENTS

Agreements

The Company has entered into several agreements and memorandums of understanding during 2013 and 2012 and through the date of this Annual Report on Form 10-K, none of which require the recording of any assets, liabilities, revenues or expenses.

Lease Commitments

The Company's headquarters are located at the Kennedy Space Center, FL on State Road 405, Building M6-306A, Room 1400. The Company intends to renew its annual lease agreement. Currently, the Company is paying office rent on a month-to-month basis for $1,607 per month plus state sales tax. In November 2013, the Company renewed an annual lease agreement for GTC office space at $3,500 per month. LTAS does not have a contractual rental allocation agreement with related party, APC, who is under a lease agreement with the landlord. The Company is also obligated under other monthly rental agreements for additional facilities and office furniture.

Rent expense for 2013 and 2012 was $119,139 and $120,727, respectively.

The estimated future minimum rental payments on non-cancelable operating leases at December 31, 2013 consist of $37,625 due during the year ended December 31, 2014.

NOTE 13. LITIGATION AND CONTINGENCIES

In the ordinary conduct of business, the Company is subject to periodic lawsuits, investigations and litigation claims, which the Company accrues for where appropriate and can be reasonably estimated. The Company cannot predict with certainty the ultimate resolution of such lawsuits, investigations and claims asserted against it. At December 31, 2012, the Company had the following material contingencies:

Brio Capital

Brio Capital, the holder of a warrant, filed an action against us on February 25, 2011 in the New York Supreme Court, County of New York, for the issuance of approximately 6.2 million shares of common stock upon the exercise of certain warrants. The Court granted a non-final Summary Judgment Order on a portion of the action in favor of Brio in December 2011 requiring us, among other things, to issue 6.2 million shares of common stock. We have issued the shares required by the Court order. We also entered into a settlement agreement to pay $57,661 in legal fees as required by the Court order, which has been satisfied. We reached a settlement with Brio resolving all remaining matters. Under the terms of the settlement, we are required to issue a number of shares of common stock in twelve (12) monthly installments equal to $31,250 divided by the average of the closing bid prices of our common stock for the last three (3) trading days of the month immediately preceding the month in which the shares are due to be issued. Pursuant to the Court's Section 3(a) (10) approval, the shares of common stock issued to Brio shall be freely tradable upon issuance. All shares issued are subject to a leak-out provision contained in the settlement agreement.

The DeCarlo Group

A lawsuit was filed by the DeCarlo Group on November 24, 2010 in Miami-Dade County Courthouse for over $400,000 claimed in connection with CFO and accounting services allegedly rendered to the Company. It is our position that we were overcharged in connection with the services rendered and that no amounts are due. DeCarlo has now filed a second amended complaint that we have responded to and intend to otherwise defend ourselves vigorously in this matter, but the outcome of the action cannot be predicted.

La Jolla Cove Investors, Inc.

On July 25, 2013, we filed a lawsuit against La Jolla Cove Investors, Inc. in the United States District Court for the Northern District of California relating to the finance documents entered into by us and La Jolla in January 2012. In the lawsuit, we allege breach of contract and other causes of action. We are seeking injunctive relief in addition to unspecified monetary damages as well as other relief. La Jolla has made counterclaims against us and is defending against our complaint. We intend to otherwise pursue this matter vigorously, but the outcome of the action cannot be predicted.

IRS

During 2010 and 2009, we, under our former name Sanswire Corp., incurred and reported to the Internal Revenue Service ("IRS") payroll tax liabilities (and deposited the appropriate withholding amounts) during the normal course of business at each payroll cycle. We reported payroll tax liabilities for all the tax periods in 2007 and 2008, however, we failed to deposit the appropriate withholding amounts for those periods. We recognized this issue and, accordingly, contacted the IRS to make arrangements to pay any taxes due. One such matter has been resolved with the IRS, and we currently estimate the amount involved in the second matter to be approximately $200,000. We may be subject to additional penalties and interest from the IRS in connection with these payroll tax matters. We are engaged in discussions and continue to cooperate with the IRS to resolve this matter.

The Company provides indemnification, to the extent permitted by law, to its officers, directors, employees and agents for liabilities arising from certain events or occurrences while the officer, director, employee, or agent is or was serving at our request in such capacity.

NOTE 14. SUBSEQUENT EVENTS

The Company has evaluated subsequent events from the balance sheet date and determined there were no subsequent events requiring disclosure.