



Our Platform Advantage

AERIE PHARMACEUTICALS **2018** ANNUAL REPORT

To Our Stockholders

In 2018 we redefined Aerie as a commercial enterprise with our successful launch of Rhopressa[®] (netarsudil ophthalmic solution) 0.02%. Now, we look forward to expanding our glaucoma franchise, continuing our global expansion and initiating our clinical programs focused on retinal disease.



The single most transformational event in 2018 was the launch of our first product, Rhopressa[®], designed to reduce intraocular pressure (IOP) in patients with glaucoma or ocular hypertension. Rhopressa[®] is a first-in-class, once-daily eye drop that has proven to be an effective new product for patients and has been well-received in the physician community. We expect Rhopressa[®] to be covered in a preferred tier for the majority of insured lives in commercial and Medicare Part D plans during the first half of 2019. We believe this expanded market access will drive continued future growth of Rhopressa[®], which already generated \$24 million in net revenues in 2018, well within the guidance range we provided investors very early in 2018. On top of that, 2019 is already off to an excellent start, with Rocklatan[™] (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%, our second product, having been granted approval by the FDA on March 12, 2019.

Soon, Rocklatan[™] will be available to prescribers through our 100 U.S. sales representatives, who cover the 14,000 prescribers that generate over 80 percent of the ophthalmology glaucoma prescriptions. Rocklatan[™] is a once-daily fixed-dose combination of Rhopressa[®] and widely-prescribed latanoprost, and represents the only product to achieve statistically superior IOP-lowering in

transforming Aerie into a global enterprise. Our regulatory filing in Europe for Rhopressa[®] (named Rhokiinsa[®] in Europe) was accepted in September 2018. If it is approved in Europe, which is the second largest glaucoma market in the world in terms of drug spend, we plan to file Rocklatan[™] (named Roclanda[™] in Europe) thereafter. Our Phase 3 trial named Mercury 3, which is comparing Roclanda[™] to a well-established fixed-dose combination containing timolol and the prostaglandin bimatoprost, is ongoing in Europe, and while not needed for regulatory approval, it is designed to improve our commercial prospects in the region. Further, for the Japan market, which is the third largest glaucoma market in the world, we recently completed successful Phase 1 studies and a pilot Phase 2 clinical trial for Rhopressa[®] on Japanese and Japanese-American patients. The results of the pilot Phase 2 trial were very promising as we evaluate our potential not only for the Japan market, but also how well the product performs on patients at lower IOPs. We recently opened our new Tokyo branch office and have already initiated our first Phase 2 clinical trial in Japan.

2018 was also an important investment year as we have taken meaningful strides in the construction of our manufacturing plant in Ireland, and we continue to target 2020 as our first full year of operations.

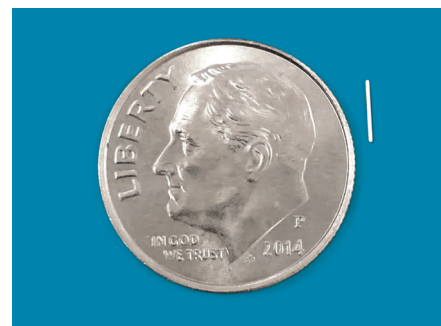
U.S. Phase 3 trials compared to latanoprost, the top selling glaucoma product in the world. The upcoming availability of such a paradigm-changing treatment is generating excitement within the ophthalmic community.

During 2018, we made excellent progress in

Our next frontier is our retina program, based on the bio-erodible polymer and implant manufacturing platform that we have built over the past two years. The moment has arrived for our two sustained-release implant product candidates to enter the clinic. This is yet another major milestone for the company as we take steps to enter this \$5 billion market in the United States alone. Our internally developed candidate, AR-13503, has demonstrated high levels of efficacy in preclinical experiments for wet AMD (age-related macular degeneration) and DME (diabetic macular edema). AR-1105 is a steroid implant with potential in macular edema due to retinal vein occlusion and has already entered the clinic in a Phase 2 trial. We will continue to focus on further enhancing our pipeline by exploring additional innovative opportunities in the glaucoma, retina, dry eye and refractive segments of the market.

We have progressed at a rapid pace in 2018 and are now keenly focused on an even further accelerated track for 2019. With our incredibly dedicated employees, now almost 400, we have many exciting days ahead as we continue building a major ophthalmic pharmaceutical company.

Vicente Anido, Jr., Ph.D.
Chief Executive Officer and Chairman of the Board



The background image on the annual report cover reveals a full array of retina implants. Above, a single implant is shown for scale.

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549**

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

or

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

For the transition period from _____ to _____

Commission File Number: 001-36152

Aerie Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

20-3109565

(IRS Employer
Identification No.)

4301 Emperor Boulevard, Suite 400

Durham, North Carolina 27703

(919) 237-5300

(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:

<u>Title of Each Class</u>	<u>Name of Each Exchange on Which Registered</u>
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 No

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files): Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of 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.

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

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with

any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 30, 2018, based upon the closing price of \$67.55 of the registrant's common stock as reported on The NASDAQ Global Market, was \$2,630,283,381.

As of February 15, 2019, the registrant had 45,911,125 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 2019 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, 2018.

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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. References to “approved products” means products approved by the U.S. Food and Drug Administration (“FDA”) or other regulatory authorities; references to “product candidates” means products that have been developed but not yet approved by the FDA or other regulatory authorities; references to “future product candidates” means products that have not yet been developed.

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 other words that 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 potential future sales of Rhopressa[®] (netarsudil ophthalmic solution) 0.02% (“Rhopressa[®]”) and the potential commercial launch and potential future sales of Rocklatan[™] (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% (“Rocklatan[™]”), previously referred to as Roclatan[™], in the United States, and any future product candidates, if approved;
- the potential future sales in jurisdictions outside of the United States of Rhopressa[®], named Rhokiinsa[®] (netarsudil ophthalmic solution) 0.02% (“Rhokiinsa[®]”) in Europe, or Rocklatan[™], named Roclanda[™] (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% (“Roclanda[™]”) in Europe, or their equivalents, and any future product candidates;
- our commercialization, marketing, manufacturing and supply management capabilities and strategies;
- third-party payer coverage and reimbursement for our approved products (currently only Rhopressa[®] in the United States), product candidates and any future product candidates, if approved;
- the glaucoma patient market size and the rate and degree of market adoption of our approved products, product candidates and any future product candidates, if approved, by eye-care professionals and patients;
- the timing, cost or other aspects of the commercial launch of our approved products, product candidates and any future product candidates, if approved;
- the success, timing and cost of our ongoing and anticipated preclinical studies and clinical trials for our product candidates and any future product candidates with respect to regulatory approval outside the United States, including statements regarding the timing of initiation and completion of the studies and trials;
- our expectations regarding the effectiveness of our approved products, product candidates and any future product candidates and results of our clinical trials and any potential preclinical studies;
- the timing of and our ability to request, obtain and maintain FDA or other regulatory authority approval of, or other action with respect to our approved products, product candidates and any future product candidates in the United States, Europe, Japan and elsewhere, including the expected timing of, and regulatory and/or other review of, filings for such product candidates;
- our expectations related to the use of proceeds from our financing activities and credit facility;
- our estimates regarding anticipated operating expenses and capital requirements and our needs for additional financing;
- our plans to pursue development of additional product candidates and technologies in ophthalmology, including development of our approved products or product candidates for additional indications, our

preclinical retinal programs and other therapeutic opportunities, and our plans to explore possible uses of our existing proprietary compounds beyond glaucoma;

- the potential advantages of our approved products, product candidates and any future product candidates;
- 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, product candidates or technologies; 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.

In particular, FDA approval of Rhopressa[®] does not constitute FDA approval of Rocklatan[™] in the United States, and there can be no assurance that we will receive FDA approval for Rocklatan[™] or any future product candidates. FDA approval of Rhopressa[®] also does not constitute regulatory approval of Rhopressa[®], or Rhokiinsa[®] as it is named in Europe, in jurisdictions outside the United States, and there can be no assurance that Rhopressa[®] or Rhokiinsa[®] will obtain regulatory approval in jurisdictions outside the United States. Our receipt of a Prescription Drug User Fee Act (“PDUFA”) goal date notification for Rocklatan[™] does not constitute FDA approval of the Rocklatan[™] New Drug Application (“NDA”), and there can be no assurance that the FDA will complete its review by the PDUFA goal date of March 14, 2019, that the FDA will not require changes or additional data that must be made or received before it will approve the NDA, if ever, or that the FDA will approve the NDA. The European Medicines Agency (“EMA”) acceptance of our Marketing Authorisation Application (“MAA”) for Rhokiinsa[®] does not constitute EMA approval of Rhokiinsa[®] and does not provide assurance that the EMA will approve Rhokiinsa[®]. In addition, the preclinical research discussed in this report is preliminary and the outcome of such preclinical studies may not be predictive of the outcome of later clinical trials. Any future clinical trial results may not demonstrate safety and efficacy sufficient to obtain regulatory approval related to the preclinical research findings discussed in this report, and we may suspend or discontinue research programs at any time for any reason.

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 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.

PART I

ITEM 1. BUSINESS

Overview

We are an ophthalmic pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with open-angle glaucoma, retinal diseases and other diseases of the eye. Our strategy is to successfully commercialize our U.S. Food and Drug Administration (“FDA”) approved product, Rhopressa[®] (netarsudil ophthalmic solution) 0.02% (“Rhopressa[®]”), and our advanced-stage product candidate, Rocklatan[™] (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% (“Rocklatan[™]”), previously referred to as Roclatan[™], if approved, in the United States. Rocklatan[™] has a Prescription Drug User Fee Act (“PDUFA”) goal date of March 14, 2019. We are also developing Rhopressa[®] and Rocklatan[™] (named Rhokiinsa[®] and Roclanda[™], respectively, in Europe) for regulatory approval in Europe and Japan and expect to commercialize on our own in Europe and likely partner for commercialization of their equivalents in Japan, if approved. We are also focused on furthering the development of our preclinical molecules and technologies focused on retinal diseases and expect to have two preclinical implants, AR-1105 and AR-13503, commence clinical trials in 2019. Further, we are screening our owned library of Rho kinase (“ROCK”) inhibitors for indications beyond glaucoma.

Rhopressa[®] is a once-daily eye drop designed to reduce elevated intraocular pressure (“IOP”) in patients with open-angle glaucoma or ocular hypertension. The active ingredient in Rhopressa[®], netarsudil, is an Aerie-owned ROCK inhibitor. We believe that Rhopressa[®] represents the first of a new drug class for reducing IOP in patients with glaucoma in over 20 years. Early indications point to healthcare professionals prescribing Rhopressa[®] as a concomitant therapy to prostaglandins or non-PGA (prostaglandin analog) medications when additional IOP reduction is desired. We believe Rhopressa[®] is primarily competing with other non-PGA products, due to its targeting of the diseased trabecular meshwork (“TM”), its demonstrated ability to reduce IOP at consistent levels across tested baselines, its preferred once-daily dosing relative to other currently marketed non-PGA products and its safety profile. Adjunctive therapies currently represent nearly one-half of the glaucoma prescription market in the United States, according to IQVIA. We believe that Rhopressa[®] may also become a preferred therapy where PGAs are contraindicated, for patients who do not respond to PGAs and for patients who choose to avoid the cosmetic issues associated with PGA products.

We launched Rhopressa[®] in the United States at the end of April 2018. Rhopressa[®] is now being sold to national and regional U.S. pharmaceutical distributors, and patients have access to Rhopressa[®] through pharmacies across the United States. In the glaucoma market in the United States, approximately half of the dispensed volumes are covered under commercial plans and half under Medicare Part D. We have obtained formulary coverage for Rhopressa[®] for approximately 90% of lives covered under commercial plans and approximately 40% of lives covered under Medicare Part D plans. We expect Medicare Part D Tier 2 equivalent coverage to increase to over 70% by the end of the first quarter of 2019.

Our advanced-stage product candidate, Rocklatan[™], is a once-daily fixed-dose combination of Rhopressa[®] and latanoprost, the most commonly prescribed drug for the treatment of patients with open-angle glaucoma. We believe, based on our clinical data, that Rocklatan[™] has the potential to provide a greater IOP-reducing effect than any currently marketed glaucoma medication. Therefore, we believe that Rocklatan[™], if approved and formulary coverage is obtained, could compete with both PGA and non-PGA therapies and become the product of choice for patients requiring maximal IOP reduction, including those with higher IOPs and those who present with significant disease progression despite using currently available therapies.

We submitted a New Drug Application (“NDA”) for Rocklatan[™] to the FDA in May 2018 under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (the “FDCA”), which provides for an abbreviated approval pathway, since Rocklatan[™] is a fixed dose combination of two FDA-approved drugs in the United States. In July 2018, we announced that the NDA was accepted for review by the FDA and the PDUFA goal date was set for March 14, 2019.

We have a commercial team that includes approximately 100 sales representatives targeting approximately 14,000 high-prescribing eye-care professionals throughout the United States. This sales force is responsible for sales of Rhopressa[®], and will also be responsible for sales of Rocklatan[™], if approved.

Our strategy also includes developing our business outside the United States, including obtaining regulatory approval in Europe and Japan on our own for Rhopressa[®] and Rocklatan[™]. If we obtain regulatory approval, we currently expect to commercialize Rhopressa[®] and Rocklatan[™] in Europe on our own, and likely partner for commercialization of their equivalents in Japan. If

approved, we expect that Rhopressa[®] and Rocklatan[™] will be marketed under the names Rhokiinsa[®] and Roclanda[™], respectively, in Europe. To optimize the commercial opportunity, we expect to launch Roclanda[™] before Rhokiinsa[®] in Europe, if approved, as the European market is oriented more toward fixed-dose combination products. We are continuing to expand our presence in Europe and are actively participating in European ophthalmology conferences and forums. We now have over 60 employees in Europe that manage the build-out and operation of our manufacturing plant in Ireland, discussed below, as well our Phase 3 clinical trial for Rocklatan[™], which is ongoing in several European countries. We are also building our clinical, medical affairs and commercial teams in Europe. In Japan, we announced the opening of our office in Tokyo and the hiring of key leadership positions to help execute our strategy in that market.

With respect to regulatory approvals of Rhopressa[®] in jurisdictions outside the United States, in October 2018, we announced that the European Medicines Agency (“EMA”) accepted for review our marketing authorisation application (“MAA”) for Rhokiinsa[®]. Additionally, we completed a Phase 1 clinical trial and a successful pilot Phase 2 clinical study in the United States on Japanese and Japanese-American subjects, which were designed to support meeting the requirements of Japan’s Pharmaceuticals and Medical Devices Agency (“PMDA”) for potential regulatory submission of Rhopressa[®] in Japan. We are also planning to initiate a Phase 2 clinical trial on Japanese patients in Japan by the end of the first quarter of 2019 to support subsequent Phase 3 registration trials that are also expected to be conducted in Japan under our direction.

With respect to Rocklatan[™] in jurisdictions outside the United States, we have completed two Phase 3 registration trials named Mercury 1 and Mercury 2, discussed further below. Both Mercury 1 and Mercury 2 will be used for European approval of Roclanda[™]. We also initiated a Phase 3 registration trial for Roclanda[™], named Mercury 3, in Europe during the third quarter of 2017. Mercury 3, a six-month efficacy and safety trial, is designed to compare Roclanda[™] to Ganfort[®], a fixed-dose combination product marketed in Europe of bimatoprost, a PGA, and timolol, a beta blocker. If successful, Mercury 3 is expected to improve our commercialization prospects in Europe. We currently expect to read out topline 90-day efficacy data for the Mercury 3 trial in 2019. We expect to submit an MAA with the EMA in early 2020 for Roclanda[™], if the EMA has approved Rhokiinsa[®] by such time.

In January 2017, we commenced establishment of our own manufacturing plant in Athlone, Ireland. This will be our first manufacturing plant, which is expected to produce commercial supplies of Rhopressa[®] and, if approved, Rocklatan[™], Rhokiinsa[®] and Roclanda[™]. Commercial supply from the plant is expected to be available in early 2020. Our current contract manufacturer produces commercial supply of Rhopressa[®] and started to manufacture Rocklatan[™] in 2018 in anticipation of potential FDA approval and commercial launch in 2019. We are also in the process of adding an additional active pharmaceutical ingredient (“API”) contract manufacturer and an additional Rhopressa[®] drug product contract manufacturer, both of which are expected to supply commercial materials in the first half of 2019. We expect to continue to use product sourced from our contract manufacturers when the Ireland plant is operational.

We also seek to enhance our longer-term commercial potential by identifying and advancing additional product candidates through our internal discovery efforts, our entry into potential research collaborations or in-licensing arrangements or our acquisition of additional ophthalmic products or technologies or product candidates that complement our current product portfolio. Our collaboration with DSM, a global science-based company headquartered in the Netherlands, provides access to their bio-erodible polymer technology, and our acquisition of assets from Envisia Therapeutics Inc. (“Envisia”), which includes the rights to use PRINT[®] manufacturing technology for ophthalmology, are designed to advance our progress in developing potential future sustained-release implant product candidates to treat retinal diseases. In August 2018, we announced the expansion of our collaboration with DSM to provide for (i) a worldwide exclusive license for all ophthalmic indications to DSM’s polyesteramide polymer technology, (ii) continuation of the collaborative research initiatives through the end of 2020, including the transfer of DSM’s formulation technology to Aerie during that time and (iii) access to a preclinical latanoprost implant.

Aided by these technologies, we are developing two preclinical sustained-release implants focused on retinal diseases. AR-13503, for which we expect to submit an Investigational New Drug application (“IND”) in the first quarter of 2019, is an Aerie-owned ROCK and Protein kinase C inhibitor with potential in the treatment of diabetic macular edema (“DME”), wet age-related macular degeneration (age-related macular degeneration, “AMD”) and related diseases of the retina. AR-13503 has shown lesion size decreases in an *in vivo* preclinical model of wet AMD at levels similar to the current market-leading wet AMD anti-vascular endothelial growth factor (vascular endothelial growth factor, “VEGF”) product. When used preclinically in combination with the market leading anti-VEGF product, AR-13503 produced greater lesion size reduction than the anti-VEGF product alone in a model of proliferative diabetic retinopathy (diabetic retinopathy, “DR”). Additionally, through the Envisia asset acquisition, we are developing AR-1105, a preclinical dexamethasone steroid implant. The IND for AR-1105 was submitted in December 2018, and in January 2019, we announced that the FDA reviewed the IND and it is now in effect, allowing Aerie to initiate human studies in the treatment of macular edema due to RVO. We expect to initiate a Phase 2 clinical study later in the first quarter of 2019.

Further, we are evaluating our owned library of ROCK inhibitors for potential indications beyond ophthalmology. There are several disease categories where ROCK inhibitors have demonstrated benefits both preclinically and clinically in past third-party studies and trials, and we are initially focused on exploring potential opportunities for our molecules in pulmonary health, dermatology and cancer. We are in the initial stages of our work on these applications.

We own the worldwide rights to all indications for Rhopressa[®] and Rocklatan[™]. We have patent protection for Rhopressa[®] and Rocklatan[™] in the United States through early 2034 and internationally, through dates ranging from 2030 to 2037. Our intellectual property portfolio contains patents and pending patent applications related to composition of matter, pharmaceutical compositions, methods of use and synthetic methods. Furthermore, we have patent protection for AR-13503 in the United States and internationally, which extends to 2030. We have also filed for patent protection for AR-1105 in the United States and internationally.

Our Strategy

Our goal is to become a leader in the discovery, development and commercialization of first-in-class therapies for the treatment of patients with open-angle glaucoma, retinal diseases and other diseases of the eye. We believe Rhopressa[®] and Rocklatan[™] have the potential to address many of the unmet medical needs in the glaucoma market, and preclinical implants AR-1105 and AR-13503 have the potential to address unmet needs in the retinal disease market. Key elements of our strategy are to:

Successfully commercialize Rhopressa[®] in North America. We own worldwide rights to all indications for Rhopressa[®] and we intend to retain our commercialization rights in North American markets. We launched Rhopressa[®] in the United States at the end of April 2018. Our sales organization is targeting approximately 14,000 high prescribing eye-care professionals throughout the United States. We have already obtained formulary coverage for approximately 90% of lives covered under commercial plans and approximately 40% of lives covered under Medicare Part D plans. We expect Medicare Part D Tier 2 equivalent coverage to increase to over 70% by the end of the first quarter of 2019.

Obtain FDA approval of Rocklatan[™] and manage a successful commercial launch, if approved. Rocklatan[™] is a fixed dose combination of two FDA-approved drugs in the United States. In July 2018, we announced that our NDA was accepted for review by the FDA and the PDUFA goal date was set for March 14, 2019, which represents a ten-month review. If approved, our existing sales force will be responsible for sales in the United States of Rocklatan[™] in addition to Rhopressa[®]. We own the worldwide rights to all indications for Rocklatan[™].

Advance the development of Rhopressa[®] and Rocklatan[™] in jurisdictions outside the United States to regulatory approval and commercialize on our own in Europe while likely securing a commercialization partner in Japan. Our strategy includes developing our business in jurisdictions outside of the United States, including obtaining regulatory approval on our own in Europe and Japan for Rhopressa[®] and Rocklatan[™]. If we obtain regulatory approval, we currently expect to commercialize Rhopressa[®] and Rocklatan[™] ourselves in Europe, which will be marketed as Rhokiinsa[®] and Roclanda[™], respectively. We will likely partner for commercialization of their equivalents in Japan, if approved. With respect to regulatory approvals for Rhopressa[®], in October 2018, we announced that the EMA accepted for review our MAA for Rhokiinsa[®]. Additionally, we completed a Phase 1 clinical trial and a successful pilot Phase 2 clinical study in the United States on Japanese and Japanese-American subjects, which were designed to support meeting the requirements of Japan's PMDA for potential regulatory submission of Rhopressa[®] in Japan. We are also preparing to initiate a Phase 2 clinical trial on Japanese patients in Japan by the end of the first quarter of 2019 to support subsequent Phase 3 registration trials that are also expected to be conducted in Japan under our direction.

With respect to Rocklatan[™], we commenced the Mercury 3 Phase 3 clinical trial in Europe during the third quarter of 2017, which is designed to compare Roclanda[™] to Ganfort[®], a fixed-dose combination product marketed in Europe of bimatoprost, a PGA, and timolol, a beta blocker. If successful, Mercury 3 is expected to improve our commercialization prospects in Europe. We currently expect to read out topline 90-day efficacy data for the trial in 2019. Since Roclanda[™] is a fixed-dose combination product that includes Rhokiinsa[®], we plan to submit an MAA for Roclanda[™] with the EMA if and when Rhokiinsa[®] is approved by the EMA. We expect to submit the MAA for Roclanda[™] in early 2020, if the EMA has approved Rhokiinsa[®] by such time.

Continue to leverage and strengthen our intellectual property portfolio. We believe we have a strong intellectual property position relating to Rhopressa[®] and Rocklatan[™]. 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 Rhopressa[®] and Rocklatan[™] in the United States, which extends through early 2034, and internationally, through dates ranging from 2030 to 2037. Furthermore, we have patent protection for AR-13503 in the United States and internationally, which extends to 2030. We have also filed for patent protection for AR-1105

in the United States and internationally. We will also continue to evaluate our owned library of ROCK inhibitors for novel uses and applications and intend to seek intellectual property protection for any such developments.

Expand our product candidate portfolio and pipeline through internal discovery efforts, research collaboration arrangements and in-licensing or acquisitions of additional product candidates, products or technologies. We continue to seek to discover and develop new compounds in our research laboratories, and our scientific staff are currently focused on evaluating our portfolio of owned ROCK inhibitors for additional indications within and beyond ophthalmology. In addition, we may enter into additional research collaborations or license arrangements or complete additional acquisitions to broaden our presence in ophthalmology, as we continually explore and discuss potential additional opportunities for new ophthalmic products, delivery alternatives and new therapeutic areas. Through business development activities, we have acquired the worldwide ophthalmic rights to a bio-erodible polymer technology from DSM, and PRINT[®] implant manufacturing technology from Envisia. With these, we have created a unique sustained-release ophthalmology platform that, initially, allows for the progression of our sustained-release retinal implant program. Using this technology, we are currently developing two preclinical sustained-release implants focused on retinal diseases, AR-1105 and AR-13503, for which we expect to commence clinical trials in 2019. We believe there is a need in the current retinal diseases treatment paradigm for new treatment pathways and less frequent injections. The U.S. retinal disease market was approximately \$5 billion in 2017.

Our Product, Product Candidate and Pipeline

Rhopressa[®], our FDA-approved product, has demonstrated that it reduces IOP through ROCK inhibition, its mechanism of action (“MOA”), by which Rhopressa[®] increases the outflow of aqueous humor through the TM, which accounts for approximately 80% of fluid drainage from the healthy eye. Our advanced-stage product candidate is once-daily Rocklatan[™], a fixed-dose combination of Rhopressa[®] and latanoprost, which reduces IOP through the same MOA as Rhopressa[®] and through a second MOA, utilizing the ability of latanoprost to increase the outflow of aqueous humor through the uveoscleral pathway, the eye’s secondary drain. Our preclinical pipeline includes AR-13503, a ROCK and Protein kinase C inhibitor being developed for DME, wet AMD and related diseases of the retina, and AR-1105, a dexamethasone steroid implant being developed for macular edema due to RVO. Both of these products are being designed as miniaturized bio-erodible implants that would be injected intravitreally every six months and both are expected to commence clinical trials in 2019.

We discovered and developed Rhopressa[®], Rocklatan[™] and AR-13503 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 Rhopressa[®] and Rocklatan[™] for preclinical *in vivo* testing following a detailed characterization of over 3,000 synthesized ROCK inhibitors, a number that has since grown to approximately 4,000. We continue to seek to discover and develop new compounds in our research laboratories, and our scientific staff with expertise in medicinal chemistry, analytical chemistry, biochemistry, cell biology, pharmacology and pharmaceutical science are currently focused on evaluating our portfolio of owned ROCK inhibitors for additional indications within and beyond ophthalmology.

The following table summarizes each of our current product, product candidate and preclinical molecules, their MOA(s) and their status, as well as our intellectual property rights.

Name and Mechanism		Status	Intellectual Property Rights
Rhopressa [®] (Rhokiinsa [®] in Europe)	ROCK inhibitor	U.S.: Marketed; launched in April 2018 Europe: MAA accepted for review by EMA Japan: Phase 2	Wholly-Owned
Rocklatan [™] (Roclanda [™] in Europe)	ROCK inhibitor and latanoprost, a PGA	U.S.: PDUFA goal date is March 14, 2019 Europe: Phase 3	Wholly-Owned
AR-13503	ROCK and Protein kinase inhibitor	U.S.: Expect to submit IND in first quarter of 2019	Wholly-Owned
AR-1105	dexamethasone steroid implant	U.S.: Expect to commence Phase 2 clinical study in first quarter of 2019	Wholly-Owned; acquired from Envisia

Rhopressa[®]

Rhopressa[®] is the first of a new class of glaucoma drug products that was discovered by our scientists. It was approved by the FDA on December 18, 2017 for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension and is not yet approved outside of the United States. Our key target markets outside the United States include Europe and Japan.

The active ingredient in Rhopressa[®] is netarsudil, a ROCK inhibitor. 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 TM fluid outflow and consequently reducing IOP.

Rhopressa[®] is competing primarily in the adjunctive therapy market, which represents approximately one-half of the U.S. glaucoma prescription market and totaled approximately 37 million prescriptions in 2017 according to IQVIA. Initial indications point to healthcare professionals prescribing Rhopressa[®] as a concomitant therapy to prostaglandins or non-PGA medications when additional IOP reduction is desired. We believe Rhopressa[®] is primarily competing with other non-PGA products, due to its targeting of the diseased TM, its demonstrated ability to reduce IOP at consistent levels across tested baselines, its preferred once-daily dosing relative to other currently marketed non-PGA products and its safety profile. Currently marketed therapies that are used adjunctively to PGAs are older generation products that are generally dosed between two and three times a day, have MOA(s) focused on reducing fluid production, often have lower efficacy levels and have systemic side effects. We believe that Rhopressa[®] may also become a preferred therapy where PGAs are contraindicated, for patients who do not respond to PGAs and for patients who choose to avoid the cosmetic issues associated with PGA products.

Rhopressa[®] in the United States

Rhopressa[®] received FDA approval on December 18, 2017 and we launched Rhopressa[®] in the United States at the end of April 2018. Rhopressa[®] is now being sold to national and regional U.S. pharmaceutical distributors, and patients have access to Rhopressa[®] through pharmacies across the United States. We have obtained formulary coverage for Rhopressa[®] for approximately 90% of lives covered under commercial plans and approximately 40% of lives covered under Medicare Part D plans. We expect Medicare Part D Tier 2 equivalent coverage to increase to over 70% by the end of the first quarter of 2019.

Rhopressa® Outside of the United States

On October 9, 2018, we announced that the EMA accepted our MAA for Rhokiinsa® for review.

Additionally, we completed a Phase 1 clinical trial and a successful pilot Phase 2 clinical study in the United States on Japanese and Japanese-American subjects, which were designed to support meeting the requirements of Japan's PMDA for potential regulatory submission of Rhopressa® in Japan.

The primary objectives of the study were to evaluate (1) the ocular hypotensive activity of two concentrations of netarsudil ophthalmic solution (0.02% and 0.04%) relative to placebo over a 28-day period, for a total of three arms all dosed in the evening, and (2) the ocular and systemic safety of netarsudil ophthalmic solution relative to placebo over the same 28-day period. The results demonstrated that netarsudil ophthalmic solution 0.02% reduced mean diurnal IOP by a range of 5.0 to 5.3 millimeters of mercury ("mmHg") for subjects with an average baseline IOP of 18.3 mmHg. The netarsudil ophthalmic solution 0.04% arm reduced IOP by a range of 5.2 mmHg to 6.6 mmHg for subjects with an average baseline IOP of 20.2 mmHg. The placebo arm reduced IOP by a range of 2.0 to 2.5 mmHg for subjects with an average baseline pressure of 19.6 mmHg. Both netarsudil arms showed higher levels of IOP reduction as compared to placebo to a statistically significant degree at day 28. The safety findings were consistent with our previous netarsudil trials.

We are also planning to initiate a Phase 2 clinical trial on Japanese patients in Japan by the end of the first quarter of 2019 to support subsequent Phase 3 registration trials that are also expected to be conducted in Japan under our direction.

Rhopressa® Additional Research

We have performed additional research on the 24-hour IOP-reduction characteristics of Rhopressa®. In a 24-hour pilot study of 12 patients designed to compare the efficacy of Rhopressa® to that of placebo, Rhopressa® demonstrated consistent levels of IOP reduction during nocturnal and diurnal periods, to a meaningfully greater extent than placebo. 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.

We also plan to perform additional research on the potential benefits of Rhopressa® on normal tension glaucoma, pseudoexfoliative glaucoma and corneal healing, among others.

Rocklatan™

Our advanced-stage product candidate is once-daily Rocklatan™, a fixed-dose combination of Rhopressa® and latanoprost. We believe, based on our Phase 3 clinical trial data, that Rocklatan™, if approved, may provide a greater IOP-reducing effect than any currently marketed glaucoma medication. Therefore, we believe that Rocklatan™, if approved and formulary coverage is obtained, could compete with both PGA and non-PGA therapies for patients requiring maximal IOP reduction, including those with higher IOPs and those who present with significant disease progression despite use of currently available therapies.

Rocklatan™ in the United States

We submitted an NDA for Rocklatan™ to the FDA in May 2018 under Section 505(b)(2) of the FDCA, which provides for an abbreviated approval pathway, since Rocklatan™ is a fixed dose combination of two FDA-approved drugs in the United States. In July 2018, we announced that the NDA was accepted for review by the FDA and the PDUFA goal date was set for March 14, 2019, which represents a ten-month review.

We have completed two Phase 3 registration trials for Rocklatan™, named Mercury 1 and Mercury 2, each discussed further below. The Mercury 2 trial design was identical to that of Mercury 1, except that Mercury 2 was a 90-day trial without the additional nine-month safety extension included in Mercury 1. The safety results for Rocklatan™ showed no treatment-related serious adverse events and minimal evidence of treatment-related systemic effects. There were no new adverse events that developed over the 12-month period relative to the 90-day results, and there were no drug-related serious or systemic adverse events. Both Mercury 1 and Mercury 2 achieved their 90-day primary efficacy endpoints of demonstrating statistical superiority of Rocklatan™ over each of its components at all measured time points in patients with maximum baseline IOPs of above 20 mmHg to below 36 mmHg.

Rocklatan™ Outside of the United States

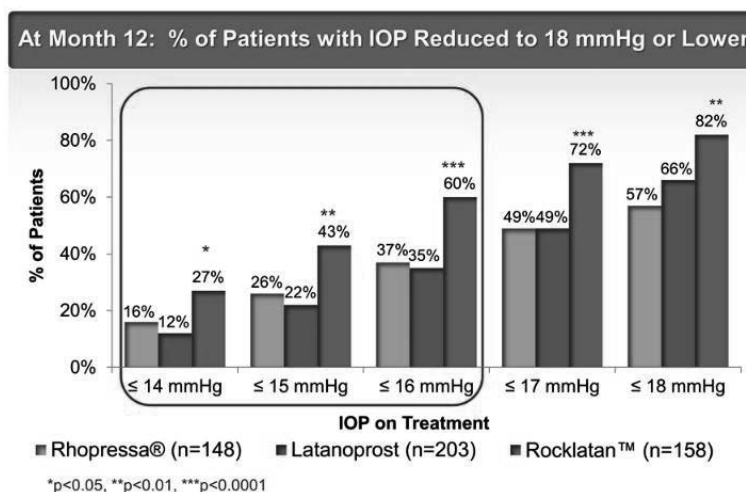
Mercury 1 and Mercury 2 will be used for European approval of Roclanda™. We also initiated a third Phase 3 registration trial for Roclanda™, named Mercury 3, in Europe during the third quarter of 2017. Mercury 3, a six-month efficacy and safety trial,

is designed to compare Roclanda™ to Ganfort®, a fixed-dose combination product marketed in Europe of bimatoprost, a PGA, and timolol, a beta blocker. If successful, Mercury 3 is expected to improve our commercialization prospects in Europe. Patients are being evaluated with maximum baseline IOPs ranging from above 20 mmHg to below 36 mmHg. We currently expect to read out topline 90-day efficacy data for the Mercury 3 trial in 2019. Since Roclanda™ is a fixed-dose combination product that includes Rhokiinsa®, we plan to submit an MAA for Roclanda™ with the EMA if and when Rhokiinsa® is approved by the EMA. We expect to submit the MAA for Roclanda™ in early 2020, if the EMA has approved Rhokiinsa® by such time.

Rocklatan™ Phase 3 Trial Data to Date

We have completed two Phase 3 registration trials for Rocklatan™, as discussed above. Mercury 1 was a 12-month safety trial with a 90-day efficacy readout. Mercury 1 achieved its primary efficacy endpoint of demonstrating statistical superiority of Rocklatan™ to each of its components, including Rhopressa® and latanoprost, in patients with maximum baseline IOPs of above 20 mmHg to below 36 mmHg. In the 90-day efficacy results, the IOP-reducing effect of Rocklatan™ exceeded that of monotherapy with latanoprost in a range of 1.3 mmHg to 2.5 mmHg and Rhopressa® in a range of 1.8 mmHg to 3.0 mmHg. In July 2017, we announced the 12-month safety results of the Mercury 1 study, which were consistent with those observed for the 90-day efficacy period, noting the safety results for Rocklatan™ showed no treatment-related serious adverse events and minimal evidence of treatment-related systemic effects. The most common Rocklatan™ adverse event was conjunctival hyperemia, which was observed in approximately 60% of patients, which was scored as mild in approximately 70% of affected patients. Other ocular adverse events reported in approximately 5% to 18% of patients in the Rocklatan™ group included corneal verticillata, conjunctival hemorrhage, eye pruritus, increased lacrimation, reduced visual acuity, blepharitis and punctate keratitis.

The graph below represents the responder analysis from the Mercury 1 90-day efficacy results, which shows the percentage of patients for whom IOP was reduced to 18 mmHg or lower, comparing Rocklatan™ to Rhopressa® and latanoprost.



Similar to Mercury 1, Mercury 2 achieved its 90-day primary efficacy endpoint of demonstrating statistical superiority over each of its components at all measured time points. The study evaluated patients with maximum baseline IOPs ranging from above 20 to below 36 mmHg at nine measured time points over the trial. The IOP-reducing effect of Rocklatan™ exceeded that of monotherapy with latanoprost in a range of 1.5 to 2.4 mmHg and Rhopressa® in a range of 2.2 to 3.3 mmHg, with efficacy levels remaining consistent for all arms of the study throughout the trial. Similar to Mercury 1, Rocklatan™ reduced mean diurnal IOPs to 16 mmHg or lower in 56% of patients, a significantly higher percentage than observed in the comparator arms of the study. The most common Rocklatan™ adverse event observed in the study was conjunctival hyperemia, which was reported in approximately 55% of patients, and was scored as mild for approximately 70% of affected patients. Other ocular adverse events reported in approximately 5% to 13% of patients in the Rocklatan™ group included corneal verticillata, conjunctival hemorrhage and corneal disorder (asymptomatic change in appearance of corneal endothelial cells). In addition, levels of IOP reduction in Mercury 2 were consistent with those observed in the Mercury 1 90-day efficacy results for all arms of the study.

Pipeline Opportunities

We are evaluating our portfolio of owned ROCK inhibitors for additional indications within and beyond glaucoma. Our owned preclinical small molecule, AR-13503 has demonstrated the potential for the treatment of DME, wet AMD and related diseases of the retina by inhibiting ROCK and Protein kinase C. AR-13503, which has the same active metabolite as Rhopressa[®], has shown lesion size decreases in an *in vivo* preclinical model of wet AMD at levels similar to the current market-leading wet AMD anti-VEGF product. When used in combination preclinically with the market leading anti-VEGF product, AR-13503 produced greater lesion size reduction than the anti-VEGF product alone in a model of proliferative DR. This molecule has not yet been tested in humans in a clinical trial setting. Pending additional studies, AR-13503 may have the potential to provide an entirely new mechanism and pathway to treat DME, wet AMD and related diseases of the retina. Since AR-13503 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.

To that end, in July 2017, we announced that we entered into a collaborative research, development and licensing agreement with DSM. The research collaboration agreement includes an option to license DSM's bio-erodible polymer implant technology for sustained delivery of certain Aerie compounds to treat ophthalmic diseases. In August 2018, we announced the expansion of our collaboration with DSM to provide for (i) a worldwide exclusive license for all ophthalmic indications to DSM's polyesteramide polymer technology, (ii) continuation of the collaborative research initiatives through the end of 2020, including the transfer of DSM's formulation technology to Aerie during that time and (iii) access to a preclinical latanoprost implant. This technology uses polyesteramide polymers to produce an injectable, thin fiber that is minute in size. Preclinical experiments have demonstrated early success in conjunction with AR-13503, including demonstration of linear, sustained elution rates over several months and achievement of target retinal drug concentrations. We expect to submit an IND for the AR-13503 sustained-release implant in the first quarter of 2019.

Further, in October 2017, we acquired the rights to use PRINT[®] technology in ophthalmology and certain other assets from Envisia. PRINT[®] is a proprietary technology capable of creating precisely-engineered sustained release products utilizing fully-scalable manufacturing processes. In addition, we acquired Envisia's intellectual property rights relating to Envisia's preclinical dexamethasone steroid implant for the potential treatment of macular edema due to RVO that utilizes the PRINT[®] technology, which we refer to as AR-1105. The IND for this sustained-release implant was submitted in December 2018. In January 2019, we announced that the FDA reviewed the IND for AR-1105 and it is now in effect, allowing Aerie to initiate human studies in the treatment of macular edema due to RVO. We expect to initiate a Phase 2 clinical study for AR-1105 in the first quarter of 2019. We are also evaluating the PRINT[®] technology platform for sustained release of therapies to the front of the eye, including to potentially treat open-angle glaucoma or ocular hypertension. We commenced operation of our current Good Manufacturing Practices ("cGMP")-validated manufacturing facility for production of ophthalmic implants using PRINT[®] technology in our Durham, North Carolina, facility in October 2018.

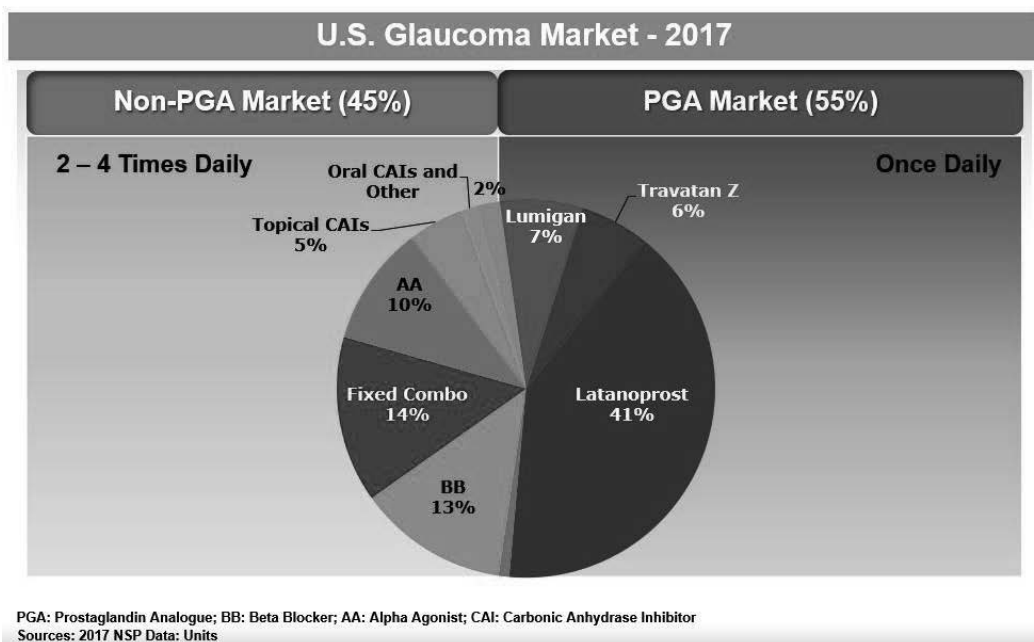
We may continue to enter into research collaboration arrangements, license, acquire or develop additional product candidates and technologies to broaden our presence in ophthalmology, and we continually explore and discuss potential additional opportunities for new ophthalmic products, delivery alternatives and new therapeutic areas with potential partners. Further, we are also currently screening our owned library of ROCK inhibitors for indications beyond glaucoma considering that third-party studies and trials have demonstrated potential for ROCK inhibition in treating certain disease categories. We are initially focused on exploring potential opportunities for our molecules in pulmonary health, dermatology and cancers. We are in the initial stages of our work on these applications.

Glaucoma Overview

Glaucoma Market Overview

Glaucoma is one of the largest segments in the global ophthalmic market. In 2017, branded and generic glaucoma product sales were approximately \$5.0 billion in the United States, Europe and Japan in aggregate, according to IQVIA. Prescription volume for glaucoma products in the United States alone was 37 million, representing 61 million bottles in 2017, 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 United States glaucoma market, as shown in the following chart, which is based on IQVIA data.



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 approximately 4.3 million by 2030. Furthermore, The Eye Diseases Prevalence Research Group has estimated that only half of the U.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 developing glaucoma, including, but not limited to, age, family history and ethnicity. 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 reduction 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.

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 such PGA monotherapy to maintain adequate control of IOP.

We believe there are significant unmet needs in the glaucoma market as is evident by the degree of use of multiple therapies to treat patients with the disease and understand that eye-care professionals are eager for new therapy choices, as we have seen with the early success of the Rhopressa® U.S. commercial launch. PGAs have side effects, contraindications and reduced efficacy in patients with low to moderately elevated IOPs relative to patients with higher IOPs. Other currently marketed 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 IQVIA. 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. Rhopressa® is the first of a new class of glaucoma drug products and may be

prescribed by eye-care professionals as a preferred adjunctive therapy for patients taking PGAs, due to its IOP-reducing ability, more convenient dosing and better tolerability profile compared to other currently marketed non-PGA adjunctive products.

Glaucoma Medical 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 reduction of IOP, measured in terms of mmHg, as the primary clinical endpoint for regulatory approval, making clinical trials for this indication relatively straight-forward due to easily measured objective parameters.

In a healthy eye, aqueous humor is continuously produced and drained from the eye in order to maintain pressure equilibrium and provide micronutrients to various tissues in the eye. An insufficient drainage of fluid can increase IOP above normal levels, which can eventually cause damage to the optic nerve. 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 between 21 and 26 mmHg at the time of diagnosis. Once damaged, the optic nerve cannot regenerate and thus damage to vision is permanent.

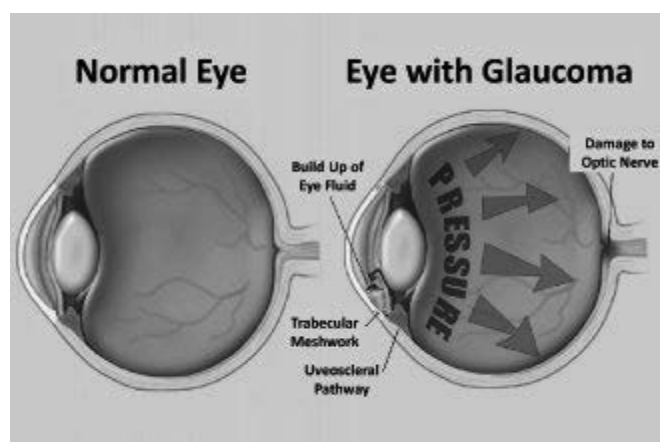
The most common form of glaucoma is open-angle glaucoma, which is characterized by abnormally high IOP as a result of impaired drainage of fluid from the eye's primary drain, the TM. Open-angle glaucoma is a progressive disease leading to vision loss and blindness for some patients as a result of irreversible 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 reduction of IOP has been shown to help in preventing additional damage to the optic nerve and further vision loss. This may require reducing 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 developing 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, episcleral venous pressure (“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.

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 reduce 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 reduced 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.

Retinal Diseases

AMD is the leading cause of irreversible vision loss in individuals over 55 years of age in developed countries. Clinically, it manifests in two forms: wet AMD and dry AMD. Wet AMD is responsible for a rapid and substantial vision decline characterized by abnormal growth and leakage of blood vessels that breaks through the Bruch’s membrane into the subretinal pigment epithelium space and/or the subretinal space, leading to exudation, hemorrhage, retinal edema, pigment epithelial detachment and fibrous scarring.

DR is the leading cause of vision loss among working age individuals in developed countries and DME is a common cause of vision loss associated with DR. DME occurs due to retinal microvasculature damage, increase in vascular permeability and loss of blood-retinal barrier leading to interstitial fluid accumulation in the retina, particularly in the region of the macula.

In both diseases, wet AMD and DME, vascular permeability, angiogenesis and inflammation play an important role and VEGF has shown to be a key mediator that has been found to be upregulated. Currently, the standard of care for treating wet AMD and DME is intravitreal injection of VEGF inhibitors (anti-VEGF). In addition, alternative therapeutic approaches for DME are directed towards stopping vascular leakage using laser photocoagulation and intravitreal injection of corticosteroids.

Existing anti-VEGF agents have similar safety and efficacy profiles. Three are the most widely used: bevacizumab, ranibizumab and aflibercept. Although anti-VEGF agents have shown a well-established efficacy profile in wet AMD and DME, a downside of these treatments is that some patients have poor response, experience a loss of efficacy after repeated injections over time or require frequent injections to maintain complete resolution of the exudation/edema. Thus, the need for alternative treatment options with prolonged treatment duration to reduce treatment burden of repeat injections and different mechanism of action to target refractory or non-response to anti-VEGF agents leaves a considerable unmet need.

RVO is the second-most common sight-threatening vascular disorder of the retina after DR. Current estimates put global prevalence at approximately 16 million people affected with the disease in one or both eyes and around 520 new cases per million are reported each year. RVO is the result of thrombus formation in the central, hemi-central or branch retinal vein, often due to compression by adjacent arteriosclerotic retinal arteries or vasculitis. The two main complications resulting from RVO are macular edema and retinal ischemia leading to retinal or iris neovascularization. Macular edema is a non-specific response of the retina to a variety of insults and involves the breakdown of the blood-retina barrier at the capillary endothelium, resulting in increased vascular permeability and subsequent leakage of fluids into the adjacent retinal tissues and significant visual disturbances. This reduction in vision may be reversible in the short-term, but chronic macular edema causes irreversible damage to the retina and permanent vision loss. Current options for treating macular edema depend upon the cause and severity

of the condition. In the case of RVO, the goal is to reduce the amount of fluid leakage and decrease the edema, thus leading to improved visual acuity. Argon laser photocoagulation was used for many years to treat macular edema associated with branch RVO, but was less effective in the treatment of central RVO, and was not successful in all patients.

Within the last 10 years, intravitreal (“IVT”) pharmacotherapy has revolutionized the therapeutic options for macular edema-associated retinal vascular diseases. Two classes of medication are currently approved to treat macular edema following RVO; corticosteroids (e.g., dexamethasone IVT implant, OZURDEX) and anti-VEGF agents (e.g., ranibizumab, LUCENTIS[®], aflibercept, EYLEA[®]). While both classes have demonstrated efficacy in RVO patients, the treatment burden remains high, with the anti-VEGFs typically requiring monthly or bi-monthly IVT injections and the dexamethasone implant typically requiring injections approximately once every three months. A corticosteroid implant that remained effective for a longer duration would provide the benefit of reducing the treatment burden on patients while treating the inflammatory components of macular edema that are not addressed by inhibition of VEGF. Additionally, if the dose of corticosteroid could be reduced without compromising efficacy, then there exists the potential for reduced corticosteroid-related adverse events such as cataract formation and increased IOP. We are developing AR-1105, a dexamethasone IVT implant, to address these unmet needs.

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, for example, Bausch Health Companies 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. Products 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 Rhopressa[®] and Rocklatan[™], if approved, are likely to be efficacy and their respective MOA(s), safety, convenience, price, tolerability and the availability of reimbursement from government and other third-party payers.

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

PGA Drug Class

- **Prostaglandin Analogues (“PGAs”).** Most PGAs are once-daily dosed eye drops generally prescribed as the initial drug to reduce IOP by increasing fluid outflow through the eye’s secondary drain. PGAs represent 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 reduction of IOP. The most commonly used drug in this class is timolol. Beta blockers are less effective than PGAs in terms of IOP reduction 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.
- **Topical 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 reduction. 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 reduction. 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 MOA(s)		
Brand	MOA / Dosing	Status
Rhopressa [®] (Aerie AR-13324)	ROCK inhibitor (qd)	U.S.: Marketed Europe: MAA accepted for review by EMA Japan: Phase 2
Rocklatan [™] (Aerie PG324)	ROCK inhibitor + PGA (qd)	U.S.: PDUFA goal date is March 14, 2019 Europe: Phase 3

New PGAs ¹		
Brand	MOA / Dosing	Status
Vyzulta [™] (Bausch)	NO donating latanoprost (qd)	U.S.: Marketed
Xelpros [™] (Sun)	Latanoprost, without BAK (qd)	U.S.: Marketed
DE-117 (Santen)	EP2 agonist (qd)	U.S.: Phase 3 Japan: approved in September 2018
DE-126 (Santen)	FP/EP3 agonist (qd)	U.S. and Japan: Phase 2b
NCX-470 (Nicox)	NO donating bimatoprost (qd)	U.S.: Phase 2

¹Not 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. Early-stage companies are also developing treatments for glaucoma, retinal diseases and other diseases of the eye and may prove to be significant competitors. We expect that our competitors will continue to develop new treatments for glaucoma, retinal diseases 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.

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, commercial and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer adverse effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

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. Our ability to compete may be affected because in many cases insurers or other third-party payers encourage the use of generic products. We expect that RocklatanTM, if approved, will be priced at a premium over competing generic products and consistent with Rhopressa[®] and other branded glaucoma drugs.

Sales and Marketing

We are commercializing Rhopressa[®] and plan to commercialize RocklatanTM, if approved, in the United States with our own focused, specialized sales force. For the launch of Rhopressa[®], we hired a commercial team that includes approximately 100 sales representatives targeting approximately 14,000 high prescribing eye-care professionals throughout the United States. This sales force will also be responsible for sales of RocklatanTM, if approved.

We have made significant progress in contracting for formulary coverage for Rhopressa[®] and will contract for formulary coverage for RocklatanTM, if approved, with U.S. payers for both commercial and Medicare Part D prescription drug plans. We have obtained formulary coverage for Rhopressa[®] for approximately 90% of lives covered under commercial plans and approximately 40% of lives covered under Medicare Part D plans. We expect Medicare Part D Tier 2 equivalent coverage to increase to over 70% by the end of the first quarter of 2019.

Outside of the United States, if we obtain regulatory approval, we currently expect to commercialize Rhokiinsa[®] and RoclandaTM in Europe on our own, and likely partner for commercialization of their equivalents in Japan.

Major Customers

For the year ended December 31, 2018, a significant percentage of our sales of Rhopressa[®] were to three large wholesale drug distributors. Sales to McKesson Corporation, Cardinal Health, Inc. and AmerisourceBergen Corporation accounted for 33.9%, 33.3% and 29.7% of total revenues, respectively, for the year then ended.

Manufacturing

We currently rely on our third-party manufacturers to produce the API and final drug product for Rhopressa[®] and RocklatanTM and we may rely on third-party manufacturers for our current and future product candidates. Our current contract manufacturer produces commercial supply of Rhopressa[®] and started to manufacture RocklatanTM in 2018 in anticipation of potential FDA approval and commercial launch in 2019.

The commercial production of the final drug product is ultimately expected to be supported by a combination of internal and outsourced manufacturing. We are also in the process of adding an additional API contract manufacturer and an additional Rhopressa[®] drug product contract manufacturer, both of which are expected to begin to supply commercial materials in the first half of 2019. Latanoprost, used in the manufacture of RocklatanTM, is available in commercial quantities from multiple reputable third-party manufacturers.

We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities. However, should a supplier or manufacturer on which we have relied to produce Rhopressa[®], RocklatanTM, Rhokiinsa[®] or any future product candidate provides us with a faulty product or such product is later recalled, we would likely experience reputational harm, delays and additional costs, each of which could be significant.

In January 2017, we commenced establishment of our own manufacturing plant in Athlone, Ireland. This will be our first manufacturing plant, which is expected to produce commercial supplies of Rhopressa[®] and, if approved, RocklatanTM, Rhokiinsa[®] and RoclandaTM. Commercial supply from the plant is expected to be available in early 2020. We need to continue to hire and train qualified employees to staff this facility. The management and operation of a pharmaceutical manufacturing facility requires the implementation and development of procedures that are compliant with the quality and other regulations dictated by regulatory authorities in the jurisdictions for which product is produced. Failure to maintain such compliance could cause us to experience delays in production, reputational harm and could negatively affect our commercial operations.

We expect third-party manufacturers to be capable of providing sufficient quantities of Rhopressa[®] and Rocklatan[™] to meet our anticipated clinical and commercial demands. If 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 could experience a delay in our ability to obtain alternative suppliers.

Intellectual Property

We have obtained patent protection for Rhopressa[®] and Rocklatan[™] (patent protection for Rocklatan[™] includes patent protection we have secured for Rhopressa[®]), in the United States and foreign jurisdictions, including in, but not limited to, Europe and Asia, and will seek and are seeking patent protection in additional foreign jurisdictions from time to time as we deem appropriate. 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. Our existing patents or patents we obtain in the future may not be commercially useful in protecting our technology. In addition, our patents may not issue on any of our pending patent applications or patent applications we file in the future. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, see “Risk Factors—Risks Related to Intellectual Property.”

Our intellectual property consists of issued patents, and pending patent applications for compositions of matter, pharmaceutical formulations, methods of use, medical devices and synthetic methods. We have patent protection for Rhopressa[®] and Rocklatan[™] in the United States through at least 2034. Additionally, we hold patents for composition of matter and method of use in certain foreign jurisdictions for Rhopressa[®] and Rocklatan[™] through dates ranging from 2030 to 2037. Furthermore, we have patent protection for AR-13503 in the United States and internationally, which extends to 2030. We have also filed for patent protection for AR-1105 in the United States and internationally. We also hold patents and have pending patent applications for other ROCK inhibitor molecules.

The following table summarizes the status of our patent portfolio as of December 31, 2018 setting forth the number of existing issued patents and pending patent applications, as well as their respective estimated expiration date ranges:

Country	Number of Issued Patents	Number of Pending Patents	Estimated Expiration Date Range
United States	34	18	2026 - 2039
Australia	10	12	2026 - 2037
Brazil	0	1	2037
Canada	2	7	2026 - 2037
China	0	3	2034
Europe	50 ⁽¹⁾	4	2026 - 2037 ⁽¹⁾
Hong Kong	0	1	2030
India	0	1	2035
Japan	6	5	2026 - 2037
Mexico	0	1	2037
Patent Cooperation Treaty	0	6	N/A
Singapore	0	1	2036
South Korea	0	2	2035 - 2037

- ⁽¹⁾ Includes patent protection in Belgium (3 issued patents; estimated expiration date: 2026-2030), France (8 issued patents; estimated expiration date: 2026-2030), Germany (8 issued patents; estimated expiration date: 2026-2030), Great Britain (8 issued patents; estimated expiration date: 2026-2030), Ireland (1 issued patent; estimated expiration date: 2030), Italy (8 issued patents; estimated expiration date: 2026-2030), Netherlands (3 issued patents; estimated expiration date: 2026-2030), Spain (8 issued patents; estimated expiration date: 2026-2030) and Switzerland (3 issued patents; estimated expiration date: 2026-2030).

Aerie[®] and Rhopressa[®] are registered U.S. trademarks of ours and we have an application pending for each trademark in Europe and Japan. We also have an application for our trademark Rocklatan[™] pending in the U.S. Patent and Trademark Office (“USPTO”). In Europe, Rhokiinsa[®] is a registered trademark of ours and we have an application pending for Roclanda[™], as well as pending applications for other trademarks in the United States and foreign jurisdictions.

Regulatory Matters

FDA Regulation and Marketing Approval

In the United States, the FDA regulates drugs under the 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 (“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 research, 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 IND, which allows clinical trials to begin unless FDA objects within 30 days;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use or uses conducted in accordance with FDA regulations, Good Clinical Practices (“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, investigators, 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 evaluate 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.

In addition, the manufacturer of an investigational drug in a Phase 2 or Phase 3 clinical trial 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.

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

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose 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 \$2.5 million for fiscal year 2019) 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 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. An NDA must also contain data to assess the safety and effectiveness of the product for the claimed indication in all relevant pediatric populations. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. 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.

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 may 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 ("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 ("ETASU"). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. These elements are negotiated as part of the NDA approval, and in some cases if consensus is not obtained until after the PDUFA review cycle, the approval date may be delayed. Once adopted, REMS are subject to periodic assessment and modification.

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

original application, including relevant pediatric data, 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 or problems the extent or severity of which were unknown may result in restrictions on the product or even complete withdrawal of the product from the market. We cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Adverse Event Reporting

The FDA requires reporting of certain information on side effects and adverse events reported during clinical studies and after marketing approval. Non-compliance with FDA safety reporting requirements may result in FDA regulatory action that may include civil action or criminal penalties. Side effects or adverse events that are reported during clinical trials can delay, impede or prevent marketing approval. Similarly, adverse events that are reported after marketing approval can result in additional limitations being placed on the product's use, require labeling changes, and, potentially, withdrawal or suspension of the product from the market.

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 Extension

Patent Term Extension ("PTE") in the United States can compensate for lost patent grant time during product development and the regulatory review process for a patent that covers a new product or its use. This PTE 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. PTEs that can be obtained are for up to five years beyond the expiration of the patent or 14 years from the date of product approval, whichever is earlier. 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 identified 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 ("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 with and accepted 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 ("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. For a drug that has been previously approved by the FDA, 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 new conditions of use 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.

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.

Advertising

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 ("PDMA"), a part of the FDCA. In addition, Title II of the Federal Drug Quality and Security Act of 2013, known as the Drug Supply Chain Security Act or the DSCSA, has imposed new "track and trace" requirements on the distribution of prescription drug products by manufacturers, distributors, and other entities in the drug supply chain. These requirements are being phased in over a ten-year period. Unless the products were packaged prior to November 27, 2018, the DSCSA requires product identifiers (i.e., serialization) on prescription drug products in order to establish an electronic interoperable prescription product system to identify and trace certain prescription drugs

distributed in the United States. The DSCSA replaced the prior drug “pedigree” requirements under the PDMA, and preempts existing state drug pedigree laws and regulations. The DSCSA also establishes new requirements for the licensing of wholesale distributors and third-party logistic providers. These licensing requirements preempt states from imposing licensing requirements that are inconsistent with, less stringent than, directly related to, or otherwise encompassed by standards established by FDA pursuant to the DSCSA. Until FDA promulgates regulations to address the DSCSA’s new national licensing standard, current state licensing requirements typically remain in effect.

Manufacturing

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 applicant under an approved NDA is subject to an annual program fee (replacing the old product and establishment fees), currently exceeding \$300,000 per prescription drug product for fiscal year 2018.

Post-Approval Testing

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.

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 (“CMS”), 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 of 1996 (“HIPAA”), as amended, and similar state laws. Pricing and rebate programs must be considered in price reports in order to 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 (“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 payers 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 payers.

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 payers, it is not clear what effect, if any, the research will have on the sales of our products, if any such products 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 products. If third-party payers 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 ("EU") 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 EU do not follow price structures of the United States and generally tend to be significantly lower.

As noted above, in the United States, we are subject to complex laws and regulations pertaining to healthcare "fraud and abuse," including, but not limited to, the Federal Anti-Kickback Statute, the Federal False Claims Act, and other state and federal laws and regulations. The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the Federal Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws, the absence of guidance in the form of regulations or court decisions, and the potential for additional legal or regulatory change in this area, it is possible that our future sales and marketing practices and/or our future relationships with eye-care professionals might be challenged under anti-kickback laws, which could harm us. Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we have developed 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 payers, 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 with requirements for manufacturers and/or marketers of pharmaceutical products. Some states require the reporting of expenses relating to the marketing and promotion of drug products and the reporting of gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the reporting of certain pricing information, including information pertaining to and justification of price increases, or prohibit prescription drug price gouging. In addition, states such as California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, as discussed in “—*Patient Protection and Affordable Care Act*” below, a similar federal requirement requires 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.

Numerous U.S. federal and state laws, including state security breach notification laws, state health information privacy laws and U.S. federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who are expected to prescribe our products and from whom we obtain patient health information, are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH”) and its implementing regulations, which imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA’s privacy and security standards directly applicable to “business associates,” such as independent contractors or agents of covered entities that receive or obtain protected health information with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities and business associates. In addition, HITECH also gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney’s fees and costs associated with pursuing these actions. As a result of HIPAA, we could be subject to criminal penalties if we obtain and/or disclose individually identifiable health information from a HIPAA-covered entity, including healthcare providers, in a manner that is not authorized or permitted by HIPAA. In addition, many U.S. states and foreign governments have enacted comparable laws addressing the privacy and security of health information, such as the General Data Protection Regulation (the “GDPR”) enacted by the EU, some of which are more stringent than HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to disrupt our operations, including recently enacted laws in a majority of states requiring security breach notification. If there are any violations of these laws, we could face significant administrative and monetary sanctions as well as reputational damage, which may have a material adverse effect on our business.

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 requiring, 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.

Government Programs for Marketed Drugs

Medicaid, the 340B Drug Pricing Program, and Medicare

Federal law requires that a pharmaceutical manufacturer, as a condition of having its products receive federal reimbursement under Medicaid and Medicare Part B, must pay rebates to state Medicaid programs for all units of its covered outpatient drugs dispensed to Medicaid beneficiaries and paid for by a state Medicaid program under either a fee-for-service arrangement or through a managed care organization. This federal requirement is effectuated through a Medicaid drug rebate agreement between the manufacturer and the Secretary of Health and Human Services. CMS administers the Medicaid drug rebate agreements, which provide, among other things, that the drug manufacturer will pay rebates to each state Medicaid agency on a quarterly basis and report certain price information on a monthly and quarterly basis. The rebates are based on prices reported to CMS by manufacturers for their covered outpatient drugs. For innovator products, that is, drugs that are marketed under approved NDAs, the basic rebate amount is the greater of 23.1% of the average manufacturer price (“AMP”) for the quarter or the difference between such AMP and the best price for that same quarter. The AMP is the weighted average of prices paid to the manufacturer (1) directly by retail community pharmacies and (2) by wholesalers for drugs distributed to retail community pharmacies. The best price is essentially the lowest price available to non-governmental entities. Innovator products are also subject to an additional rebate that is based on the amount, if any, by which the product’s current AMP has increased over the baseline AMP, which is the AMP for the first full quarter after launch, adjusted for inflation. For non-innovator products, generally generic drugs marketed under approved abbreviated new drug applications, the basic rebate amount is 13% of the AMP for the quarter. Until amendments to the statute were enacted, this was the only rebate applicable to non-innovator products. However, as a result of a November 2015 amendment, non-innovator products are subject to an additional rebate. The additional rebate is similar to that discussed above for innovator products, except that the baseline AMP quarter is the fifth full quarter after launch (for non-innovator multiple source drugs launched on April 1, 2013 or later) or the third quarter of 2014 (for those launched before April 1, 2013). The statutory definition of AMP was amended in 2010 by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, “PPACA”). In February 2016, CMS published a final rule to further define AMP and provide clarification on other parts of the rebate program.

The terms of participation in the Medicaid drug rebate program impose an obligation to correct the prices reported in previous quarters, as may be necessary. Any such corrections could result in additional or lesser rebate liability, depending on the direction of the correction. In addition to retroactive rebates, if a manufacturer were found to have knowingly submitted false information to the government, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

A manufacturer must also participate in a federal program known as the 340B drug pricing program in order for federal funds to be available to pay for the manufacturer’s drugs under Medicaid and Medicare Part B. Under this program, the participating manufacturer agrees to charge certain safety net healthcare providers no more than an established discounted price for its covered outpatient drugs. The formula for determining the discounted price is defined by statute and is based on the AMP and the unit rebate amount as calculated under the Medicaid drug rebate program, discussed above. Manufacturers are required to report pricing information to the Health Resources and Services Administration (“HRSA”) on a quarterly basis effective the first quarter of 2019. HRSA has also issued regulations relating to the calculation of the ceiling price as well as imposition of civil monetary penalties for each instance of knowingly and intentionally overcharging a 340B covered entity.

Federal law also requires that manufacturers report data on a quarterly basis to CMS regarding the pricing of drugs that are separately reimbursable under Medicare Part B. These are generally drugs, such as injectable products, that are administered “incident to” a physician service and are not generally self-administered. The pricing information submitted by manufacturers is the basis for reimbursement to physicians and suppliers for drugs covered under Medicare Part B. As with the Medicaid drug rebate program, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

Medicare Part D provides prescription drug benefits for seniors and people with disabilities. Medicare Part D beneficiaries have a gap in their coverage (between the initial coverage limit and the point at which catastrophic coverage begins) where Medicare does not cover their prescription drug costs, known as the coverage gap. However, by 2020, Medicare Part D beneficiaries will pay 25% of drug costs after they reach the initial coverage limit - the same percentage they were responsible for before they reached that limit - thereby closing the coverage gap. The cost of closing the coverage gap is being borne by innovator companies and the government through subsidies. Beginning in 2011, each manufacturer of drugs approved under NDAs was required to enter into a Medicare Part D coverage gap discount agreement and provide a 50% discount on those drugs dispensed to Medicare beneficiaries in the coverage gap, in order for its drugs to be reimbursed by Medicare Part D. The Bipartisan Budget Act of 2018 increased the manufacturer’s subsidy under this program from 50% to 70% of the negotiated price, beginning in 2019.

Federal Contracting/Pricing Requirements

Manufacturers are also required to make their covered drugs, which are generally drugs approved under NDAs, available to authorized users of the Federal Supply Schedule (“FSS”) of the General Services Administration. The law also requires manufacturers to offer deeply discounted FSS contract pricing for purchases of their covered drugs by the Department of Veterans Affairs, the Department of Defense (“DoD”), the Coast Guard, and the Public Health Service (including the Indian Health Service) in order for federal funding to be available for reimbursement or purchase of the manufacturer’s drugs under certain federal programs. FSS pricing to those four federal agencies for covered drugs must be no more than the Federal Ceiling Price (“FCP”), which is at least 24% below the Non-Federal Average Manufacturer Price (“Non-FAMP”) for the prior year. The Non-FAMP is the average price for covered drugs sold to wholesalers or other middlemen, net of any price reductions.

The accuracy of a manufacturer’s reported Non-FAMPs, FCPs, or FSS contract prices may be audited by the government. Among the remedies available to the government for inaccuracies is recoupment of any overcharges to the four specified federal agencies based on those inaccuracies. If a manufacturer were found to have knowingly reported false prices, in addition to other penalties available to the government, the law provides for civil monetary penalties of \$100,000 per incorrect item. Finally, manufacturers are required to disclose in FSS contract proposals all commercial pricing that is equal to or less than the proposed FSS pricing, and subsequent to award of an FSS contract, manufacturers are required to monitor certain commercial price reductions and extend commensurate price reductions to the government, under the terms of the FSS contract Price Reductions Clause. Among the remedies available to the government for any failure to properly disclose commercial pricing and/or to extend FSS contract price reductions is recoupment of any FSS overcharges that may result from such omissions.

Tricare Retail Pharmacy Network Program

The DoD provides pharmacy benefits to current and retired military service members and their families through the Tricare healthcare program. When a Tricare beneficiary obtains a prescription drug through a retail pharmacy, the DoD reimburses the pharmacy at the retail price for the drug rather than procuring it from the manufacturer at the discounted FCP discussed above. In order for the DoD to realize discounted prices for covered drugs (generally drugs approved under NDAs), federal law requires manufacturers to pay refunds on utilization of their covered drugs sold to Tricare beneficiaries through retail pharmacies in DoD’s Tricare network. These refunds are generally the difference between the Non-FAMP and the FCP and are due on a quarterly basis. Absent an agreement from the manufacturer to provide such refunds, DoD will designate the manufacturer’s products as Tier 3 (non-formulary) and require that beneficiaries obtain prior authorization in order for the products to be dispensed at a Tricare retail network pharmacy. However, refunds are due whether or not the manufacturer has entered into such an agreement.

Branded Pharmaceutical Fee

A branded pharmaceutical fee is imposed on manufacturers and importers of branded prescription drugs, generally drugs approved under NDAs. In each year between 2011 and 2018, the aggregate fee for all such manufacturers will range from \$2.5 billion to \$4.1 billion, and then will remain at \$2.8 billion in 2019 and subsequent years. This annual fee is apportioned among the participating companies based on each company’s sales of qualifying products to or utilization by certain U.S. government programs during the preceding calendar year. The fee became effective January 1, 2011, and is not deductible for U.S. federal income tax purposes. Utilization of generic drugs, generally drugs approved under ANDAs, is not included in a manufacturer’s sales used to calculate its portion of the fee.

Patient Protection and Affordable Care Act

In March 2010, the 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:

- As discussed above, effective in 2010, PPACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers’ rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic agents to 23.1% of AMP and adding a new rebate calculation for “line extensions” (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. PPACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by expanding the population potentially eligible for Medicaid drug benefits. CMS expanded Medicaid rebate liability to the territories of the United States as well, effective April 1, 2020. 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, also provided for the public availability of pharmacy acquisition of cost data, which could negatively impact our sales.

- 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.
- 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"). The Bipartisan Budget Act of 2018 increased the manufacturer's subsidy under this program from 50% to 70% of the negotiated price, beginning in 2019.
- 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. Effective January 1, 2022, we will also be required to report on transfers of value to, among others, physician assistants and nurse practitioners or clinical nurse specialists. 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.

There have been ongoing discussions within the U.S. federal government regarding the future of PPACA. There is uncertainty with respect to the impact these changes, if any, may have, and any changes likely will take time to unfold.

European Union

European Union Drug Development

In the EU, our products and product candidates will also be subject to extensive regulatory requirements. Regulatory laws for pharmaceuticals are largely harmonized throughout the EU, so that applicable EU law is most significant and national laws have less importance. 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 EU are subject to significant regulatory controls. Phases 1 to 3 of clinical trials in humans are comparable to those regulated in the United States, and GCP requirements in the EU for these studies follow internationally accepted standards.

Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trial regulatory framework for pharmaceuticals by setting out common rules for the control and authorization of clinical trials in the EU, 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 ("NCA") and one or more Ethics Committees ("ECs"). 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. All clinical trials will have to conform to current GCP guidelines issued by the EU and the International Council on Harmonisation of Technical

Requirements for Registration of Pharmaceuticals for Human Use, in particular when the results of such trials are being used in marketing authorization procedures, and audits by EU inspectors on regulatory conformance of such clinical trials are likely.

In 2014, the new EU Clinical Trial Regulation 546/2014 was enacted. When it becomes applicable (currently expected beginning in 2020), it will govern all newly-commenced clinical trials. The new Regulation aims to make more uniform and streamline the clinical trials authorization process, ensure consistent rules for conducting clinical trials throughout the EU, increase the efficiency of clinical trials, and increase the transparency of authorization, conduct and results of clinical trials. All currently conducted clinical trials remain subjected to the Clinical Trials Directive of 2001.

Generally, in the European Economic Area (“EEA”), for every product candidate, a pediatric investigation plan (“PIP”) will have to be submitted and approval be obtained, in addition to clinical trials conducted in adults. The clinical studies that sponsoring companies must carry out on children are to be set out in detail in the PIP. In most cases, the PIP will become a commitment when applying for a marketing authorization for a product candidate. A PIP may entail significant cost.

European Union Drug Review Approval

In the EEA, which is currently comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization (“MA”) which is comparable to an NDA in the United States. There are two types of marketing authorizations in the EEA: 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 (“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 each Member State of the EEA and only authorizes marketing in that Member State’s national territory and not in 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 EU. 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 State 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 (“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.

Our current EU application seeks to obtain a Centralized MA for Rhokiinsa[®]. We have submitted our application directly to the EMA, which has accepted our application. The EMA is responsible for the validation and scientific evaluation of the application but the European Commission will decide upon our application. The EMA’s CHMP will carry out a scientific assessment of the application and will give a recommendation on whether the medicine should be authorized or not. A favorable opinion is accompanied by a draft summary of the product’s characteristics, the package leaflet and the proposed text for the packaging.

The time limit for the evaluation procedure is 210 days, subject to extensions if additional questions need to be addressed. Within 15 days of the adoption, the EMA will forward its opinion to the European Commission to start the decision-making phase. Within 15 days a draft implementing decision is sent by the Commission to the Standing Committee on Medicinal Products for Human Use, allowing for its scrutiny by EU countries. These have 15 days to return their linguistic comments, and 22 days for substantial ones. Once a favorable opinion is reached, the draft decision is adopted via an empowerment procedure. The adoption of the decision should take place within 67 days of the opinion of the EMA. The Commission’s Secretariat-General then notifies the marketing authorization holder of the decision. The decision is subsequently published in the Community Register.

Marketing authorizations are initially valid for five years. Applications for renewal must be made to the EMA at least six months before this five-year period expires.

Files Required for Obtaining an EU Marketing Authorization

Similar to the United States, applications for MAs in the EU must be supported by an extensive dossier that shows the product candidate has the required quality, efficacy and safety suitable for the intended use, and additional administrative documents. The content and format of the dossier must follow the so-called Common Technical Document (“CTD”) format. Amongst other things, the applicant must submit all relevant data from pharmaceutical, pre-clinical and clinical trials, and all relevant information as regards the composition, quality and manufacturing process of the product. These requirements are laid down in applicable EU legislation and very detailed EMA guidelines.

In the course of the MAA process, an inspection of the veracity and the compliance of the clinical trials that form the basis of the MAA may be conducted by EU inspectors. If it turns out that a clinical trial does not meet GCP and other applicable regulatory standards, it may not serve as a basis for proving efficacy and safety of the product at issue.

Also, the manufacturing sites for the active ingredients of the product candidate may be inspected by the EU in order to establish that the manufacturing indeed complies with cGMP standards.

Applicants are responsible for ensuring the safety profile of their medicine is adequately characterized at the time of submitting their MAA. Applicants are required to submit a risk management plan as part of their MAA. Risk management plans describe existing knowledge on the safety of a medicine and future pharmacovigilance activities designed to further study or monitor the product's safety. Part of that plan will be that a qualified person responsible for pharmacovigilance is being retained.

Post-approval Obligations of an MA Holder in the EU

Even after approval of a product candidate by the European Commission, an MA holder will face various ongoing actions and obligations and must ensure that it has a suitable organization in place that is able to meet these obligations.

Reportable suspected adverse events must be reported to competent authorities via EudraVigilance, a centralized European information system of suspected adverse reactions to medicines. EudraVigilance will re-route the case safety reports to EU member states. The EMA will make the reports of individual cases of suspected adverse reactions also available to the WHO Uppsala Monitoring Centre. Patients and healthcare professionals will continue to report adverse reactions to national competent authorities.

For public health reasons, the EMA may require the MA holder to provide additional data post-authorization, as necessary to provide additional data about the safety and, in certain cases, the efficacy or quality of authorized medicinal products.

The EMA is responsible for harmonizing and coordinating pharmacovigilance inspections at EU level, which involves, among others:

- Preparing a risk-based program of routine pharmacovigilance inspections in relation to centrally authorised products.
- Preparing and developing guidance on pharmacovigilance inspections.
- Coordinating advice on the interpretation of pharmacovigilance requirements and related technical issues.

The EMA is also responsible for coordinating inspections to verify compliance with cGMP, GCP, good laboratory practice and good pharmacovigilance practice, and any other aspects of the supervision of authorized medicinal products.

Member States and the Commission must inform other member states, the EMA and the Commission if concerns result from the evaluation of data from pharmacovigilance activities. This may result in the suspension or revocation of the marketing authorization.

Member states have systems in place which aim at preventing dangerous medicinal products from reaching the patient, and cover the receipt and handling of notifications of suspected falsified medicines or quality defects. Rapid alerts must be sent to all member states and a recall may be initiated if such medicines have already reached patients.

An MA holder must:

- Continuously operate a pharmacovigilance system, part of which requires a permanently and continuously available appropriately qualified person responsible for pharmacovigilance.

- Establish a risk management system, take account of scientific and technical progress and adapt accordingly, and continuously provide the competent authorities with information which might involve amendment of its marketing authorization.
- Inform the competent authorities of positive and negative results in clinical trials or studies and any defects, and on request have at its disposal details regarding, for example, the volume of sales.
- Ensure that a package information leaflet is made available on request from patients' organizations, in formats appropriate for the blind and partially-sighted.
- Inform the EMA of changes related to the placement of the medicinal product on the market, for example withdrawal or suspension.

Data Exclusivity and Similar Protection in the EU

An innovator company enjoys a period of "data exclusivity" during which its preclinical and clinical trials data may not be referenced in the regulatory filings of another company (typically a generic company) for the same drug substance.

The period of data exclusivity in Europe has been harmonized as eight years from the date of first authorization in Europe. There is an additional period of two years of "market exclusivity". This is the period of time during which a generic company may not market an equivalent generic version of the originator's pharmaceutical product (although their application for authorization may be processed during this period, such that they are in a position to market their product on the expiry of this additional two-year period).

After that period of a total of 10 years, generic companies can market their "essentially similar" products by referencing the innovator's data, unless the innovator product qualifies for a further one year of exclusivity. This additional one year may be obtained if the innovator company is granted an MA for a significant new indication for the relevant medicinal product within the first eight years of its marketing. In such a situation, the generic companies can only market their copy products after 11 years from the grant of the innovator company's initial MA.

In addition, the innovator company may be eligible to receive a Supplementary Protection Certificate ("SPC"). This is an intellectual property right that serves as an extension to a patent right, comparable to a PTE in the U.S. SPCs aim to offset the loss of patent protection for pharmaceutical products that occurs due to the compulsory lengthy testing and clinical trials these products require prior to obtaining regulatory marketing approval.

An SPC can extend an eligible patent right for a maximum of five years. An additional six-month extension is available in accordance with Regulation (EC) No 1901/2006 if the SPC relates to a medicinal product for children for which data has been submitted according to a PIP, as outlined above.

Reimbursement in the EU

The EU does not have a centralized healthcare system. Healthcare is provided through very different systems at the national level. This jurisdictional divide may lead to delayed or restricted patient access. Generally, the reimbursement prices must be negotiated with national healthcare carriers on a state-by-state process.

EU and national laws impose a number of restrictions on pricing. Directive 89/105/EEC relating to the transparency of measures regulating the prices of medicinal products ("Transparency Directive") aims to ensure the transparency of national pricing and reimbursement. It sets procedural requirements to help monitor national decisions and their compatibility with pharmaceutical trade in the EU internal market. For example, member states must ensure that decisions on prices are made within a certain timeframe and communicated to the applicant with a statement of reason based on objective and verifiable criteria. Member states must also ensure that such decisions are open to judicial review.

Another important restriction on pricing is Article 102 of the Treaty on the Functioning of the European Union ("TFEU"), which prohibits dominant pharmaceutical companies from abusing this dominance in their relevant markets.

EU Privacy Laws

The GDPR came into effect in the European Union on May 25, 2018, and has changed the way that personal data can be held and processed. Non-compliance can lead to substantial fines, amounting to up to 4% of annual global revenue or €20 million, whichever is greater.

The GDPR expands and formalizes many rights that existed under former laws. It also requires that organizations inventory their data and document the legal basis for processing personal information. Further, the GDPR provides EU data subjects with rights they may exercise in connection with their data such as the “right to be forgotten”.

Generally, personal data of third parties must only be held and used by a company (the “Data Controller”) when covered by an informed consent of the person concerned, or by a legitimate and vital interest, as defined in the GDPR. Any consent must be informed, freely given and specific, and, if applicable, also include the right to transfer personal data to a country outside of the EU. The Data Controller is responsible for GDPR compliance, but can outsource certain tasks to third parties, so-called “Data Processors”. Affected third parties must be informed in some detail on the storage and use of their data, e.g. as clinical trial subjects, or as prescribers, and have the right to deny their consent.

It is important for companies to ensure they have a nominated data protection officer. They must also brief and train their staff, so they are aware and aligned. Companies should keep records of their approach to GDPR and how they have prepared for it. Preparation should also extend to a response in the event of an access request or complaint from a data subject, or with regards to a GDPR breach.

Brexit

Unless otherwise agreed with the other member states of the EU, the United Kingdom will leave the EU in March 2019 (“Brexit”). As one of the Brexit consequences, the EMA will relocate from London to Amsterdam. It is unclear what impacts Brexit will have with respect to the cross-border acknowledgment of clinical trial results and MAs; however, it is possible that a separate marketing application and approval will be required to market a product in the United Kingdom, and that significant delays will occur before the product can be marketed in the United Kingdom. Likewise, a no deal Brexit could cause the United Kingdom to be treated as a third country under GDPR requiring use of GDPR sanctioned mechanisms for data transfers.

Japan

Right of Reference

In Japan, clinical trial data collected for obtaining an approval in foreign countries can be used for obtaining an approval for a drug in accordance with the requirements stipulated in the notification by Ministry of Health, Labor and Welfare (the “MHLW”). The collection of such clinical data and drafting of the submission must meet the requirements under the normal Japanese regulations (Article 43 of the Enforcement Regulations of Pharmaceuticals and Medical Devices Law). The clinical trial data are required to include (i) pharmacodynamics, dose response, efficacy and safety in the foreign countries, (ii) clinical test data clearly exhibiting dose response, efficacy and safety (planned and performed in accordance with Japan rules, such as the Ministerial Ordinance on Good Clinical Practice for Drugs, and GCP; well-managed and using proper test controls; and using proper endpoints, and (iii) pharmacodynamics characteristic in the Japanese population. Further, the MHLW usually requests that a company submit bridging data from testing that is performed in Japan so that the clinical test data in foreign countries are demonstrated to be able to be generalized to the Japanese population. Generally, when the bridging data demonstrate that the dose response, efficacy and safety in Japan are similar to those in the foreign countries, the MHLW recognizes that the test results in the foreign countries can be generalized to the Japanese population. When the dose of the Japanese population in the bridging data is different from that of the test in the foreign countries, the MHLW will request that a company submit pharmacodynamics test results. When the number of samples in the bridging study or studies is limited, the MHLW will request that a company further submit test data demonstrating safety. When the bridging data cannot demonstrate efficacy and safety, the MHLW will request that a company submit clinical test results for the Japanese population.

Obtaining Approval

In practice, there are three basic ways for a non-Japanese company to obtain approval for pharmaceuticals manufactured overseas:

- Option 1—establish a Japanese corporation that obtains the necessary approvals and licenses. This provides the most durable presence in Japan. It also entails high initial time and expense (including hiring staff) and must be done in compliance with the provisions of the Pharmaceuticals and Medical Devices Law.
- Option 2—designate an existing Japanese company to obtain the necessary approvals and licenses. The manufacturing/sales approval for the drug will be registered in the Japanese company's name. This can raise potential problems if the overseas company does not strictly control the Japanese approval holder.
- Option 3—use the designated marketing approval holder (“DMAH”) system under Article 19-2 of the Pharmaceuticals and Medical Devices Law and select a Japanese company approved by the MHLW to act as

a DMAH. This option provides several benefits, including the manufacturing/sales approval being held directly by the non-Japanese company. In addition, the costs for obtaining/maintaining drug approval are lower than in the first two options. Since the approval is under the non-Japanese company's name, there are fewer concerns about the Japanese company acting on its own. If there are problems with the DMAH, the non-Japanese company can designate another company as the DMAH. Compared with the first option, the costs for a DMAH are lower, since there is no need to establish a new company. DMAHs are authorized by the MHLW, licensed for manufacture/sales of pharmaceuticals and provide full support in the drug approval process.

Japan Privacy Laws

Japan has regulatory provisions for privacy protection for personal information, including of patients in clinical trials. Most importantly, the Act on the Protection of Personal Information covers the protection of personal information. Personal information as used in the Act means information about a living individual that can identify the specific individual by name, date of birth or other description contained in such information (including such information as will allow easy reference to other information and will thereby enable the identification of the specific individual).

Pharmaceutical companies in Japan typically adopt their own internal privacy policies based on this law. The requirements tend to be general and leave a good deal of discretion to individual companies, but typically pharmaceutical companies establish policies covering appropriate safeguarding of personal information, prior consent for disclosure, and protection of personal data from leaks or other unauthorized access or disclosure.

The Clinical Research Act establishing clinical research guidelines, similarly, requires persons conducting clinical studies to obtain informed consent of participants and protect participants' personal data.

Other Countries

In addition to regulations in the United States, the EU, Japan, and potentially the United Kingdom, 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.

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 353 full-time employees as of December 31, 2018. 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 4301 Emperor Boulevard, Suite 400, Durham, North Carolina 27703 and our telephone number is (919) 237-5300. 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. The SEC maintains a website that

contains reports, proxy and information statements and other information regarding our filings at <http://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.

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 FDA-approved product, Rhopressa[®], and our advanced-stage product candidate, Rocklatan[™]. If we are unable to successfully commercialize Rhopressa[®] or Rocklatan[™], if approved, 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 depend on the successful commercialization of our FDA-approved product Rhopressa[®], which began in April 2018, and the successful development, regulatory approval and commercialization of our current and any future product candidates for the treatment of patients with open-angle glaucoma, retinal diseases and other diseases of the eye. Rhopressa[®] has been approved by the FDA in the United States, but it has not received regulatory approval in any other jurisdiction and no sales can be made in any jurisdictions outside the United States unless such approval occurs. We have invested a significant portion of our efforts and financial resources in the development of Rhopressa[®] and Rocklatan[™], and our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize Rhopressa[®] and Rocklatan[™], if approved, in the United States. The success of Rhopressa[®], Rocklatan[™] and any future product candidates in the United States depends on several factors, including:

- successfully completing clinical trials;
- receiving and maintaining regulatory approvals from applicable regulatory authorities;
- developing and maintaining effective sales, marketing and distribution capabilities;
- establishing adequate internal manufacturing capacity or arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- establishing commercial markets;
- obtaining reimbursement from third-party payers; and
- successfully competing with other products.

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 Rhopressa[®], Rocklatan[™] or any future 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.

The commercial success of Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, will depend on the degree of market acceptance among eye-care professionals, patients, patient advocacy groups, healthcare payers and the medical community.

Commercial activities for Rhopressa[®] began in April 2018 and our sales force is working to gain market acceptance among eye-care professionals, patients, patient advocacy groups, healthcare payers, including pharmacy benefit managers, and the medical community. The commercial success of Rhopressa[®] in the United States will depend on the degree of such market acceptance. Similarly, Rhopressa[®], if approved in jurisdictions outside the United States, and Rocklatan[™] and any future product candidates in any jurisdiction in which they may receive approval, may not gain market acceptance among eye-care professionals, patients, patient advocacy groups, healthcare payers, including pharmacy benefit managers, and the medical community. There are a number of available therapies marketed for the treatment of open-angle glaucoma, retinal diseases 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 payers. Insurers and other third-party payers may also encourage the use of generic products, either in preference to or prior to the use of brand therapies. The degree of market acceptance of Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, will depend on a number of factors, including:

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

- the possibility that third-party payers will not give favorable positions on their formularies or will place restrictions on their use, including through use of step therapy or prior authorization programs;
- the timing of market introduction;
- their effectiveness as compared with currently available products;
- eye-care professional willingness to prescribe and patient willingness to adopt them 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;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in labeling;
- limitations in the approved clinical indications and MOA(s);
- our success in demonstrating their benefits including relative convenience and ease of initiation, prescription and administration;
- the strength of our selling, marketing and distribution capabilities;
- the quality of our relationships with eye-care professionals, patient advocacy groups, third-party payers and the medical community;
- the continuous availability of quality manufactured products;
- sufficient third-party coverage or reimbursement; and
- the degree to which the products are subject to material product liability claims.

As we have done with Rhopressa[®], it is possible that we may find it necessary or desirable to provide rebates on Rocklatan[™] or any future product candidates, if approved, to customers or third-party payers or to implement patient assistance programs, including co-pay assistance programs, which could affect our profitability. In addition, we do not know how eye-care professionals, patients and third-party payers will continue to respond to the pricing of Rhopressa[®] in the United States or how they will respond to the pricing of Rhopressa[®] in jurisdictions outside the United States, or the pricing of Rocklatan[™] or any future product candidates in any jurisdiction, if approved.

The market opportunity for our currently marketed or potential products, if approved, are difficult to precisely estimate. Our estimates of these market opportunities for Rhopressa[®] in the United States and the potential market opportunity for Rhopressa[®] in jurisdictions outside the United States, Rocklatan[™] or any future product candidates, if approved, 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 any of our products post-regulatory approval is smaller than we expect or if we fail to maintain market acceptance or fail to achieve market acceptance, 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 coverage and reimbursement for Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, by third-party payers, potential future sales would be materially adversely affected.

The course of treatment for patients with open-angle glaucoma, retinal diseases and other diseases of the eye includes primarily older drugs, and the leading products for the treatment of open-angle glaucoma, retinal diseases and other diseases of the eye currently in the market, including latanoprost and timolol, in the case of glaucoma treatment, are available as generic drugs. Therefore, there will be no commercially viable market for Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, without adequate coverage and reimbursement from third-party payers, and any reimbursement policy may be affected by future healthcare reform measures. We have currently obtained formulary coverage for approximately 90% of lives covered under commercial plans and approximately 40% of lives covered under Medicare Part D plans for Rhopressa[®] in the United States. However, we cannot be certain that those levels of coverage will continue to increase, or that we will be able to maintain those levels of coverage. Further, we cannot be certain that adequate coverage and reimbursement will be available for Rhopressa[®] in jurisdictions outside the United States or for Rocklatan[™] or any future product candidates, if approved. Additionally, even if there is a commercially viable market, if the level of coverage or reimbursement is below our expectations, our anticipated revenue and gross margins will be adversely affected.

Third-party payers, such as government or private healthcare insurers and pharmacy benefit managers, 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 payers, 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 payers, including Medicare, may question the coverage of, and challenge the prices charged for, medical products and services, and many third-party payers limit coverage of or reimbursement for newly approved healthcare products. In particular, third-party payers may limit the covered indications. Cost-control initiatives in the U.S. healthcare industry could decrease the price we have established for Rhopressa[®] or the price we might establish for Rocklatan[™] or any future product candidates, if approved, which could result in product revenues being lower than anticipated. Rhopressa[®] is currently priced 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 payers may not be willing to reimburse for Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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 believe that U.S. third-party payers consider the efficacy, cost effectiveness, safety and tolerability of Rhopressa[®] and will consider such factors of Rocklatan[™] and any future product candidates, if approved, and whether use of any such products should be a covered benefit under its health plan in determining whether to approve coverage and 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 maintain approval for reimbursement of Rhopressa[®] or we do not receive approval for reimbursement of Rocklatan[™] or any future product candidates, if approved, from third-party payers on a timely or satisfactory basis or if pricing is set at unsatisfactory levels. 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 any of our approved products.

Reimbursement in the EU 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 any of our products, if approved by the appropriate regulatory authorities, to other available therapies. If the prices for any of our products, if approved by the appropriate regulatory authorities, decrease or if governmental and other third-party payers do not provide adequate coverage and reimbursement levels, our revenue, potential for future cash flows and prospects for profitability will suffer. Also, we may not be able to launch the product uniformly throughout the EU but may have to commence commercial operations on a country-by-country basis, which could complicate the launching process and negatively affect our sales.

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 open-angle glaucoma, retinal diseases and other diseases of the eye. We currently compete directly against companies producing existing and future glaucoma treatment products. To the extent we develop proprietary compounds for use beyond glaucoma, we will face competition from companies, academic institutions, government agencies and private and public research institutions operating in such new therapeutic areas.

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. Early-stage companies are also developing treatments for open-angle glaucoma, retinal diseases and other diseases of the eye and may prove to be significant competitors. In September 2018, Sun Pharmaceuticals Industries Ltd. received FDA approval for a PGA indicated for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension. We expect that our competitors will continue to develop new treatments for open-angle glaucoma, retinal diseases 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 open-angle glaucoma, retinal diseases and 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 any products that we may develop. In addition, 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 payers encourage the use of generic products. Ophthalmology 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. Rhopressa[®] is priced at a premium over competitive generic products and consistent with other branded glaucoma drugs and we expect that Rocklatan[™], if approved, will be priced similarly. 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 in all current and potential commercial jurisdictions for our products;
- attract and retain key personnel;
- develop effective manufacturing capabilities and continue to build an effective selling and marketing infrastructure;
- demonstrate the advantages of our products compared to alternative therapies, including, in the case of Rhopressa[®] and Rocklatan[™], if approved, other currently marketed PGA and non-PGA products;
- identify and develop additional product candidates to expand our current product portfolio;
- compete against other products with fewer contraindications; and
- obtain and sustain adequate reimbursement from third-party payers.

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

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

We have no experience selling, marketing or distributing any drug product in any jurisdictions outside the United States, and we currently are just beginning to establish a commercially-oriented presence in jurisdictions outside the United States. Other companies have experienced unsuccessful product launches and failed to meet expectations of market potential, including companies with significantly more experience and resources than us, and there can be no guarantee that we will successfully launch any product in any jurisdictions outside the United States. To achieve commercial success for Rhopressa[®] in jurisdictions outside the United States, we must either develop a sales and marketing organization in such jurisdictions or outsource these functions to third parties. We currently plan to commercialize Rhokiinsa[®] and Roclanda[™], if approved, in Europe on our own and likely partner for commercialization in Japan. We will 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 in jurisdictions outside the United States. We may not be able to successfully establish these capabilities on our expected timing or at all despite these additional expenditures.

Factors that may inhibit our efforts to successfully establish a sales force in jurisdictions outside the United States include:

- an 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;
- an inability to effectively manage a geographically dispersed sales and marketing organization in such jurisdictions;

- the inability of sales personnel to obtain access to adequate numbers of eye-care professionals to prescribe any future approved products;
- failure to adhere to regulatory requirements governing the sale of products in any jurisdiction;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- a delay in bringing products to market after efforts to hire and train our sales force have already commenced.

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

We have not obtained regulatory approval for Rhopressa[®] outside the United States or for Rocklatan[™] in any jurisdiction.

Rhopressa[®], which has been approved by the FDA for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension, is our only product that has received regulatory approval. We do not yet have any products that have received regulatory approval in any jurisdictions outside the United States. We cannot guarantee that we will ever have any other 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.

With respect to approval of Rhopressa[®] outside the United States, we completed a Phase 3 registration trial, named “Rocket 4,” designed to generate adequate six-month safety data for European regulatory approval. In the fourth quarter of 2018, the EMA accepted our MAA for Rhopressa[®], which will be marketed under the name Rhokiinsa[®] in Europe, if approved. The acceptance of our filing in no way means that the EMA agrees with our interpretation of the outcome of the clinical trial data or will issue an approval for the product in the EU. Additionally, we completed a Phase 1 clinical trial and a successful pilot Phase 2 clinical study in the United States on Japanese and Japanese-American subjects, which were designed to support meeting the requirements of Japan’s Pharmaceuticals and Medical Devices Agency (“PMDA”) for potential regulatory submission of Rhopressa[®] in Japan. We are also planning to initiate a Phase 2 clinical trial on Japanese patients in Japan by the end of the first quarter of 2019 to support subsequent Phase 3 registration trials that are expected to be conducted in Japan.

We cannot predict how long it will take to obtain approval in Japan and if our clinical trials ultimately are successful. We will need to ensure that our planned Phase 2 clinical trial on Japanese patients in Japan and subsequent Phase 3 registration trials in Japan comply with all applicable regulations. Any failure to fully comply with Japanese regulations could result in the regulatory authorities requesting corrections or requiring new clinical trials be conducted, which could cause delay in obtaining the approval.

We submitted an NDA for Rocklatan[™] to the FDA in May 2018 under Section 505(b)(2) of the FDCA, because Rocklatan[™] is a fixed dose combination of two FDA-approved drugs in the United States, Section 505(b)(2) permits us to rely on the FDA’s prior findings of safety and effectiveness for Rhopressa[®] and latanoprost. In July 2018, the FDA accepted the NDA for review and the PDUFA goal date was set for March 14, 2019, which represents a ten-month review. This was communicated by the FDA via a “Day 74” letter, which also stated that the application is sufficiently complete to permit a substantive review and that the FDA had not identified any application deficiencies. The “Day 74” letter did not mention the need for an advisory committee. The issuance of the “Day 74” letter without mention of deficiencies or an advisory committee does not mean that FDA will not identify deficiencies during its substantive review that may preclude approval or that the FDA will not later determine that an advisory committee is appropriate. It is possible that the “shutdown” of the U.S. federal government that began in December 2018 and ended in January 2019 will affect FDA’s ability to meet its goal of reviewing our application by March 14, 2019, which could cause delay in our obtaining approval, if ever.

We have completed two Phase 3 registration trials for Rocklatan[™], named Mercury 1 and Mercury 2. Both Mercury 1 and Mercury 2 achieved their 90-day primary efficacy endpoints of demonstrating statistical superiority of Rocklatan[™] over each of its components at all measured time points in patients with maximum baseline IOPs of above 20 mmHg to below 36 mmHg.

With respect to Rocklatan[™] in jurisdictions outside the United States, Mercury 1 and Mercury 2 will also be used to apply for EMA approval of Roclanda[™]. In addition, we initiated a third Phase 3 registration trial for Roclanda[™], named Mercury 3. If successful, Mercury 3 is expected to improve our commercialization prospects in Europe. We currently expect to read out topline 90-day efficacy data for the trial in 2019 and expect to submit an MAA with the EMA for Roclanda[™] in Europe in early 2020, if Rhokiinsa[®] is approved by the EMA. See “Business—Overview” for more information about Mercury 1, Mercury 2 and Mercury 3.

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. FDA approval of Rhopressa[®] does not constitute FDA approval of Rocklatan[™], and there can be no assurance that we will receive FDA approval for Rocklatan[™] or any future product candidates. FDA approval of Rhopressa[®] and the EMA acceptance of our MAA for Rhokiinsa[®] do not constitute regulatory approval of Rhopressa[®] or Rhokiinsa[®] in jurisdictions outside the United States, and there can be no assurance that we will receive regulatory approval for Rhopressa[®] or Rhokiinsa[®] in jurisdictions outside the United States.

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. 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. Although we believe our NDA for Rocklatan[™] contained substantial evidence of effectiveness for the product, we cannot guarantee that the NDA will be approved by the FDA. In addition, we may be required to supplement the Rocklatan[™] NDA with additional information and/or receive unfavorable feedback from the FDA regarding the likelihood of obtaining FDA approval for Rocklatan[™]. Further, restructuring efforts are underway at the FDA pursuant to which the organizational positioning within the FDA of the Ophthalmic Group is being reevaluated, which may affect the FDA's focus on new ophthalmic therapies.

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 Rhopressa[®], Rocklatan[™], Rhokiinsa[®], Roclanda[™] and any future 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 any products we may develop, certain changes to the product, such as changes in manufacturing processes and additional labeling claims, will be subject to additional review and approval by the FDA and other regulatory authorities. Also, regulatory approval for Rhopressa[®], Rocklatan[™], Rhokiinsa[®], Roclanda[™] or any future product candidates, if approved, may be withdrawn. If we are unable to obtain regulatory approval for Rhopressa[®] or Rocklatan[™] (named Rhokiinsa[®] and Roclanda[™] in Europe, respectively) outside the United States or for Rocklatan[™] or any future 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 Rhopressa[®] in jurisdictions outside the United States or for Rocklatan[™] or any future product candidates in any jurisdiction if regulatory authorities require additional time or studies to assess the safety and efficacy.

We may be unable to initiate or complete development of Rhopressa[®] or Rocklatan[™] (named Rhokiinsa[®] and Roclanda[™] in Europe, respectively) in jurisdictions outside the United States on schedule, if at all. If applicable regulatory authorities require additional time or studies to assess the safety or efficacy of any 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 any of our product candidates. Preclinical studies and clinical trials required to demonstrate the quality, safety and efficacy of drug products 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 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 applicable 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 (“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 any of our product candidates;
- our inability to obtain approval from IRBs to conduct clinical trials at their respective sites;
- the failure of a third party to comply with applicable 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.

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 IRBs 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 our product candidates beyond those that are 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.

In addition, unless otherwise agreed with the other member states of the EU, the United Kingdom will leave the EU in March 2019 (“Brexit”). As one of the Brexit consequences, the EMA is in the process of relocating from London to Amsterdam, and it is possible that approvals for new medicinal products, and other regulatory actions involving the EMA, may be considerably delayed. It is uncertain what other impacts Brexit will have with respect to the cross-border acknowledgment of clinical trial results and marketing authorizations. It is possible that a separate marketing application and approval will be required to market a product in the United Kingdom. There are political endeavors to minimize the effects of Brexit in this area but there is no certainty that these efforts will be successful. If Brexit results in market access delays in Europe or the requirement for additional marketing approvals, our business may be materially harmed.

The failure by U.S. Congress to timely approve a budget for the federal government and its agencies, including the FDA, could have a material adverse effect on our business.

On an annual basis, U.S. Congress must approve budgets that govern spending by the federal agencies, including the FDA. If Congress cannot agree on a budget, or if the President vetoes a budget approved by Congress, then the federal government may be shut down and non-essential federal employees, including many FDA employees, may be furloughed. Such a shutdown would prevent the FDA from performing many of its duties, which are crucial to our business. On December 22, 2018, due to a lapse in appropriations for the federal government, most of the federal government was shut down, including many functions of the FDA, and most of the federal employees were furloughed. The federal government received appropriations to temporarily reopen as of January 25, 2019 and received the remainder of the appropriations for the fiscal year as of February 15, 2019. Although the federal government has now reopened, the recent and any future government shutdown could affect, among other things, the FDA approval process of RocklatanTM, which could have a material adverse effect on our business. For example, the FDA may need additional time to review the NDA for RocklatanTM due to the time that the government was shut down and therefore approval by the FDA, if obtained, may occur after the PDUFA date of March 14, 2019. Additionally, the FDA may have a backlog due to the government shutdown and as such, supplier qualifications, IND review and acceptance and other functions that the FDA performs may be delayed. Such a backlog could delay our NDA review process for RocklatanTM and subsequent commercialization, if approved, among other things, which could have a material adverse effect on our business.

Failure can occur at any stage of clinical development. If the clinical trials 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 Rhopressa[®] in jurisdictions outside the United States or for RocklatanTM or any future product candidates in any jurisdiction.

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.

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, IRBs 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 any of our clinical trials 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 regulatory approval for Rhopressa[®] and RocklatanTM in jurisdictions outside the United States 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, other than Rhopressa[®], have been approved in the United States. In April 2015, we announced that Rocket 1 did not meet its primary efficacy endpoint of demonstrating non-inferiority of IOP reduction 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 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 reducing effect throughout the 12-month period at the specified timepoint.

Our clinical trials were designed to test the use of Rhopressa[®] and Rocklatan[™] as a monotherapy, rather than as an adjunctive therapy. Accordingly, the efficacy of Rhopressa[®] and Rocklatan[™] as a monotherapy 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[®].

The breadth of the labeling of any product or product candidate, if approved, will depend upon providing evidence of such product's MOA(s) that is satisfactory to the applicable regulatory authority. Failure to do so will limit the types of claims we will be able to make in our marketing and labeling of Rhopressa[®], Rhokiinsa[®], Rocklatan[™] and any future product candidates, if approved. For example, based on the results of our preclinical and clinical studies, we believed Rhopressa[®] and Rocklatan[™] reduced IOP through additional MOAs; however, Rhopressa[®] received FDA approval for one MOA, ROCK inhibition or the mechanism by which Rhopressa[®] increases outflow of aqueous humor through the TM, as reflected in the Rhopressa[®] product labeling.

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 product candidates, including:

- clinical trials 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 may be larger than we anticipate, enrollment in these clinical trials may be slower than we estimate 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 IRBs 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 based on a finding that the participants are being exposed to health risks;
- the cost of clinical trials may be greater than we anticipate;
- the supply or quality of product candidates or other materials necessary to conduct clinical trials may be insufficient or inadequate; and
- product candidates may have undesirable adverse effects or other unexpected characteristics.

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

Rhopressa[®], Rocklatan[™] or any future product candidates may have undesirable or adverse effects, which may result in the delay, denial or withdrawal of regulatory approval or may require our products to be taken off the market, require them to include safety warnings or otherwise limit their sales after regulatory approval is received.

Unforeseen adverse effects from Rhopressa[®], Rocklatan[™] or any future product candidates could arise either during clinical development or, even after approval, after the approved product has been marketed. To date, the main tolerability finding of Rhopressa[®] has been mild conjunctival hyperemia, or eye redness. In our Phase 3 registration trials, some patients also experienced conjunctival hemorrhages, or petechiae, corneal verticillata, blurry vision, and decreased visual acuity as adverse events. Rocklatan[™] combines Rhopressa[®] with latanoprost. To date, the main tolerability finding of Rocklatan[™] has also been mild conjunctival hyperemia, which was reported in approximately 63% of patients and was scored as mild for approximately 70% of affected patients in the 12-month safety data from Mercury 1. In our Phase 3 registration trials, some patients also experienced conjunctival hemorrhage, eye pruritus, increased lacrimation, reduced visual acuity, blepharitis, punctate keratitis and corneal disorder as adverse events. 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.

While the FDA granted approval of Rhopressa[®] based on the data included in the NDA, we do not know whether the results when a larger number of patients in broader populations are exposed to Rhopressa[®], including results related to safety and efficacy, will be consistent with the results from our earlier clinical studies of Rhopressa[®] that served as the basis of FDA approval of Rhopressa[®]. New data relating to Rhopressa[®], including from any adverse event reports or any negative results during clinical development for additional indications of Rhopressa[®], may emerge at any time.

Any undesirable or adverse effects that may be caused by any such products or product candidates could interrupt, delay or halt clinical trials and could result in the delay, denial or withdrawal of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from successfully commercializing Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, and generating or continuing to generate revenues from their sale. In addition, if we or others identify undesirable or adverse effects caused by Rhopressa[®] or, if approved, Rocklatan[™] or any future product candidates after regulatory approval we could face one or more of the following consequences:

- regulatory authorities may re-review the product and impose restrictions on its distribution;
- 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 (“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 promoted or administered, conduct additional clinical trials or recall such 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 or continuing to generate revenues from its sale.

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. If we fail to successfully 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. As part of this strategy, in March 2015 and April 2015, we formed Aerie Limited and Aerie Ireland Limited, respectively. Additionally, in January 2017, we commenced establishment of our own manufacturing plant in Athlone, Ireland, which is expected to produce commercial supplies of Rhopressa[®] and, if approved, Rocklatan[™], Rhokiinsa and Roclanda[™] in early 2020. We also opened an office in Tokyo in October 2018 to assist with our expected expansion into Japan. 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;
- changes in tariffs, trade barriers and other regulatory requirements including those governing data privacy;

- 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 the tax reform law that was enacted in the United States in December 2017 that creates uncertainty with respect to the 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, tsunamis, 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.

If we are found in violation of U.S. 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 U.S. federal or state healthcare programs, which may adversely affect our business, financial condition and results of operation.

In the United States, our current and future arrangements with healthcare providers, healthcare organizations, third-party payors and customers expose us to broadly applicable anti-bribery, fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our product candidates. Restrictions under applicable federal and state anti-bribery and healthcare laws and regulations, include the following:

- 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 payers, 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.

In addition, certain manufacturers of covered drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with certain exceptions, are required to report annually to CMS information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members, with the information made publicly available on a searchable website. Effective January 1, 2022, transfers of value to physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives must also be reported.

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 payers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties.

Furthermore, the government purchasing and reimbursement programs include remedies such as the obligation to correct reported prices and pay additional rebates (depending on the direction of the correction) or pay restitution to the extent the government overpaid for covered drugs. In addition, federal law provides for civil monetary penalties for conduct such as failure to provide required information, late submission of required information, false information, and knowingly and intentionally overcharging a 340B covered entity.

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.

Existing 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 payers 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 payers.

In 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. Among other things, PPACA increased manufacturers' rebate liability under the Medicaid Drug Rebate Program, imposed a significant annual fee on companies that manufacture or import branded prescription drug

products and required 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,” which was increased to 70% of the negotiated price beginning in 2019. There have been efforts by the Trump Administration and Congress to seek to repeal all or portions of PPACA, and in December 2017, President Trump signed into law the Tax Act (as defined herein), which eliminated certain requirements of PPACA, including the individual mandate. There is uncertainty with respect to the impact these or future changes, if any, may have.

In addition, the Trump Administration has indicated an intent to address prescription drug pricing and recent Congressional hearings have brought increased public attention to the costs of prescription drugs. The Trump Administration has proposed a regulation intended to eliminate the rebate-oriented model used for pricing pharmaceutical products under Medicare Part D and Medicaid Managed Care, with the policy objective of lower costs to consumers. If this proposal is finalized, a similar approach may be adopted by commercial insurance plans as well. In addition, the Trump Administration has made other proposals that are in earlier stages. Numerous bills have been introduced in Congress by members of both parties seeking to reduce drug prices using a variety of approaches. These actions and the uncertainty about the future of the PPACA and healthcare laws are likely to continue the downward pressure on pharmaceutical pricing and increase our regulatory burdens and operating costs. While we currently do not believe the implementation of any such initiatives would negatively impact our net sales or operating margins, these initiatives are in early stages.

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 potential products may be. While we may establish procedures to react to the current laws and regulations, one or more laws or regulations may be enacted that will require us to alter or refresh our existing procedures. In addition, increased scrutiny by the U.S. Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing approval testing and other requirements.

If we face allegations of noncompliance with the law and encounter sanctions, our reputation, revenues and liquidity may suffer, and Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be materially adversely affected. Additionally, if we are unable to generate revenues from our product sales, our potential for achieving profitability will be diminished and the need to raise capital to fund our operations will be increased.

Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, subject us to ongoing regulatory requirements and we may face future development, manufacturing and regulatory difficulties.

Rhopressa[®] is, and Rocklatan[™] or any future product candidates, if approved, will 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, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work are required to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We are also required to report certain adverse reactions and production problems, if any, to the FDA and the EMA and other similar agencies and to comply with certain requirements concerning advertising and promotion. 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, we may not promote any product for indications, uses or claims for which they are not approved, even though physicians may prescribe them for those uses. If we want to expand any such indications for which we may market a product, we will need to obtain additional regulatory approvals, which may not be granted.

If a regulatory agency discovers previously unknown problems with Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, such as adverse events of unanticipated severity or frequency, or problems with the facility where such product is manufactured, or disagrees with the promotion, marketing or labeling of such product, or finds that we have engaged in the promotion of off-label use, it may impose restrictions on that product or us, including requiring withdrawal of that

product from the market. If Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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.

We may not be able to identify additional therapeutic opportunities for Rhopressa[®], Rocklatan[™] or any future 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 or acquisitions and may seek to commercialize a portfolio of new ophthalmic drugs or technologies in addition to Rhopressa[®] and Rocklatan[™]. For example, in 2017, we entered into a collaboration arrangement with DSM, which was expanded in the third quarter of 2018, and acquired the rights to certain assets from Envisia, both of which are expected to support the development of our ongoing preclinical retinal programs. In addition to our preclinical retinal programs, we are conducting preclinical studies to evaluate potential additional indications for Rhopressa[®] and potentially Rocklatan[™]. We are also evaluating our owned library of ROCK inhibitors for potential indications beyond ophthalmology. Our clinical operations to date have been limited to developing product candidates for the treatment of glaucoma and ocular hypertension, and there can be no assurance that we will successfully develop, license or acquire any drugs or technologies in new therapeutic areas or at all.

Preclinical studies require additional research and development, which in some cases may include significant preclinical, clinical and other testing, prior to initiating clinical development or seeking regulatory approval to market new indications, technologies and/or product candidates. Accordingly, these additional indications, technologies and product candidates will not be commercially available for a number of years, if at all. In particular, although we are currently exploring additional indications for Rhopressa[®], we cannot guarantee that we will pursue or receive the regulatory approvals required to promote Rhopressa[®] for any additional indications. Failure to receive such approvals will prevent us from promoting and commercializing Rhopressa[®] beyond its currently approved indication.

Research programs, including through collaboration arrangements, to pursue the development of Rhopressa[®], Rocklatan[™] and any future product candidates for additional indications and to identify new product candidates, technologies, therapeutic areas 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, technologies, therapeutic areas 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, technologies, therapeutic areas and/or product candidates;
- potential additional indications, technologies, therapeutic areas or product candidates may, after further study, fail to demonstrate efficacy sufficient to warrant further clinical development;
- potential technologies or 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 or to develop suitable potential product candidates or technologies, whether through internal research programs,

research collaboration arrangements or acquisitions, than we possess, thereby limiting our ability to diversify and expand our product portfolio.

We are currently developing two preclinical sustained-release implants focused on retinal diseases. AR-13503, for which we expect to submit an IND in the first quarter of 2019, and AR-1105, for which we submitted an IND in the fourth quarter of 2018. The IND for AR-1105 was accepted for review by the FDA, and we expect to initiate a Phase 2 clinical study later in the first quarter of 2019. The decision whether to pursue, and the timing of, any additional preclinical research programs is subject to a number of factors and we may suspend or discontinue research programs at any time.

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 or develop additional therapeutic opportunities for Rhopressa[®] or Rocklatan[™] or any future product candidates or any uses for our existing proprietary compounds beyond glaucoma or to develop suitable potential product candidates or technologies through internal research programs, research collaboration arrangements or acquisitions, which could materially adversely affect our future growth and prospects.

Rhopressa[®] and Rocklatan[™] are designed to treat patients with open-angle glaucoma or ocular hypertension, and the success or failure of either of them could impact sales of the other or other potential ROCK inhibitor products in the future.

Rhopressa[®] and Rocklatan[™] are designed to be once-daily dosed ROCK inhibitor eye drops to be applied topically to reduce IOP for the treatment of glaucoma or ocular hypertension. While we believe there is space for both Rhopressa[®] and Rocklatan[™], we cannot guarantee that cannibalization of sales will not occur in the future. While increased sales for one of Rhopressa[®] or Rocklatan[™], if approved, may negatively impact sales for the other, our commercialization strategy is unique for each. Because each of Rhopressa[®] and Rocklatan[™] are ROCK inhibitor eye drops designed to treat patients with glaucoma or ocular hypertension, any challenges or failures with respect to either of Rhopressa[®] and Rocklatan[™] could negatively impact sales or the public perception of the other or any other potential ROCK inhibitor products we may develop in the future.

Risks Related to Manufacturing

We currently have limited manufacturing capacity and anticipate continued reliance on third-party manufacturers for the development and commercialization of Rhopressa[®], Rocklatan[™] and any future product candidates in accordance with manufacturing regulations until we have completely developed our internal manufacturing capabilities, if at all.

We do not currently operate manufacturing facilities for clinical or commercial production of Rhopressa[®], Rocklatan[™] and any future product candidates, other than AR-13503 and AR-1105. We currently lack the resources and the capabilities to manufacture Rhopressa[®], Rocklatan[™] and any future product candidates, other than AR-13503 and AR-1105, on a clinical or commercial scale.

With respect to the commercial production of Rhopressa[®], we currently are outsourcing the production of the API and final drug product until such a time when we can develop internal manufacturing capabilities, if at all. We have entered into a contractual relationship for drug product manufacturing for the commercialization of Rhopressa[®], and we are working to establish an additional contractual relationship for the commercial production of Rhopressa[®]. This process is difficult and time consuming and we can give no assurance that we will enter any future commercial supply agreements with any additional manufacturers on favorable terms or at all.

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 clinical or commercial supplies.

Our current manufacturing capability is limited to the production of the clinical product supply necessary for Aerie's two lead development programs focused on retinal diseases for the preclinical sustained-release implants AR-13503 and AR-1105. We commenced operation of our cGMP-validated manufacturing facility for production of ophthalmic implants using the proprietary PRINT[®] technology platform in the fourth quarter of 2018. This facility is currently only being used to support clinical trials of AR-13503 and AR-1105 implants. This facility is not being used to produce commercial or clinical supply of Rhopressa[®] or Rocklatan[™].

In January 2017, we commenced establishment of our own manufacturing plant in Athlone, Ireland. This will be our first manufacturing plant, which is expected to produce commercial supplies of Rhopressa[®] and, if approved, Rocklatan[™],

Rhokiinsa[®] and Roclanda[™]. We expect that commercial supply from the plant will be available in early 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 “—*We have no experience developing manufacturing facilities or manufacturing Rhopressa[®] or Rocklatan[™] and we cannot assure you that we will be able to develop our manufacturing plant or manufacture Rhopressa[®] or Rocklatan[™] 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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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.

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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, or otherwise do not satisfactorily perform according to the terms of their agreements with us;
- delays in obtaining regulatory approval for Rhopressa[®] outside the United States or for Rocklatan[™] or any future 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 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 in February 2017 upon receiving confirmation from the contract manufacturer that it was prepared for FDA inspection and the Rhopressa[®] NDA was subsequently approved in December 2017.

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 Rhopressa[®], Rocklatan[™] or any future product candidates 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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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 do not have a compliance status acceptable to the FDA, regulatory approval and/or commercial supply of the active pharmaceutical ingredients of Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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 reputation, 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 or other regulatory 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 or commercial production of a product. The new facility will also be subject to pre-approval inspection. In addition, we have to demonstrate that the product made at the new facility is equivalent to the product made at the former facility by physical and chemical methods, which are costly and time consuming. It is also possible that the FDA may require clinical testing as a way to prove equivalency, which would result in additional costs and delay.

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

We are in process of establishing our own manufacturing plant in Athlone, Ireland, for the future commercial production of Rhopressa[®] and, if approved, Rocklatan[™], Rhokiinsa[®] and Roclanda[™]. We expect that commercial supply from the plant will be available in early 2020. We have no experience in developing manufacturing facilities or manufacturing drug products. 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 permission or approval from the FDA and other regulatory authorities to allow the plant to manufacture Rhopressa[®] and Rocklatan[™], if approved, for export to the United States and other markets. If we are unable to obtain such permission or approval in a timely manner, our ability to successfully manufacture and commercialize Rhopressa[®] and Rocklatan[™], if approved, 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 Rhopressa[®] and Rocklatan[™], if approved, 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 “—*We currently have limited manufacturing capacity and anticipate continued reliance on third-party manufacturers for the development and commercialization of Rhopressa[®], Rocklatan[™] and any future product candidates in accordance with manufacturing regulations until we have completely developed our 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 Rhopressa[®] and Rocklatan[™], if approved. 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 Rhopressa[®] and Rocklatan[™], if approved, and we would lose potential revenues.

Risks Related to Our Financial Position and Need for Additional Capital

We have recently begun commercializing Rhopressa[®], our first FDA-approved product, have limited revenue and may never become profitable.

We have a limited operating history and have only recently begun commercializing our first product, Rhopressa[®]. We have never been profitable and only have one product approved for commercial sale. Even though we received FDA approval for Rhopressa[®] and began commercial sales in the United States, we are still in the process of obtaining regulatory approval in jurisdictions outside the United States and there is no guarantee that Rhopressa[®] will be approved in any such jurisdictions. We do not have regulatory approval for Rocklatan[™] or any future product candidates in any jurisdiction. FDA approval of Rhopressa[®] does not guarantee FDA approval of Rocklatan[™] or any future product candidates and also does not guarantee regulatory approval of Rhopressa[®] in jurisdictions outside the United States.

Our ability to generate product revenue depends on a number of factors, including our ability to:

- maintain an acceptable price for Rhopressa[®] in the United States and set an acceptable price for Rhopressa[®] in jurisdictions outside the United States, if approved, and obtain adequate reimbursement from third-party payers in jurisdictions outside the United States;
- set an acceptable price for Rocklatan[™] and any future product candidates, if approved, and obtain adequate reimbursement from third-party payers;
- manufacture or obtain commercial quantities of Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, at acceptable cost levels;
- successfully market and sell Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, in the United States and other jurisdictions; and
- successfully complete clinical development, and receive regulatory approval, for our current and any future product candidates.

In addition, because of the numerous risks and uncertainties associated with product development, commercialization and manufacturing, we are unable to precisely 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 though we have begun commercial sales of Rhopressa[®], we are still incurring and anticipate continuing to incur significant costs associated with the commercialization of Rhopressa[®] and commercial launch of Rocklatan[™], if approved.

Our ability to become and remain profitable depends on our ability to generate revenue. Although we have generated revenues from the sale of Rhopressa[®], even if we are able to generate revenues from Rocklatan[™] and any future product candidates, if approved, 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 materially 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 Rhopressa[®] and Rocklatan[™], if approved, are commercially successful, if at all.

We have incurred losses in each year since our inception in June 2005. Our net losses were \$232.6 million, \$145.1 million and \$99.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of \$696.4 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 historical 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, which were converted into shares of common stock in July 2018, and the issuance and sale of common stock pursuant to our registration statements on Form S-3 and prior “at-the-market” sales agreements. Rhopressa[®] will continue to require significant marketing efforts and substantial investment to maintain and increase revenues. Rocklatan[™] and any future 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 activities. In addition, as we have now launched Rhopressa[®], we have incurred and expect to continue to incur increased manufacturing, selling and marketing expenses. As a result, we expect to continue to incur operating losses until our products generate adequate commercial revenue to render Aerie profitable. These losses have had and will continue to have a material adverse effect on our stockholders’ equity, financial position, cash flows and working capital.

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 Rhopressa[®], Rocklatan[™] or any future 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 through December 31, 2018, we have raised additional net proceeds of approximately \$122.9 million from the issuance of the 2014 Convertible Notes, which were converted into shares of common stock in July 2018, and approximately \$487.7 million through the issuance and sale of common stock under our shelf registration statements on Form S-3 and prior “at-the-market” sales agreements. In July 2018, we entered into an agreement with respect to a senior secured delayed draw term loan facility (the “credit facility”), which will allow us to borrow up to \$100 million in one or more borrowings. No amounts were drawn at closing or as of December 31, 2018. See “—Borrowings under the Credit Facility could adversely affect our financial condition and restrict our operating flexibility.”

We may need to obtain additional financing to fund our future operations. Additionally, we may need to obtain additional financing to conduct additional trials for the approval of Rhopressa[®] in jurisdictions outside the United States or of Rocklatan[™] or any future product candidates, and for completing the development of any additional product candidates or technologies and executing our international expansion strategy. 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 commercial success with Rhopressa[®] and our ability to successfully commercialize Rocklatan[™] and any future product candidates, if approved;
- the amount of sales and other revenues from Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, including the selling prices for such potential products and the availability of adequate third-party reimbursement;
- selling and marketing costs associated with Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, 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 or technologies;
- costs of any new business strategies;

- 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 expected cash flows will be sufficient to support the expected approval and planned commercialization of Rocklatan™ in the United States and to support product commercialization of Rhopressa® through at least the next twelve months. We also intend to use these funds for general corporate purposes and for strategic growth opportunities, including the development and commercialization of Rhokiinsa® and Roclanda™, if approved, in Europe, the execution of clinical trials in Japan, the expansion of our international operations, the construction of our manufacturing plant in Ireland and the continuation of preclinical activity in support of our product pipeline. In July 2018, we entered into an agreement with respect to a senior secured delayed draw term loan facility, which will allow us to borrow up to \$100.0 million in one or more borrowings. See “—*Borrowings under the Credit Facility could adversely affect our financial condition and restrict our operating flexibility.*” We do not currently intend to draw down on the credit facility but may do so if and as needed.

Until we can generate a sufficient amount of revenue, we are able to finance future cash needs through additional debt financings or other available sources. 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 incorrect and changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. Our inability to obtain additional funding when we need it could seriously harm our business.

Borrowings under the credit facility could adversely affect our financial condition and restrict our operating flexibility.

In July 2018, we entered into an agreement with respect to a senior secured delayed draw term loan facility, pursuant to which we may borrow up to \$100 million in aggregate in one or more borrowings at any time prior to July 23, 2020. The credit facility includes fees upon drawdown of 1.75% of amounts drawn, an 8.625% annual interest rate on drawn amounts, annual fees on undrawn amounts of 1.5% and an exit fee of \$1.5 million. No amounts were drawn at closing or as of December 31, 2018. Interest payments, fees, covenants and restrictions under the credit facility could have important consequences, including the following:

- impairing our ability to successfully continue to commercialize Rhopressa® or complete the development of Rocklatan™ and any future product candidates, which would prevent us from generating a source of revenue and becoming profitable;
- 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, and making it more difficult for us to satisfy our obligations with respect to any such additional financing; and
- increasing our vulnerability to general economic downturns, competition and industry conditions, which could place us at a competitive disadvantage compared to our competitors with no debt obligations or with debt obligations on more favorable terms.

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 the credit facility and any other indebtedness.

Although the agreement governing the credit facility contains restrictions on the incurrence of additional indebtedness, these restrictions are subject to a number of significant qualifications and exceptions, and any additional indebtedness incurred in compliance with these restrictions could be substantial. If new debt is incurred in addition to debt incurred under the credit

facility, the related risks that we face would be increased.

The terms of the credit facility may restrict our current and future operations, particularly our ability to respond to changes in our business or to take certain actions.

The credit facility 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 credit facility includes covenants that, among other things, restrict or otherwise limit our ability to:

- incur additional indebtedness and create liens;
- make restricted payments;
- undergo fundamental changes;
- dispose of assets;
- make investments; and
- enter into transactions with affiliates.

If not cured, as applicable, a breach of any of these provisions could result in a default under the credit facility that would allow our lenders to declare any outstanding debt immediately due and payable. In addition, the credit facility is secured by substantially all of our existing and hereafter created or acquired domestic assets, including our intellectual property, accounts receivable, equipment, general intangibles, inventory and investment property, and all of the proceeds and products of the foregoing. If we are unable to pay any amounts due and payable under the credit facility because we do not have sufficient cash on hand or are unable to obtain alternative financing on acceptable terms, the lenders could initiate a bankruptcy proceeding or proceed against any assets that serve as collateral to secure the credit facility.

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 credit facility.

We may sell additional debt or equity 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, or if we decide based on ongoing forecast updates, new strategic initiatives, market conditions or for other reasons that additional financings are desirable or needed, we may sell additional debt or equity securities, which would result in dilution to all of our stockholders or impose restrictive covenants that adversely impact our business. In September 2016, our automatic shelf registration statement on Form S-3 became effective upon filing with the SEC, pursuant to which we may offer an unlimited amount of common stock from time to time, and, through the date of this report, we have issued and sold approximately 7.4 million shares of common stock pursuant to such shelf registration statement. 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 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, developing our product candidates, advancing Rhopressa[®] and Rocklatan[™] to FDA approval and the commercial launch of Rhopressa[®]. We have not yet demonstrated our ability to develop a manufacturing plant or manufacture a widely-sold commercial scale product. 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 are in the process of transitioning from a company with a product development focus to a company capable of supporting commercial and manufacturing activities. We may not be successful in completing such 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 capital structure and leverage, changes to our transfer pricing practices, tax deductions attributed to equity and other compensation and limitations on such deductions 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 carryforwards 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 carryforwards. 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, 2018, we had U.S. federal and state net operating losses (“NOLs”) of approximately \$387.7 million and \$411.2 million, respectively. If not utilized, federal NOLs that arose before 2018 and state NOLs begin to expire at various dates beginning in 2031 and 2024, respectively. Federal NOLs that arose on or after January 1, 2018 can be carried forward indefinitely to be utilized against future income, but can only be used to offset a maximum of 80% of our federal taxable income in any year. 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 and state NOL carryforwards. Those federal and state NOLs that are not limited are included as deferred tax assets and have been fully offset by a valuation allowance as of December 31, 2018. As of December 31, 2018, we also had foreign NOLs of \$44.1 million which are available solely to offset taxable income of our foreign subsidiaries, subject to any applicable limitations under foreign law.

Changes to the United States tax laws could materially impact our financial position and results of operations.

In December 2017, the Tax Act was signed into law. The Tax Act makes extensive changes to the U.S. tax laws and includes provisions that, among other things, reduce the U.S. corporate tax rate, repeal the corporate alternative minimum tax (“AMT”) and refund certain existing AMT credits over several years, introduce a capital investment deduction, limit the interest deduction, limit the use of net operating losses to offset future taxable income, limit the deduction for compensation paid to certain executive officers and make extensive changes to the U.S. international tax system, including the taxation of foreign earnings of U.S. multinational corporations. Further, due to the expansion of our international business activities, changes enacted in the Tax Act with respect to the U.S. taxation of such activities may increase our worldwide effective tax rate and adversely affect our financial position and results of operations. The U.S. Treasury Department has released regulations implementing the Tax Act and is expected to release additional regulations and the U.S. tax laws may be further amended in the future. The Tax Act is complex and far-reaching and we cannot predict with certainty the resulting impact its enactment will have on us.

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.

In addition, jurisdictions outside the United States could challenge aspects of the Tax Act or implement reactionary legislation or regulations that could adversely affect us and/or negate or minimize any favorable impact that we may derive from the Tax Act in the future.

Risks Related to Our Reliance on Third Parties

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 the related data collection and analysis. We expect to rely on these third parties to conduct clinical trials of any future product candidates that we develop. These parties are not our employees and we cannot control the amount or timing of resources that they devote to our programs. 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 and commercial supply. Any performance failure on the part of our distributors could delay, as applicable, clinical development, regulatory approval or commercialization of Rhopressa[®], Rocklatan[™] or any future product candidates, 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.

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 Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, could be harmed, our costs could increase and our ability to obtain regulatory approval (as applicable) and commence product sales could be delayed.

If we fail to manage an effective distribution process in the United States or establish an effective distribution process in jurisdictions outside the United States, our business may be adversely affected.

We have established the infrastructure necessary for distributing pharmaceutical products in which third-party logistics wholesalers warehouse Rhopressa[®] and distribute it to pharmacies and will need to establish such infrastructures in jurisdictions outside the United States. This distribution network requires significant coordination with our sales and marketing and finance organizations, and the failure to coordinate financial systems could negatively impact our ability to accurately report product revenue. If we are unable to effectively manage the distribution process, the continued commercialization of Rhopressa[®] could be disrupted or the commercial launch and sales of Rhopressa[®] in jurisdictions outside the United States, in any such case, or of Rocklatan[™] or any future product candidates, if approved, will be delayed or severely compromised and our results of operations may be harmed.

Any collaboration arrangement that we may enter into may not be successful, which could adversely affect our ability to develop and commercialize any future product candidates or technologies or to enter new therapeutic areas.

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 or technologies. For example, in 2017, we entered into a collaborative research, development and licensing agreement with DSM, which was expanded in the third quarter of 2018. We will face, to the extent that we decide to enter into additional collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are often complicated 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. Any such termination or expiration may adversely affect us financially and could harm our business reputation.

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 standards of patentability as well as 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 and potential products may prevent us from obtaining or enforcing patents relating to such product 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, medical devices and synthetic methods. As of December 31, 2018, we own 43 patents and have seven pending patent applications in the United States and certain foreign jurisdictions for Rhopressa[®] and Rocklatan[™]. Patent protection for Rocklatan[™] includes the U.S. patents that cover Rhopressa[®]. The patents cover composition of matter and method of use. We own 59 patents and have 55 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:

- our patents may not be broad or strong enough to prevent competition from other products that are identical or similar to Rhopressa[®] and Rocklatan[™],

- there can be no assurance that the term of a patent can be extended under the provisions of PTE 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 Rhopressa[®] and Rocklatan[™];
- we do not currently own or control foreign patents issued outside of Australia, Canada, Europe and Japan that would prevent generic entry into those markets for Rhopressa[®] and Rocklatan[™];
- 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 of competent jurisdiction 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 of competent jurisdiction 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 Rocklatan[™] 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 Rhopressa[®] by submitting ANDAs to the FDA in which our competitors claim that our patents are invalid, unenforceable and/or not infringed. Our competitors may employ similar strategies with respect to Rocklatan[™], if approved.

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 having competent 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 Rhopressa[®] and Rocklatan[™] and any future product candidates, as well as successfully defending our current and future patents against third-party challenges. As of December 31, 2018, we own 102 patents and have 62 pending patent applications in the United States and certain foreign jurisdictions relating to Rhopressa[®], Rocklatan[™] and 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. Our issued patents include 43 patents for composition of matter and method of use covering our FDA-approved product, Rhopressa[®] in the United States and certain foreign jurisdictions. These patents also

cover our advanced-stage product candidate Rocklatan™ to the extent that Rhopressa® forms a part of Rocklatan™. 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 Rhopressa®, Rocklatan™ or our 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 enforceability, 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 disrupt the commercialization of or increase the costs of commercializing Rhopressa® or stop us from commercializing or increase the costs of commercializing Rocklatan™ or any future product candidates, if approved.

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 Rhopressa® or any product candidates 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 Rhopressa®, Rocklatan™ or any future product candidates infringe. For example, pending applications may exist that claim or can be amended to claim subject matter that Rhopressa®, Rocklatan™ or any future product candidates 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 Rhopressa®, Rocklatan™ or any future 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 Rhopressa®, Rocklatan™ or any future product candidates or methods either do not infringe the claims of the relevant patent or that the patent claims asserted are invalid or unenforceable, 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 Rhopressa® or Rocklatan™ or any future product candidates, if approved, 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 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 current product and potential products 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 members 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 members of 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

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 regulatory 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 Rocklatan[™] to our now FDA-approved product and our advanced-stage product candidate, respectively, in 2014 and 2018, respectively, with the trademark applications for registration for Rhopressa[®] accepted by the USPTO and the trademark application for registration for Rocklatan[™] pending from the USPTO. The trade name Rhopressa[®] was approved by the FDA. If the EMA approves Rhopressa[®], it will be marketed as Rhokiinsa[®], for which the USPTO has already accepted our application for trademark registration. Rocklatan[™] and any other names we intend to use for our current or any future product candidates will require approval from the FDA and applicable non-U.S. regulatory authorities regardless of whether we have secured a formal trademark registration from the USPTO or applicable non-U.S. regulatory authorities. 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. Regulatory authorities outside the United States conduct their own investigations. If the FDA or applicable non-U.S. authorities object to any of our proposed product names, we may be required to adopt an alternative name for Rhopressa[®] or Rhokiinsa[®] outside the United States, Rocklatan[™] or any future product candidates. In 2018, the EMA approved the name Roclanda[™] for Rocklatan[™] in Europe. A trademark application for Roclanda[™] was filed in Europe on October 25, 2018, which remains pending. If, however, we adopt an alternative name, we would lose the benefit of our existing trademark applications for such product or 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 or applicable non-U.S. authorities. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would disrupt our commercialization of Rhopressa[®] outside the United States and limit our ability to commercialize Rocklatan[™] or any future 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 Rhopressa[®], Rocklatan[™] or any future product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA regulatory approval for Rhopressa[®] and Rocklatan[™] and any future product candidates, one or more of our U.S. patents may be eligible for limited PTE 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 extension term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. PTEs, 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 PTE 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 PTE. The FDA approved the Rhopressa[®] NDA on December 18, 2017. On February 8, 2018, we timely filed an application with the USPTO for PTE for our US8394826 patent, which covers Rhopressa[®] and Rocklatan[™]. The petition remains pending. We may not be granted an extension because of, for example, 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 PTE or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain earlier approval of competing products, and our ability to generate revenues could be materially adversely affected.

Risks Related to Our Business Operations and Industry

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

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

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. In particular, the loss of Vicente Anido, Jr., our Chairman of the Board of Directors and Chief Executive Officer, Thomas A. Mitro, our President and Chief Operating Officer, Richard J. Rubino, our Chief Financial Officer, Casey C. Kopczynski, our Chief Scientific Officer, John LaRocca, Esq., our General Counsel, or Kathleen McGinley, our Vice President of Human Resources and Corporate Services, 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 have increased the size of our organization, and we may experience difficulties in managing our growth.

We have increased the size of our organization. We have 353 full-time employees as of December 31, 2018 compared to 160 full-time employees as of December 31, 2017. We are currently expanding our employment base as we continue to expand internationally, including for the future operation of our manufacturing plant in Ireland, and for continued research activities to further expand our pipeline. We expect to expand our employment base to approximately 400 full-time employees when we are in the full commercial and manufacturing stage for Rhopressa[®] and Rocklatan[™], if approved, in the United States.

Growth imposes significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate new employees. Our future financial performance and our ability to commercialize Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved, 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 research programs, clinical trials and the regulatory process effectively;
- manage the development and eventual operation of our manufacturing plant and the manufacturing of Rhopressa[®], Rocklatan[™] and any future product candidates for clinical and commercial use;
- integrate current and additional management, administrative, financial, manufacturing and sales and marketing personnel;
- hire additional personnel necessary to effectively commercialize and manufacture Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved;
- 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 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 may be negatively impacted by macroeconomic conditions.

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

Interest rates and the ability to access credit markets could also adversely affect the ability of patients, payers and distributors to purchase, pay for and effectively distribute Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved. Similarly, these macroeconomic factors could affect the ability of our 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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, or develop additional product candidates or technologies.

A significant portion of our revenue currently comes from a limited number of distributors, and any decrease in revenue from these distributors could harm our business.

A significant portion of our revenue comes from a limited number of distributors. In the year ended December 31, 2018, three distributors represented approximately 33.9%, 33.3% and 29.7% of total revenues. We further expect that a significant portion of our revenue will continue to depend on sales to a limited number of distributors in the foreseeable future. We do not have long-term commitments from our distributors to carry our products, and any of our distributors may from quarter to quarter comprise a significant concentration of our revenues. Our dependence on a few distributors could expose us to the risk of substantial losses if any single large distributor stops purchasing our products, purchases a lower quantity of our products or goes out of business and we cannot find substitute distributors on equivalent terms without delays, if at all. While we may be able to shift our business to one of our other existing distributors or to a new distributor, there may be disruption in the interim. In addition, any reduction in the prices we receive for our products could adversely impact our revenues and financial condition. If we lose our relationship with any of our significant distributors, we could experience delays in the distribution of our products and could also experience declines in our revenues which in turn could materially adversely affect our business, results of operations or financial condition.

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. For example, in October 2017, we acquired the rights to use PRINT[®] technology and certain other assets from Envisia Therapeutics Inc. Further, in August 2018 we entered into an Amended and Restated Collaborative Research, Development, and License Agreement with DSM, which provides for (i) a worldwide exclusive license for all ophthalmic indications to DSM's polyesteramide polymer technology, (ii) continuation of the collaborative research initiatives through the end of 2020, including the transfer of DSM's formulation technology to Aerie during that time and (iii) access to a preclinical latanoprost implant. We have no present agreement regarding any material acquisitions. However, if we

do undertake any acquisitions or additional 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.

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

Our principal executive office and research facility is located in Durham, North Carolina, our regulatory, commercial support and other administrative activities are located in Irvine, California, and our clinical and finance operations are located in Bedminster, New Jersey. We also lease space for a manufacturing plant in Athlone, Ireland and small offices in Malta, Ireland, the United Kingdom and Japan. We are vulnerable to natural disasters, such as severe storms, and other adverse events that could disrupt our operations. We carry limited insurance for natural disasters and other adverse events 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, cyber-attacks or other security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, sales force, collaborators and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, malware, ransomware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusions, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Computer hackers may attempt to penetrate our computer systems and, if successful, misappropriate our proprietary and confidential information including e-mails and other electronic communications. In addition, an employee, supplier, collaboration partner or other third party with whom we do business may attempt to obtain such information and may purposefully or inadvertently cause a breach involving such information. 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 commercialization efforts, damage our reputation, provide competitors with valuable information and subject us to additional liabilities, including criminal penalties and civil sanctions. We have not been subject to cyber-attacks or other cyber incidents to date which, individually or in the aggregate, have been material to our business, but the actions we take to prevent or detect the risk of cyber incidents and protect our information technology networks and infrastructure may be insufficient to prevent or detect a major cyber-attack or other cyber incident in the future.

In addition, there is a risk created by our lack of redundancy across our systems and if any of these events were to occur, this could result in a loss of materials that would be difficult to replace, such as proprietary information including intellectual property and business information and/or customer, supplier, employee, business partner and, in certain instances, patient

personally identifiable information. 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. Likewise, we rely on third parties to manufacture Rhopressa[®], and similar events relating to their systems could also have a material adverse effect on our business. 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 commercialization of Rhopressa[®] and the further development or commercialization of Rocklatan[™] and any future product candidates could be delayed.

Our actual or perceived failure to comply with U.S. federal, state, and foreign governmental regulations and other legal obligations related to privacy, data protection and information security could harm our reputation and business.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information, data about our clinical participants, suppliers and business partners and personally identifiable information. The secure storage, maintenance, and transmission of and access to this information is important to our operations and reputation. Any access, disclosure or other loss of information could result in legal claims or proceedings, disruption of our operations and damage to our reputation, all of which could materially adversely affect our business. In addition, we are subject to various U.S. federal and state and international privacy and security regulations. For example, the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. In addition, many U.S. states have enacted comparable laws addressing the privacy and security of health information, some of which are more stringent than HIPAA. With our increasing international presence, we are also subject to the laws of jurisdictions outside the United States. Privacy and data protection laws may be interpreted and applied differently from country to country and may create inconsistent or conflicting requirements, which could increase the costs incurred by us in complying with such laws.

The EU member states, Switzerland, Japan and other countries have established, or are in the process of establishing, legal frameworks for privacy and data security that impose significant compliance obligations with which our customers, our vendors or we must comply. For example, the GDPR, which became effective on May 25, 2018, imposes strict requirements on data controllers and processors of personal data. The GDPR is wide-ranging in scope and imposes numerous requirements, including requirements relating to processing sensitive data (including health, biometric and genetic information), obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches and taking certain measures when engaging third-party processors. In addition, the GDPR grants individuals an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the EU, including to the United States and other regions.

The GDPR introduced new fines and penalties for a breach of requirements, which may result in significant fines of up to 4% of annual global revenues, or €20.0 million, whichever is greater. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, in particular as regards data processing in the context of clinical trials. As a result of the implementation of the GDPR, we were required to put in place additional mechanisms to ensure compliance with the new data protection rules, although there is a risk that the measures will not be implemented correctly or that individuals within our business will not be fully compliant with the new procedures. If there are any breaches of these measures, we could face significant administrative and monetary sanctions as well as reputational damage, which may have a material adverse effect on our business.

Our disclosure controls and procedures and our systems to implement such 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.

We are in the process of implementing a new global enterprise resource planning (“ERP”) system. This ERP system will replace many of our existing financial systems. Such an implementation is a significant undertaking, both financially and from a management and personnel perspective. Any disruptions, delays or deficiencies in the design and implementation of our new ERP system could adversely affect our ability to process financial transactions, maintain effective disclosure or internal controls and procedures, fulfill contractual obligations or could otherwise materially adversely affect our business.

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 face an additional risk from our commercial sales of Rhopressa[®] and will face an even greater risk when we commercially sell Rocklatan[™] or any future product candidates, if approved. We maintain primary product liability insurance and excess product liability insurance that cover our clinical trials, and we have and plan to maintain insurance against product liability lawsuits for commercial sale of Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved. 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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved, 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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved. 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 Rhopressa[®] or Rocklatan[™] or any future product candidates, if approved;
- 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 increased our insurance coverage when Rhopressa[®] received FDA approval. However, the product liability insurance we will need to maintain in connection with the continued commercial sales of Rhopressa[®], and will need to obtain in connection with commercial sales of Rocklatan[™] and any future product candidates if and when they receive regulatory approval, may be unavailable in adequate 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 inhibit the continued commercial production and sale of Rhopressa[®] or the development and commercial production and sale of Rocklatan[™] or any future 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 success of our commercial launch of Rhopressa[®] in the United States, including associated sales volumes, revenues and profitability;
- the anticipated approval of Rocklatan[™] by the FDA, and the success of the commercial launch in the United States, if approved;
- overall company profitability and ability to generate positive cash flows, and elimination of the additional costs associated with financing overhang;
- our ability to maintain adequate product supply to meet demand;
- our ability to obtain regulatory approval in jurisdictions outside the United States;
- the results of our testing and clinical trials;
- 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 Rhopressa[®], Rocklatan[™] 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;
- actual versus expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our quarterly or annual operating results;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the 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 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.

Any securities litigation could result in substantial damages and may divert management's time and attention from our business.

A putative securities class action lawsuit was filed against us and certain of our officers and directors in 2015, which 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 52.7% of our common stock as of December 31, 2018. 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 entities 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.

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 credit facility 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 (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. We have made, and will continue to make, changes to our corporate governance standards, disclosure controls and financial reporting and accounting systems to continue to meet our reporting obligations. However, the measures we take may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

We are subject to Section 404(b) of the Sarbanes-Oxley Act (“Section 404”), which requires that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting, among other additional requirements. Compliance with Section 404 is costly and time consuming for management and could result in the detection of internal control deficiencies. 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. Any failure to file accurate and timely quarterly and annual reports that we are required to file with the SEC under the Exchange Act 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 (“DGCL”), could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions include:

- establishing a classified board of directors such that not all members of the board are elected at one time;
- allowing the authorized number of our directors to be changed only by resolution of our board of directors;
- limiting the removal of directors by the stockholders;
- authorizing the issuance of “blank check” preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; and
- requiring the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal our bylaws.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal executive office and research facility is located in Durham, North Carolina, our regulatory, commercial support and other administrative activities are located in Irvine, California, and our clinical, finance and legal operations are located in Bedminster, New Jersey. We also lease space for a manufacturing plant in Athlone, Ireland. Our Durham, North Carolina, facility consists of approximately 61,000 square feet of laboratory and office space under leases that expire between June 2020 and June 2024 and our Irvine, California, location consists of approximately 37,300 square feet of office space under a lease that expires in January 2022. We terminated our previous lease and entered into a lease for our new Bedminster, New Jersey, location, which consists of approximately 34,000 square feet of office space under a lease that expires in October 2029. Our manufacturing plant in Athlone, Ireland, consists of approximately 30,000 square feet of interior floor space and is under lease through at least September 2027. We also have small offices in Malta, Ireland, the United Kingdom and Japan. 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. We are not a party to any known litigation, are not aware of any material unasserted claims and do not have contingency reserves established for any litigation liabilities.

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

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

Market Information

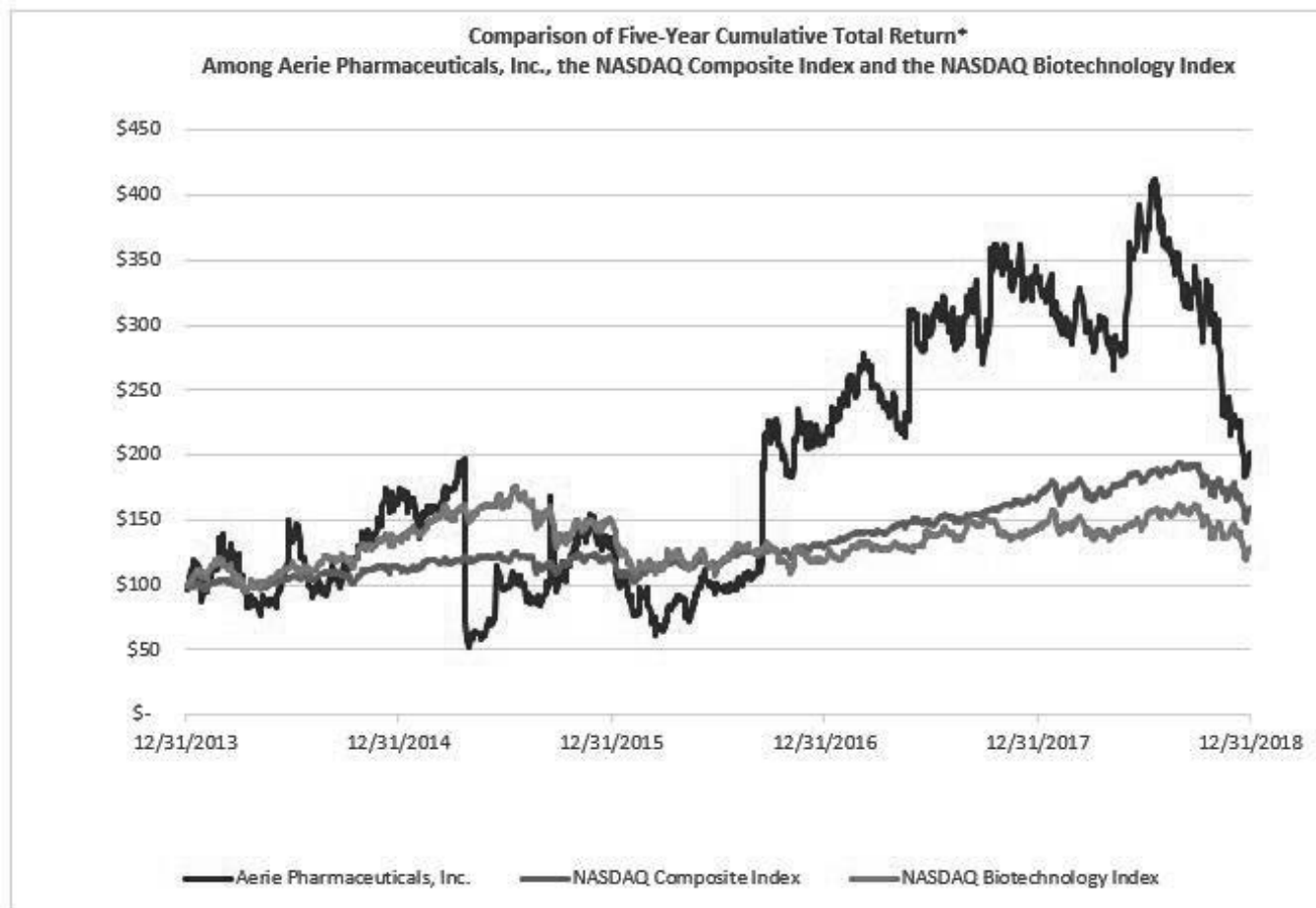
Our common stock is traded on The NASDAQ Global Market under the symbol "AERI."

Stockholders

As of February 15, 2019, we had 45,911,125 shares of common stock outstanding held by approximately 294 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.

Stock Performance Graph

The following graph illustrates a comparison of the five-year cumulative total stockholder return on our common stock since December 31, 2013 to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of \$100 on December 31, 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.

Use of Proceeds from Registered Securities

None.

ITEM 6. SELECTED FINANCIAL DATA

The following table sets forth our selected financial data for the periods and as of the dates indicated. You should read the following selected financial data together with the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this report and our audited consolidated financial statements and the accompanying notes included elsewhere in this report. We have derived the statements of operations data for the years ended December 31, 2018, 2017 and 2016 and the balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements included elsewhere in this report. We have derived the statements of operations data for the years ended December 31, 2015 and 2014 and the balance sheet data as of December 31, 2016, 2015 and 2014 from our audited consolidated financial statements not included in this report. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	YEAR ENDED DECEMBER 31,				
	2018	2017	2016	2015	2014
	(in thousands, except share and per share data)				
Product revenues, net ⁽¹⁾	\$ 24,181	\$ —	\$ —	\$ —	\$ —
Total revenues, net	24,181	—	—	—	—
Costs and expenses:					
Cost of goods sold	641	—	—	—	—
Selling, general and administrative	120,614	56,905	34,706	30,635	20,103
Pre-approval commercial manufacturing	26,545	16,710	9,772	—	—
Research and development	86,123	72,078	52,394	44,451	29,869
Total costs and expenses	233,923	145,693	96,872	75,086	49,972
Loss from operations	(209,742)	(145,693)	(96,872)	(75,086)	(49,972)
Other income (expense), net ⁽²⁾	(22,824)	(1,170)	(1,994)	862	1,839
Loss before income taxes	(232,566)	(146,863)	(98,866)	(74,224)	(48,133)
Income tax expense (benefit)	3	(1,758)	193	139	—
Net loss	\$ (232,569)	\$ (145,105)	\$ (99,059)	\$ (74,363)	\$ (48,133)
Net loss per common share—basic and diluted	\$ (5.58)	\$ (4.11)	\$ (3.40)	\$ (2.88)	\$ (2.00)
Weighted average number of common shares outstanding—basic and diluted	41,663,958	35,324,472	29,135,583	25,781,230	24,086,651

- (1) The Company launched its first product, Rhopressa[®], in the United States in April 2018 and commenced generating product revenues in the second quarter of 2018.
- (2) Includes the value of additional shares of Aerie common stock issued to complete the conversion of the 2014 Convertible Notes in July 2018.

	AS OF DECEMBER 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents	\$ 202,818	\$ 197,569	\$ 197,945	\$ 91,060	\$ 85,586
Investments	—	52,086	35,717	59,310	72,614
Total assets	285,044	290,276	248,254	159,127	159,835
Convertible notes, net	—	123,845	123,539	123,236	122,906
Total stockholders’ equity	227,806	135,599	105,344	18,775	28,042

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following management's discussion and analysis should be read in conjunction with our audited financial statements and related notes that appear elsewhere in this Annual Report on Form 10-K. This management's discussion and analysis contains forward-looking statements that involve risks and uncertainties. Please see "Special Note Regarding Forward-Looking Statements" for additional factors relating to such statements, and see "Risk Factors" in Part I, Item 1A of this report for a discussion of certain risk factors applicable to our business, financial condition and results of operations. Past operating results are not necessarily indicative of operating results in any future periods.

Overview

We are an ophthalmic pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with open-angle glaucoma, retinal diseases and other diseases of the eye. Our strategy is to successfully commercialize our FDA-approved product, Rhopressa[®], in the United States and advance our product candidate, Rocklatan[™], to regulatory approval. We have a commercial team that includes approximately 100 sales representatives targeting approximately 14,000 high prescribing eye-care professionals throughout the United States. This sales force is responsible for sales of Rhopressa[®], and will also be responsible for sales of Rocklatan[™], if approved.

We seek to enhance our longer-term commercial potential by identifying and advancing additional product candidates through our internal discovery efforts, our entry into potential research collaborations or in-licensing arrangements or our acquisition of additional ophthalmic products or technologies or product candidates that complement our current product portfolio, such as our collaboration with DSM, whereby we have access to their bio-erodible polymer technology, and our acquisition of assets from Envisia, designed to advance our progress in developing potential future sustained-release product candidates to treat retinal diseases, as discussed below.

Our strategy also includes developing our business outside of the United States, including obtaining regulatory approval in Europe and Japan on our own for Rhopressa[®] and Rocklatan[™]. If we obtain regulatory approval, we currently expect to commercialize Rhokiinsa[®] and Roclanda[™] in Europe on our own, and likely partner for commercialization of their equivalents in Japan. To optimize the commercial opportunity, we expect to launch Roclanda[™] before Rhokiinsa[®] in Europe, if approved, as the European market is oriented more toward fixed-dose combination products. We are continuing to expand our presence in Europe and are actively participating in European ophthalmology conferences and forums. We now have over 60 employees in Europe that manage the build-out and operation of our manufacturing plant in Ireland, discussed below, as well our Phase 3 clinical trial for Roclanda[™], which is ongoing in several European countries. We are also building our clinical, medical affairs and commercial teams in Europe. In Japan, we announced the opening of our office in Tokyo and the hiring of key leadership positions to help execute our strategy in that market.

In January 2017, we commenced establishment of our own manufacturing plant in Athlone, Ireland. This will be our first manufacturing plant, which is expected to produce commercial supplies of Rhopressa[®] and, if approved, Rocklatan[™], Rhokiinsa[®] and Roclanda[™]. Commercial supply from the plant is expected to be available in early 2020. Our current contract manufacturer produces commercial supply of Rhopressa[®] and started to manufacture Rocklatan[™] in 2018 in anticipation of potential FDA approval and commercial launch in 2019. We are also in the process of adding an additional API contract manufacturer and an additional Rhopressa[®] drug product contract manufacturer, both of which are expected to supply commercial materials in the first half of 2019. We expect to continue to use product sourced from our contract manufacturers when the Ireland plant is operational.

We own the worldwide rights to all indications for Rhopressa[®] and Rocklatan[™]. We have patent protection for Rhopressa[®] and Rocklatan[™] in the United States through early 2034 and internationally, through dates ranging from 2030 to 2037. Our intellectual property portfolio contains patents and pending patent applications related to composition of matter, pharmaceutical compositions, methods of use, and synthetic methods. Furthermore, we have patent protection for AR-13503 in the United States and internationally, which extends to 2030. We have also filed for patent protection for AR-1105 in the United States and internationally.

Product and Product Candidate Overview

Rhopressa[®], our FDA-approved product, has demonstrated that it reduces IOP through ROCK inhibition, its MOA, by which Rhopressa[®] increases the outflow of aqueous humor through the TM, which accounts for approximately 80% of fluid drainage from the healthy eye. Our advanced-stage product candidate is once-daily Rocklatan[™], a fixed-dose combination of

Rhopressa[®] and latanoprost, reduces IOP through the same MOA as Rhopressa[®] and through a second MOA, utilizing the ability of latanoprost to increase the outflow of aqueous humor through the uveoscleral pathway, the eye's secondary drain. Both are taken once-daily in the evening and have shown in preclinical and clinical trials to be effective in reducing IOP, with a favorable safety profile.

Rhopressa[®]

Rhopressa[®] is a once-daily eye drop designed to reduce elevated IOP in patients with open-angle glaucoma or ocular hypertension. The active ingredient in Rhopressa[®], netarsudil, is an Aerie-owned ROCK inhibitor. We believe that Rhopressa[®] represents the first of a new drug class for reducing IOP in patients with glaucoma in over 20 years. Initial indications point to healthcare professionals prescribing Rhopressa[®] as a concomitant therapy to prostaglandins or non-PGA medications when additional IOP reduction is desired. We believe Rhopressa[®] is primarily competing with other non-PGA products, due to its targeting of the diseased TM, its demonstrated ability to reduce IOP at consistent levels across tested baselines, its preferred once-daily dosing relative to other currently marketed non-PGA products and its safety profile. Adjunctive therapies currently represent nearly one-half of the glaucoma prescription market in the United States, according to IQVIA. We believe that Rhopressa[®] may also become a preferred therapy where PGAs are contraindicated, for patients who do not respond to PGAs and for patients who choose to avoid the cosmetic issues associated with PGA products.

Rhopressa[®] received FDA approval on December 18, 2017 and we launched Rhopressa[®] in the United States at the end of April 2018. Rhopressa[®] is now being sold to national and regional U.S. pharmaceutical distributors, and patients have access to Rhopressa[®] through pharmacies across the United States. We have obtained formulary coverage for Rhopressa[®] for approximately 90% of lives covered under commercial plans and approximately 40% of lives covered under Medicare Part D plans. We expect Medicare Part D Tier 2 equivalent coverage to increase to over 70% by the end of the first quarter of 2019.

In October 2018, we announced that the EMA accepted our MAA for review for Rhokiinsa[®]. Additionally, we completed a Phase 1 clinical trial and a successful pilot Phase 2 clinical study in the United States on Japanese and Japanese-American subjects, which were designed to support meeting the requirements of Japan's PMDA for potential regulatory submission of Rhopressa[®] in Japan. We are also planning to initiate a Phase 2 clinical trial on Japanese patients in Japan by the end of the first quarter of 2019 to support subsequent Phase 3 registration trials that are also expected to be conducted in Japan under our direction.

Rocklatan[™]

Our advanced-stage product candidate, Rocklatan[™], is a once-daily fixed-dose combination of Rhopressa[®] and latanoprost, the most commonly prescribed drug for the treatment of patients with open-angle glaucoma. We believe, based on our clinical data, that Rocklatan[™] has the potential to provide a greater IOP-reducing effect than any currently marketed glaucoma medication. Therefore, we believe that Rocklatan[™], if approved and formulary coverage is obtained, could compete with both PGA and non-PGA therapies and become the product of choice for patients requiring maximal IOP reduction, including those with higher IOPs and those who present with significant disease progression despite using currently available therapies.

We submitted an NDA for Rocklatan[™] to the FDA in May 2018 under Section 505(b)(2) of the FDCA, which provides for an abbreviated approval pathway, since Rocklatan[™] is a fixed dose combination of two FDA-approved drugs in the United States. In July 2018, we announced that the NDA was accepted for review by the FDA and the PDUFA goal date was set for March 14, 2019.

With respect to Rocklatan[™] in jurisdictions outside the United States, we also initiated a Phase 3 registration trial for Roclanda[™], named Mercury 3, in Europe during the third quarter of 2017. Mercury 3, a six-month efficacy and safety trial, is designed to compare Roclanda[™] to Ganfort[®], a fixed-dose combination product marketed in Europe of bimatoprost, a PGA, and timolol, a beta blocker. If successful, Mercury 3 is expected to improve our commercialization prospects in Europe. We currently expect to read out topline 90-day efficacy data for the trial in 2019. Since Roclanda[™] is a fixed-dose combination product that includes Rhokiinsa[®], we plan to submit an MAA for Roclanda[™] with the EMA if and when Rhokiinsa[®] is approved by the EMA. We expect to submit the MAA for Roclanda[™] in early 2020, if the EMA has approved Rhokiinsa[®] by such time.

Pipeline Opportunities

Our stated objective is to build a major ophthalmic pharmaceutical company. We are evaluating our portfolio of owned ROCK inhibitors for additional indications within and beyond glaucoma. Our owned preclinical small molecule, AR-13503, is a ROCK and Protein kinase C inhibitor sustained-release implant with potential in the treatment of DME, wet AMD and related diseases of the retina. AR-13503, which has the same active metabolite as Rhopressa[®], has shown lesion size decreases in an *in*

in vivo preclinical model of wet AMD at levels similar to the current market-leading wet AMD anti-VEGF product. When used in combination preclinically with the market-leading anti-VEGF product, AR-13503 produced greater lesion size reduction than the anti-VEGF product alone in a model of proliferative DR. This molecule has not yet been tested in humans in a clinical trial setting. Pending additional studies, AR-13503 may have the potential to provide an entirely new mechanism and pathway to treat DME, wet AMD and related diseases of the retina. Since AR-13503 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.

To that end, in July 2017, we announced that we entered into a collaborative research, development and licensing agreement with DSM, a global science-based company headquartered in the Netherlands. The research collaboration agreement includes an option to license DSM's bio-erodible polymer implant technology for sustained delivery of certain Aerie compounds to treat ophthalmic diseases. In August 2018, we announced the expansion of our collaboration with DSM to provide for (i) a worldwide exclusive license for all ophthalmic indications to DSM's polyesteramide polymer technology, (ii) continuation of the collaborative research initiatives through the end of 2020, including the transfer of DSM's formulation technology to Aerie during that time and (iii) access to a preclinical latanoprost implant. This technology uses polyesteramide polymers to produce an injectable, thin fiber that is minute in size. Preclinical experiments have demonstrated early success in conjunction with AR-13503, including demonstration of linear, sustained elution rates over several months and achievement of target retinal drug concentrations. We expect to submit an IND for AR-13503 by the end of the first quarter of 2019.

Further, in October 2017, we acquired the rights to use PRINT[®] technology in ophthalmology and certain other assets from Envisia. PRINT[®] is a proprietary technology capable of creating precisely-engineered sustained release products utilizing fully-scalable manufacturing processes. In addition, we acquired Envisia's intellectual property rights relating to Envisia's preclinical dexamethasone steroid implant for the potential treatment of macular edema due to RVO that also utilizes the PRINT[®] technology, which we refer to as AR-1105. The IND for this sustained-release implant was submitted in December 2018. In January 2019, we announced that the FDA reviewed the IND for AR-1105 and it is now in effect, allowing Aerie to initiate human studies in the treatment of macular edema due to RVO. We expect to initiate a Phase 2 clinical study for AR-1105 in the first quarter of 2019.

We are also evaluating the PRINT[®] technology platform for sustained release of therapies to the front of the eye, including to treat glaucoma or ocular hypertension, as examples. We commenced operation of our cGMP-validated manufacturing facility for production of ophthalmic implants using PRINT[®] technology in our Durham, North Carolina, facility in October 2018.

We may continue to enter into research collaboration arrangements, license, acquire or develop 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. We are also currently screening our owned library of ROCK inhibitors for indications beyond ophthalmology considering that third-party studies and trials have demonstrated potential for ROCK inhibition in treating certain disease categories. We are initially focused on exploring potential opportunities for our molecules in pulmonary health, dermatology and cancers.

Financial Overview

Our cash and cash equivalents totaled \$202.8 million as of December 31, 2018. We believe that our cash and cash equivalents and projected cash flows from revenues will provide sufficient resources for our current ongoing needs through at least the next twelve months, though there may be need for additional financing activity as we continue to grow, including the potential use of the currently undrawn \$100 million credit facility. See "—Liquidity and Capital Resources" below and Note 9 to our consolidated financial statements included elsewhere in this report for further discussion.

We have incurred net losses since our inception in June 2005. Until 2018, when we commenced commercial operations, our business activities were primarily limited to research and development and raising capital. As of December 31, 2018, we had an accumulated deficit of \$696.4 million. We recorded net losses of \$232.6 million, \$145.1 million and \$99.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. Our capital resources and business efforts are largely focused on activities relating to the commercialization of Rhopressa[®], advancing our product pipeline, international expansion and construction of our manufacturing facility in Athlone, Ireland. We expect to continue to incur operating losses until our products generate adequate commercial revenue to render Aerie profitable. If we do not successfully commercialize Rhopressa[®], or Rocklatan[™] or any future product candidates, if approved, we may be unable to generate adequate product revenues to achieve such profitability. We may be required to draw down on the credit facility, or to obtain further funding through public or private debt or equity offerings or other arrangements. Adequate additional funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce or eliminate our research and development programs or commercialization or manufacturing efforts.

Product Revenues, Net

We launched Rhopressa[®] in the United States in late April 2018 and commenced generating product revenues from sales of Rhopressa[®] during the second quarter of 2018. Our product revenues are recorded net of provisions relating to estimates for (i) trade discounts and allowances, such as discounts for prompt payment and distributor fees, (ii) estimated rebates to Third-party Payers, estimated payments for Medicare Part D prescription drug program coverage gap (commonly called the “donut hole”), patient co-pay program coupon utilization, chargebacks and other discount programs and (iii) reserves for expected product returns. These estimates reflect current contractual and statutory requirements, known market events and trends, industry data and forecasted customer mix. Actual amounts may ultimately differ from these estimates. If actual results vary, estimates may be adjusted in the period such change in estimate becomes known, which may have an impact on earnings in the period of adjustment.

We will not generate any revenue from Rocklatan[™] or any future product candidates unless and until we obtain regulatory approval and commercialize such products.

Cost of Goods Sold

Cost of goods sold consists of direct and indirect costs to procure and manufacture Rhopressa[®] product sold, including third-party manufacturing costs. We began capitalizing inventory costs for Rhopressa[®] after receipt of FDA approval of Rhopressa[®] on December 18, 2017. Prior to receiving FDA approval, such costs were expensed as pre-approval commercial manufacturing expenses. Cost of goods sold in 2019 will continue to be favorably impacted by sales of Rhopressa[®] inventory that was expensed prior to FDA approval; however, we do not expect the impact to be material.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of employee-related expenses, including salaries, benefits and stock-based compensation for all officers and employees in general management, sales and marketing, finance and administration. Other significant expenses include selling and marketing expenses, facilities expenses, shipping and handling costs and professional fees for audit, tax, legal and other services.

We expect that our selling, general and administrative expenses will increase modestly for 2019 as compared to 2018 reflecting a full year of expenses related to our sales force.

Pre-approval Commercial Manufacturing Expenses

Pre-approval commercial manufacturing expenses consist of costs incurred for commercial-related manufacturing activities for Rhopressa[®] and Rocklatan[™] prior to FDA approval. These costs include those associated with the manufacturing of inventory in anticipation of commercial launch, expenses associated with the establishment of both our manufacturing plant in Athlone, Ireland, and our additional API and drug product contract manufacturers, as well as employee-related expenses, which includes salaries, benefits and stock-based compensation for commercial-related manufacturing personnel prior to regulatory approval.

If we obtain regulatory approval of our additional API and drug product contract manufacturers in the first half of 2019, we expect that our pre-approval commercial manufacturing expenses will decrease in 2019 as compared to 2018 as the cost of commercial material produced by these manufacturers following regulatory approval will be capitalized as inventory.

Research and Development Expenses

We expense research and development costs to operations as incurred. Research and development expenses consist primarily of costs incurred for the research and development of our preclinical and clinical candidates, which include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense for research and development personnel;
- expenses incurred under agreements with CROs, contract manufacturing organizations and service providers that assist in conducting clinical trials and preclinical studies;
- costs associated with any collaboration arrangements, licenses or acquisitions of preclinical molecules, product candidates or technologies;
- costs associated with preclinical activities and development activities;
- costs associated with regulatory operations; and

- depreciation expense for assets used in research and development activities.

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

We expect that our research and development expenses will be relatively consistent for 2019 as compared to 2018.

Other Income (Expense), Net

Other income (expense) primarily includes interest income, interest expense, foreign exchange gains and losses, and other income and expense. Interest income primarily consists of interest earned on our cash, cash equivalents and investments, and amortization or accretion of discounts and premiums on our investments. Interest expense consists of interest expense under the 2014 Convertible Notes, including the amortization of debt discounts and issuance costs incurred prior to the conversion of the 2014 Convertible Notes on July 23, 2018. Interest expense also includes the amortization of issuance costs and commitment fees incurred on the credit facility entered into on July 23, 2018. Foreign exchange gains and losses are primarily due to the remeasurement of our Euro-denominated liability related to our build-to-suit lease obligation, which is held by a subsidiary with a U.S. dollar functional currency. Other expense includes the value of additional shares of Aerie common stock issued to complete the conversion of the 2014 Convertible Notes in July 2018. See Note 9 to our consolidated financial statements included elsewhere in this report for additional information.

Critical Accounting Policies and Use of Estimates

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

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

Revenue Recognition

We recognize revenue when our customers obtain control of our product in an amount that reflects the consideration we expect to receive from our customers in exchange for that product. To determine revenue recognition for contracts that are determined to be in scope of the Financial Accounting Standards Board Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("ASC Topic 606"), we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy the performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services transferred to our customer. Once the contract is determined to be within the scope of ASC Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied. Shipping and handling costs related to our product sales are included in selling, general and administrative expenses.

Net product revenues for the year ended December 31, 2018, were derived from sales of Rhopressa[®] in the United States to customers, which principally include a limited number of national and select regional wholesalers (the "Distributors"). These Distributors subsequently resell the product, primarily to retail pharmacies that dispense the product to patients. We expense

incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that would have been recognized is one year or less or the amount is immaterial. The product that is ultimately used by patients is generally covered by third-party payers, such as government or private healthcare insurers and pharmacy benefit managers (“Third-party Payers”) and may be subject to rebates and discounts payable directly to those Third-party Payers.

Product revenue is recorded net of trade discounts, allowances, rebates, chargebacks, estimated returns and other incentives, discussed below. These reserves are classified as either reductions of accounts receivable or as current liabilities. Amounts billed or invoiced are included in accounts receivable, net on the consolidated balance sheet. We did not have any contract assets (unbilled receivables) at December 31, 2018, as customer invoicing generally occurs before or at the time of revenue recognition. We did not have any contract liabilities at December 31, 2018, as we did not receive payments in advance of fulfilling our performance obligations to our customers.

Net product revenue is typically recognized when the Distributors obtain control of our product, which occurs at a point in time, typically upon delivery of Rhopressa[®] to the Distributors. For the year ended December 31, 2018, three Distributors accounted for 33.9%, 33.3% and 29.7% of total revenues, respectively. We evaluate the creditworthiness of each of our Distributors to determine whether it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur. We do not assess whether a contract has a significant financing component if the expectation is such that the period between the transfer of the promised goods to the customer and the receipt of payment will be less than one year. Standard credit terms do not exceed 75 days.

We calculate our net product revenue based on the wholesale acquisition cost that we charge our Distributors for Rhopressa[®] less provisions for (i) trade discounts and allowances, such as discounts for prompt payment and Distributor fees, (ii) estimated rebates to Third-party Payers, estimated payments for Medicare Part D prescription drug program coverage gap (commonly called the “donut hole”), patient co-pay program coupon utilization, chargebacks and other discount programs and (iii) reserves for expected product returns. The estimates of reserves established for variable consideration reflect current contractual and statutory requirements, known market events and trends, industry data and forecasted customer mix. Provisions for revenue reserves reduced product revenues by \$19.6 million in aggregate for the year ended December 31, 2018. The transaction price may be subject to constraint and is included in the net product revenues only to the extent that it is probable that a significant reversal of the amount of the cumulative revenues recognized will not occur in a future period. Actual amounts may ultimately differ from these estimates. If actual results vary, estimates may be adjusted in the period such change in estimate becomes known, which could have an impact on earnings in the period of adjustment.

Trade Discounts and Allowances: We generally provide discounts on sales of Rhopressa[®] to our Distributors for prompt payment and pay fees for distribution services and for certain data that Distributors provide to us. We expect our Distributors to earn these discounts and fees, and accordingly deduct the full amount of these discounts and fees from our gross product revenues at the time such revenues are recognized.

Rebates, Chargebacks and Other Discounts: We contract with Third-party Payers for coverage and reimbursement of Rhopressa[®]. We estimate the rebates and chargebacks we expect to be obligated to provide to Third-party Payers and deduct these estimated amounts from our gross product revenue at the time the revenue is recognized. We estimate the rebates and chargebacks that we expect to be obligated to provide to Third-party Payers based upon (i) our contracts and negotiations with these Third-party Payers, (ii) estimates regarding the payer mix for Rhopressa[®] and (iii) historical industry information regarding the payer mix for comparable pharmaceutical products and product portfolios. Other discounts include our co-pay assistance programs for commercially-insured patients meeting certain eligibility requirements. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to pay associated with product that has been recognized as revenue.

Product Returns: We estimate the amount of Rhopressa[®] that will be returned and deduct these estimated amounts from our gross revenue at the time the revenue is recognized. We currently estimate product returns based on historical industry information regarding rates for comparable pharmaceutical products and product portfolios, the estimated remaining shelf life of Rhopressa[®] shipped to Distributors, and contractual agreements with our Distributors intended to limit the amount of inventory they maintain. Reporting from the Distributors includes Distributor sales and inventory held by Distributors, which provide us with visibility into the distribution channel to determine when product would be eligible to be returned.

Inventories

Manufacturing costs related to commercial production are expensed as pre-approval commercial manufacturing expenses before we obtain regulatory approval for our product candidates. Once regulatory approval is obtained, such costs are capitalized as inventory. Inventories are stated at the lower of cost or net realizable value. We determine the cost of inventory

using the first-in, first-out (“FIFO”) method. We analyze our inventory levels at least quarterly and write down inventory that is expected to expire prior to being sold, inventory in excess of expected sales requirements and inventory that fails to meet commercial sale specifications, with a corresponding charge to cost of goods sold. The determination of whether inventory costs will be realizable requires estimates by management of future expected inventory requirements based on sales forecasts. If actual net realizable value is less than our estimate or if actual market conditions are less favorable than our projections, additional inventory write-downs may be required. Charges for inventory write-downs are not reversed if it is later determined that the product is saleable.

Accrued Expenses

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

- fees paid to CROs in connection with clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturing organizations and service providers that assist in conducting preclinical and clinical trials or that produce commercial inventory prior to FDA approval; and
- fees paid to service providers for audit, tax, legal and other services.

We accrue our expenses related to clinical trials based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct research activities and/or manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the level of effort varies from our estimate, we will adjust the accrual accordingly.

If we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. Although we do not currently anticipate the future settlement of existing accruals to differ materially from our estimates, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low for any period. There have been no material changes in estimates for the periods presented.

Fair Value Measurements

We record certain financial assets and liabilities at fair value based on the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants. As of December 31, 2017, the estimated fair value of the 2014 Convertible Notes was \$327.6 million. In July 2018, the entire outstanding principal amount of the 2014 Convertible Notes was converted into shares of Aerie common stock. See Note 9 to our consolidated financial statements included elsewhere in this report for additional information.

Acquisitions

We evaluate acquisitions to determine whether the acquisition is a business combination or an acquisition of assets under Financial Accounting Standards Board (“FASB”) Accounting Standards Codification Topic 805: *Business Combinations* (“ASC Topic 805”). Business combinations are accounted for using the acquisition method of accounting, whereby assets acquired and liabilities assumed are recorded as of the acquisition date at their respective fair values and any excess of the fair value of the consideration transferred over the fair value of the net assets acquired is recorded as goodwill. In an asset acquisition that does not constitute a business, no goodwill is recognized, and the net assets acquired are generally recorded at cost. In January 2017, the FASB issued Accounting Standards Update (“ASU”) 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* (“ASU 2017-01”). The ASU clarifies the definition of a business and provides a screen to determine when an integrated set of assets and activities is not a business. The screen requires that when substantially all of the fair value

of the gross assets acquired, or disposed of, is concentrated in a single identifiable asset or a group of similar identifiable assets, the set is not a business. The new standard was effective for us beginning on January 1, 2018; however, we elected to early adopt this ASU as of July 1, 2017. Under ASC Topic 805, including the provisions of ASU 2017-01, the October 4, 2017 transaction to acquire assets from Envisia was determined to meet the criteria of an asset acquisition rather than a business combination, resulting in a \$24.8 million charge to research and development expense on the consolidated statement of operations and comprehensive loss in the three months ended December 31, 2017 for acquired in-process research and development (“IPR&D”). Significant judgment is required in estimating the fair value of intangible assets and in a determination of whether an acquisition is a business combination or an acquisition of assets. The fair value estimates are based on available historical information and on future expectations and assumptions deemed reasonable by management but are inherently uncertain.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees ratably over the requisite service period, which in most cases is the vesting period of the award for employees, based on the estimated fair value of the awards on the date of grant. Compensation expense for options granted to non-employees is determined as the fair value of consideration received or the fair value of the equity instruments issued, whichever is more reliably measured. The fair value of the awards granted to non-employees is remeasured each period until the related service is complete. The fair value of restricted stock awards (“RSAs”), including restricted stock awards with non-market performance and service conditions (“PSAs”) is determined based on the fair value of our common stock on the date of grant. Compensation expense related to RSAs is recognized ratably over the vesting period. As the PSAs have multiple performance conditions, compensation expense is recognized for each vesting tranche over the respective requisite service period of each tranche if and when we deem it probable that the performance conditions will be satisfied. Compensation expense for stock purchase rights under our employee stock purchase plan is measured and recognized on the date that we become obligated to issue shares of our common stock and is based on the difference between the fair value of our common stock and the purchase price on such date. The fair value of the stock appreciation rights (“SARs”) is estimated using the Black-Scholes option pricing model and is marked to market through stock-based compensation expense. SARs are liability-based awards as they may only be settled in cash.

Significant Factors, Assumptions and Methodologies Used in Determining Fair Value

Determining the appropriate fair value measurement of stock-based awards requires the use of subjective assumptions. We estimate the fair value of options to purchase common stock using the Black-Scholes option pricing model, which is affected by our common stock fair values as well as assumptions regarding a number of other subjective variables. These other variables include the expected term of the options, our expected stock price volatility over the expected term of the options, risk-free interest rates and expected dividends.

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

- *Fair Value of our Common Stock.* The fair value for our underlying common stock is determined using the closing price on the date of grant as reported on The NASDAQ Global Market.
- *Volatility.* We calculate expected volatility based on our historical volatility in combination with reported data for a selected group of similar publicly traded companies, or guideline peer group, for which the relevant historical information is available. We selected representative companies from the pharmaceutical industry with similar characteristics to us, including stage of product development and commercialization.
- *Expected Term.* We used the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, as we do not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. The simplified method is based on the vesting period and the contractual term for each grant, or for each vesting-tranche for awards with graded vesting. The midpoint between the vesting date and the maximum contractual expiration date is used as the expected term under this method.
- *Risk-free Rate.* The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected time to exercise.
- *Forfeiture.* Forfeitures are recognized in the period in which they occur. Prior to 2017, forfeitures were estimated such that we only recognized expense for the shares expected to vest, and adjustments were made if actual forfeitures differed from those estimates.

- *Dividend Yield.* Except for a one-time cash dividend related to the spin-off of certain non-core intellectual property that occurred in 2012, we have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future.

Key weighted average assumptions utilized in the fair value calculation for the underlying common stock as of December 31, 2018, 2017 and 2016 appear in the table below.

	YEAR ENDED DECEMBER 31,		
	2018	2017	2016
Expected term (years)	6.0	6.0	6.0
Expected stock price volatility	78%	84%	84%
Risk-free interest rate	2.7%	2.0%	1.4%
Dividend yield	—	—	—

Tax Valuation Allowance

A valuation allowance is recorded if it is more likely than not that a deferred tax asset will not be realized. Realization of future tax benefits is dependent on our ability to generate sufficient taxable income within the carryforward period. Due to our history of operating losses and lack of available evidence supporting future taxable income, we maintain a valuation allowance on all of our deferred tax assets as of December 31, 2018, with the exception of a release of valuation allowance during the year ended December 31, 2017 on a deferred tax asset related to a \$1.7 million AMT refund that we expect to receive under the Tax Act. The amount of refund expected to be received is recorded as a receivable as of December 31, 2018 and 2017.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes the results of our operations for the years ended December 31, 2018 and 2017:

	YEAR ENDED DECEMBER 31,		CHANGE	% CHANGE
	2018	2017		
	(in thousands, except percentages)			
Product revenues, net	\$ 24,181	\$ —	\$ 24,181	*
Total revenues, net	24,181	—	24,181	*
Costs and expenses:				
Cost of goods sold	641	—	641	*
Selling, general and administrative expenses	120,614	56,905	63,709	112%
Pre-approval commercial manufacturing	26,545	16,710	9,835	59%
Research and development expenses	86,123	72,078	14,045	19%
Total costs and expenses	233,923	145,693	88,230	61%
Loss from operations	(209,742)	(145,693)	(64,049)	44%
Other income (expense), net	(22,824)	(1,170)	(21,654)	*
Loss before income taxes	\$ (232,566)	\$ (146,863)	\$ (85,703)	58%

*Percentage not meaningful

Product revenues, net

Product revenues, net was \$24.2 million for the year ended December 31, 2018 and relate to sales of Rhopressa[®], which we launched in the United States at the end of April 2018. Rhopressa[®] is our first product to receive regulatory approval, and we did not generate any revenues prior to the second quarter of 2018.

Cost of goods sold

Cost of goods sold was \$0.6 million for the year ended December 31, 2018. Our gross margin percentage of 97.3% was favorably impacted during the year ended December 31, 2018 by sales of Rhopressa[®] with certain materials produced prior to FDA approval and therefore expensed in prior periods. If inventory sold during the year ended December 31, 2018 was valued at cost, our gross margin for the period then ended would have been 96.4%.

Selling, general and administrative expenses

Selling, general and administrative expenses increased by \$63.7 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. This increase was primarily associated with the expansion of our employee base to support the growth of our operations and selling and marketing expenses incurred in connection with our commercial launch of Rhopressa[®].

Employee-related expenses increased by \$34.1 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017 primarily due to increased headcount to build our commercial infrastructure, including the addition of our sales force which increased by \$19.0 million in 2018. Employee-related expenses also included an increase in stock-based compensation expense of \$7.8 million. Selling and marketing expenses increased by \$24.1 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017 related to our commercial launch of Rhopressa[®] in the United States and the preparation for our planned commercial launch of Rocklatan[™] in the United States, if approved.

Pre-approval commercial manufacturing expenses

Pre-approval commercial manufacturing expenses increased by \$9.8 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. Employee-related expenses increased by \$4.8 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017 primarily due to increased headcount in our manufacturing plant in Ireland. Other commercial manufacturing expenses increased by \$5.1 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017, primarily related to the build-out and operation of our manufacturing plant in Ireland.

Research and development expenses

Research and development expenses increased by \$14.0 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. This increase is primarily comprised of an increase of \$19.4 million related to early-stage pipeline activities, including \$12.6 million related to our expanded collaboration agreement with DSM, an increase of \$9.4 million of employee-related expenses related to an increase in headcount and an increase of \$5.3 million in expenses for Rhopressa[®], as discussed below. These increases were partially offset by a decrease of \$24.8 million of research and development expenses related to our Envisia asset acquisition that occurred in 2017 for acquired IPR&D that was expensed during the year ended December 31, 2017, and a decrease of \$2.7 million in expenses for Rocklatan[™], as discussed below.

Research and development expenses for Rhopressa[®] totaled \$10.7 million and \$5.3 million for the years ended December 31, 2018 and 2017, respectively. The \$5.3 million increase in expenses for Rhopressa[®] for the year ended December 31, 2018 as compared to the year ended December 31, 2017 primarily related to costs incurred in 2018 for our clinical trials to support the potential regulatory submission of Rhopressa[®] in Japan. Research and development expenses for Rocklatan[™] totaled \$6.3 million and \$9.0 million for the years ended December 31, 2018 and 2017, respectively. The \$2.7 million decrease in expenses for Rocklatan[™] for the year ended December 31, 2018 as compared to the year ended December 31, 2017 primarily related to a decrease in development and regulatory activities for U.S. approval in 2018 as compared to 2017, partially offset by costs incurred in 2018 related to the Mercury 3 registration trial in Europe and the \$2.4 million NDA filing fee incurred upon submission of the NDA for Rocklatan[™] to the FDA.

Other income (expense), net

Other income (expense), net consists of the following:

	YEAR ENDED DECEMBER 31			
	2018	2017	CHANGE	% CHANGE
	(in thousands, except percentages)			
Interest income	\$ 3,429	\$ 1,753	\$ 1,676	96%
Interest expense	(2,531)	(2,368)	(163)	7%
Other income (expense)	(23,722)	(555)	(23,167)	*
Other income (expense), net	\$ (22,824)	\$ (1,170)	\$ (21,654)	*

*Percentage not meaningful

Other income (expense), net changed by \$21.7 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017. The change was primarily related to the value of the additional 329,124 shares of Aerie common stock issued to Deerfield in the amount of \$24.1 million, which was recorded as other expense during the third quarter of 2018 in connection with the induced conversion of the entire outstanding principal amount of the 2014 Convertible Notes in July 2018. See Note 9 to our consolidated financial statements included in this report for additional information. This expense was partially offset by an increase in interest income primarily due to the increase in our cash, cash equivalents and investments balances.

Comparison of the Years Ended December 31, 2017 and 2016

The following table summarizes the results of our operations for the years ended December 31, 2017 and 2016:

	YEAR ENDED DECEMBER 31,			
	2017	2016	CHANGE	% CHANGE
	(in thousands, except percentages)			
Selling, general and administrative expenses	\$ 56,905	\$ 34,706	\$ 22,199	64%
Pre-approval commercial manufacturing	16,710	9,772	6,938	71%
Research and development expenses	72,078	52,394	19,684	38%
Total operating expenses	145,693	96,872	48,821	50%
Loss from operations	(145,693)	(96,872)	(48,821)	50%
Other income (expense), net	(1,170)	(1,994)	824	*
Loss before income taxes	\$ (146,863)	\$ (98,866)	\$ (47,997)	49%

*Percentage not meaningful

Selling, general and administrative expenses

Selling, general and administrative expenses increased by \$22.2 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. Employee-related expenses increased by \$12.0 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016, driven primarily by the growth of our operations. The increase in employee-related expenses includes an increase in employee stock-based compensation expense of \$6.0 million. Expenses related to our pre-launch sales and marketing planning activities increased by \$5.2 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016, in preparation for the Rhopressa[®] commercial launch.

Pre-approval commercial manufacturing expenses

Pre-approval commercial manufacturing expenses increased by \$6.9 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. Our preparatory commercial manufacturing activities were primarily related to the validation and scale-up of our manufacturing capabilities in preparation for Rhopressa[®] launch and increased by \$3.1 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. Employee-related expenses increased by \$3.0 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016, primarily due to increased headcount in our manufacturing plant in Ireland.

Research and development expenses

Research and development expenses increased by \$19.7 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. The increase was primarily related to the acquisition of assets from Envisia in which \$24.8 million of acquired IPR&D was expensed during the year ended December 31, 2017. Excluding the impact of the Envisia asset acquisition, research and development expenses decreased by \$5.1 million primarily related to the completion of the Phase 3 registration trials for Rhopressa[®] and Rocklatan[™] for U.S. approval, partially offset by expenses incurred for Rocklatan[™] registration trials for European approval and for Rhopressa[®] clinical trials designed for potential future approval in Japan.

Research and development expenses for Rhopressa[®] totaled \$5.3 million and \$12.0 million for the years ended December 31, 2017 and 2016, respectively. Research and development expenses for Rocklatan[™] totaled \$9.0 million and \$18.0 million for the years ended December 31, 2017 and 2016, respectively. In addition, employee-related expenses increased by \$6.4 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016 due to an increase in headcount to support the growth of our operations.

Other income (expense), net

Other income (expense), net consists of the following:

	YEAR ENDED DECEMBER 31		CHANGE	% CHANGE
	2017	2016		
	(in thousands, except percentages)			
Interest income	\$ 1,753	\$ 639	\$ 1,114	*
Interest expense	(2,368)	(2,537)	169	(7)%
Other income (expense)	(555)	(96)	(459)	*
Other income (expense), net	\$ (1,170)	\$ (1,994)	\$ 824	*

*Percentage not meaningful

Other income (expense), net changed by \$0.8 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. The change was primarily related to additional interest income for the year ended December 31, 2017 as compared to the year ended December 31, 2016 due to the increase in our cash, cash equivalents and investments, partially offset by an increase in unrealized foreign exchange loss included in other expense related to the remeasurement of our Euro-denominated build-to-suit lease obligation, which is held by a subsidiary with a U.S. dollar functional currency.

Liquidity and Capital Resources

Since our inception, we have funded operations primarily through the sale of equity securities and the issuance of convertible notes. We have incurred losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses until such a time when one or more of our products are commercially successful, if at all. We received FDA approval for Rhopressa[®] on December 18, 2017 and we launched Rhopressa[®] in the United States at the end of April 2018. As a result, we commenced generating product revenues related to sales of Rhopressa[®] in the second quarter of 2018. We will not generate any revenue from Rocklatan[™] or any future product candidates unless and until we obtain regulatory approval and commercialize such products. Rocklatan[™] has a PDUFA goal date of March 14, 2019.

Sources of Liquidity

Since our initial public offering in October 2013, we have:

- issued \$125.0 million aggregate principal amount of the 2014 Convertible Notes, which was subsequently converted into shares of Aerie's common stock in July 2018,
- issued approximately 11.0 million shares of our common stock through December 31, 2017, for which we received net proceeds of approximately \$351.3 million, after deducting fees and expenses. This includes approximately \$207.7 million of net proceeds from our prior "at-the-market" sales agreements, of which approximately \$61.1 million were received during the year ended December 31, 2017, and approximately \$143.6 million of net proceeds from the issuance of shares of our common stock pursuant to underwriting

agreements, related to registered public offerings, of which approximately \$72.7 million were received during the year ended December 31, 2017,

- issued approximately 2.3 million additional shares of our common stock during the year ended December 31, 2018, for which we received net proceeds of approximately \$136.4 million, after deducting fees and expenses. This includes approximately \$62.3 million of net proceeds from our “at-the-market” sales agreement (“ATM”) and approximately \$74.1 million of net proceeds from the issuance of shares of our common stock pursuant to an underwriting agreement, dated January 23, 2018, related to a registered public offering, and
- commenced generating product revenues related to sales of Rhopressa[®] in the second quarter of 2018 following our commercial launch of Rhopressa[®] in the United States. Product revenues, net amounted to \$24.2 million for the year ended December 31, 2018 and relate to sales of Rhopressa[®]. Accounts receivable, net amounted to \$2.7 million as of December 31, 2018.

As of December 31, 2018, our principal sources of liquidity were our cash and cash equivalents, which totaled approximately \$202.8 million. In July 2018, we entered into a \$100 million senior secured delayed draw term loan facility that matures on July 23, 2024. No funds were drawn at closing or as of December 31, 2018. See Note 9 to our consolidated financial statements included in this report for additional information. We believe that our cash and cash equivalents and projected cash flows from revenues will provide sufficient resources for our current ongoing needs through at least the next twelve months. See “— Operating Capital Requirements.”

Cash Flows

The following table summarizes our sources and uses of cash:

	YEAR ENDED DECEMBER 31,		
	2018	2017	2016
Net cash (used in) provided by:	(in thousands)		
Operating activities	\$ (152,576)	\$ (93,213)	\$ (79,840)
Investing activities	20,789	(42,807)	18,100
Financing activities	137,036	135,644	168,625
Net increase (decrease) in cash and cash equivalents	<u>\$ 5,249</u>	<u>\$ (376)</u>	<u>\$ 106,885</u>

Operating Activities

During the years ended December 31, 2018, 2017 and 2016, our operating activities used net cash of \$152.6 million, \$93.2 million and \$79.8 million, respectively. The increase in net loss from operations for the year ended December 31, 2018 as compared to the year ended December 31, 2017 and for the year ended December 31, 2017 as compared to the year ended December 31, 2016 was primarily due to the expansion of our employee base as well as an increase in cash used for commercial operations and manufacturing activities for the U.S. launch of Rhopressa[®] and development activities related to our product pipeline, including costs associated with executing our international expansion strategy primarily in Europe and Japan.

Investing Activities

During the year ended December 31, 2018, our investing activities provided net cash of \$20.8 million primarily related to proceeds from maturities and sales of available-for-sale investments of \$108.3 million, which were partially offset by purchases of available-for-sale investments of \$56.2 million and purchases of property, plant and equipment of \$31.3 million, primarily related to the build-out of our manufacturing plant in Ireland. During the year ended December 31, 2017, our investing activities used net cash of \$42.8 million primarily related to purchases of available-for-sale investments of \$104.5 million, purchases of property, plant and equipment of \$16.0 million, primarily related to the build-out of our manufacturing plant in Ireland, and a \$10.5 million cash payment for the acquisition of assets from Envisia, which were partially offset by maturities and sales of available-for-sale investments of \$88.2 million. During the year ended December 31, 2016, our investing activities provided net cash of \$18.1 million primarily related to maturities and sales of available-for-sale investments of \$58.3 million, which were partially offset by purchases of available-for-sale investments of \$35.2 million and purchases of property, plant and equipment of \$5.1 million to support the growth of our operations.

Financing Activities

During the years ended December 31, 2018, 2017 and 2016, our financing activities provided net cash of \$137.0 million, \$135.6 million and \$168.6 million, respectively. The net cash provided by financing activities during the years ended December 31, 2018, 2017 and 2016 was primarily related to the issuance and sale of common stock under our prior “at-the-market” sales agreements and under underwriting agreements related to registered public offerings, from which we received net proceeds of approximately \$136.0 million, \$134.2 million and \$167.4 million, respectively.

Operating Capital Requirements

We expect to incur ongoing operating losses until such a time when Rhopressa[®] or Rocklatan[™] or any other product, if approved in the future, generates adequate revenues to render Aerie profitable.

Our principal liquidity requirements are for: working capital; operating expenses including for commercialization and manufacturing activities; expenses associated with developing our pipeline opportunities, including pursuing strategic growth opportunities; costs associated with executing our international expansion strategy, including clinical and potential commercialization activities in Europe and Japan; contractual obligations; and capital expenditures, including completing our manufacturing plant in Ireland.

In January 2017, we entered into a lease agreement for a new manufacturing plant in Ireland under which we are leasing approximately 30,000 square feet of interior floor space for build-out. Capital expenditures related to the manufacturing plant totaled approximately \$24.8 million in 2018. We expect the plant to be operational in early 2020.

We believe that our cash and cash equivalents and projected cash flows from revenues will provide sufficient resources to support our operations through at least the next twelve months. Additionally, we have the borrowing capacity of up to \$100 million under a delayed draw term loan facility. The first two years of payments on any drawn amounts will be on an interest-only basis. We do not currently intend to draw down on the credit facility but may do so if and as needed.

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

- commercial performance of Rhopressa[®] and Rocklatan[™] or any future product candidates, if approved;
- costs of commercialization activities for Rhopressa[®] and Rocklatan[™] and any future product candidates, if approved;
- costs of building inventory to support sales growth and other associated working capital needs;
- costs, timing and outcome of seeking regulatory approval;
- timing and costs of our ongoing and future clinical trials and preclinical studies including those related to our international expansion;
- costs of any follow-on development or products, including the exploration and/or development of any additional indications or additional opportunities for new ophthalmic product candidates, delivery alternatives and new therapeutic areas;
- terms and timing of any acquisitions, collaborations or other arrangements;
- costs related to the credit facility; and
- costs related to filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims.

We based our projections on assumptions that may prove to be incorrect or unreliable or may change due to circumstances beyond our control, and as a result, we may consume our available capital resources earlier than we originally projected. Accordingly, we may be required to draw down on the credit facility or obtain further funding through public or private debt offerings, or other sources, or we may decide, based on various factors, that additional financings are desirable. If such funding is required, we cannot guarantee that it will be available to us on favorable terms, if at all.

Income Taxes and Net Operating Loss Carryforwards

We have incurred significant NOLs since our inception in June 2005. We expect to continue to incur NOLs until such a time when Rhopressa[®] or Rocklatan[™] or any other product, if approved in the future, generates adequate revenues to render Aerie profitable. We received FDA approval for Rhopressa[®] on December 18, 2017, and we launched Rhopressa[®] in the United States at the end of April 2018. As a result, we commenced generating product revenues related to sales of Rhopressa[®] in the second

quarter of 2018; however, we did not generate taxable income in 2018. The NOLs may be utilized to offset taxable income generated in the future.

As of December 31, 2018, we had federal and state NOL carryforwards of approximately \$387.7 million and \$411.2 million, respectively. Federal NOLs that arose prior to 2018 and state NOLs will begin to expire at various dates beginning in 2031 and 2024, respectively. Federal NOLs that arose on or after January 1, 2018, can be carried forward indefinitely to be utilized against future income, but can only be used to offset a maximum of 80% of our federal taxable income in any year. As of December 31, 2018, we had foreign NOL carryforwards of \$44.1 million, which are available solely to offset taxable income of our foreign subsidiaries, subject to any applicable limitations under foreign law.

NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of our company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. State NOLs and tax credit carryforwards may be subject to similar limitations under state laws.

In December 2017, the Tax Act was signed into law and enacted significant changes to the Internal Revenue Code of 1986, as amended. This new tax legislation, among other changes, reduced the federal corporate income tax rate from 35% to 21% effective January 1, 2018. Under U.S. GAAP, deferred tax assets and liabilities are required to be revalued during the period in which the new tax legislation is enacted, which resulted in the remeasurement of our federal deferred tax assets and liabilities as of December 31, 2017 to reflect the effects of the enacted changes in tax rate. As we provide a full valuation allowance on our net deferred tax assets, there was no impact to income tax expense in our consolidated statement of operations and comprehensive loss for the year ended December 31, 2017 as a result of the remeasurement. The Tax Act also repealed the corporate AMT for tax years beginning after December 31, 2017 and provides that existing AMT credit carryovers are refundable in tax years beginning after December 31, 2017. We have approximately \$1.7 million of AMT credit carryovers that we expect to be fully refunded between 2019 and 2022. The Tax Act also limits various business deductions, modifies the maximum deduction of NOLs and includes various international tax provisions. Many provisions in the Tax Act were generally effective in tax years beginning in 2018, and we will continue to analyze additional information and guidance related to certain aspects of the Tax Act in assessing the potential impact on Aerie in the future.

Indebtedness

In July 2018, our \$125.0 million aggregate principal amount of 2014 Convertible Notes was converted into shares of Aerie common stock. Also, in July 2018, we entered into a \$100 million senior secured delayed draw term loan facility, pursuant to which we may borrow up to \$100 million in aggregate in one or more borrowings at any time prior to July 23, 2020. The credit facility includes fees upon drawdown of 1.75% of amounts drawn, an 8.625% annual interest rate on drawn amounts, and annual fees on undrawn amounts of 1.5%. There is also an exit fee of \$1.5 million payable upon termination of the credit facility (whether at maturity or otherwise). Fees on undrawn amounts are not payable until July 23, 2020, and no principal payments will be due on drawn amounts, if any, until July 23, 2020. The credit facility matures on July 23, 2024 in respect of drawn amounts. The credit facility includes affirmative and negative covenants and prepayment terms. No amounts were drawn at closing or as of December 31, 2018. See Note 9 to our consolidated financial statements appearing elsewhere in this report for more information.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2018:

	TOTAL	LESS THAN 1 YEAR	1 TO 3 YEARS	3 TO 5 YEARS	MORE THAN 5 YEARS
	(in thousands)				
Lease obligations ⁽¹⁾	\$ 25,975	\$ 4,798	\$ 9,633	\$ 3,627	\$ 7,917
Credit facility fees ⁽²⁾	4,500	—	4,500	—	—
Purchase obligations ⁽³⁾	33,007	12,557	13,307	7,143	—
	<u>\$ 63,482</u>	<u>\$ 17,355</u>	<u>\$ 27,440</u>	<u>\$ 10,770</u>	<u>\$ 7,917</u>

- (1) Our lease obligations are primarily related to our principal executive office and research facility in Durham, North Carolina, and corporate offices in Bedminster, New Jersey, Irvine, California and other foreign offices. Additionally, the table reflects rental payments related to a lease agreement we entered into in January 2017 for a new manufacturing plant in Athlone, Ireland, under which we are leasing approximately 30,000 square feet of interior floor space for build-out. We are permitted to terminate the lease agreement beginning in September 2027. Obligations denominated in foreign currencies have been translated to U.S. dollars at the foreign exchange rates in effect at December 31, 2018.
- (2) In July 2018, the entire outstanding principal amount of the 2014 Convertible Notes was converted into shares of Aerie common stock. Also, in July 2018, we entered into a credit facility, which matures on July 23, 2024. The credit facility includes fees upon drawdown of 1.75% of amounts drawn, an 8.625% annual interest rate on drawn amounts, and annual fees on undrawn amounts of 1.5%. There is also an exit fee of \$1.5 million payable upon termination of the credit facility (whether at maturity or otherwise). No funds were drawn at closing or as of December 31, 2018, and therefore, fees included in the table above relate to fees due on undrawn amounts, including the exit fee. Refer to Note 9 to our consolidated financial statements included elsewhere in this report for further information.
- (3) Purchase obligations primarily include non-cancelable commitments under our contract manufacturing agreements.

We have agreements with third-parties with contingent milestone payments that are potentially payable by us, as more fully described in Note 1 to our consolidated financial statements appearing elsewhere in this report, which are not reflected in the table above. These payments are contingent upon achieving certain development and/or regulatory milestones that may or may not ever be achieved. Therefore, our requirement to make such payments in the future, if at all, as well as the timing of any such payments is highly uncertain.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under SEC regulations.

Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements included elsewhere in this report regarding the impact of certain recent accounting pronouncements on our consolidated financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our cash and cash equivalents consisted of cash and money market funds. We do not currently engage in any hedging activities against changes in interest rates. Given the short-term nature of our cash and cash equivalents, we do not believe that a change in market interest rates would have a material impact on our financial condition or results of operations. Any amounts drawn under the credit facility, if any, will carry a fixed interest rate and, as such, will not be subject to interest rate risk.

We face market risks attributable to fluctuations in foreign currency exchange rates and exposure on the remeasurement of foreign currency-denominated monetary assets or liabilities into U.S. dollars. In particular, our operations and subsidiary in Ireland may enter into certain obligations or transactions in Euros or other foreign currencies but has a U.S. dollar functional currency. We do not currently have any derivative instruments or a foreign currency hedging program. To date and during the year ended December 31, 2018, foreign currency exposure and foreign currency financial instruments have not been material.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The financial statements required by this item are set forth beginning at page F-1 of this report and are incorporated herein by reference.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15(d)-15(e)), as of the end of the period covered by this report. Based upon the evaluation, the Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2018, the disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed in the reports we file or submit under the Exchange Act is (i) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (ii) accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, our principal executive officer and principal financial officer and effected by our Board of Directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in conformity with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our Chief Executive Officer and Chief Financial Officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control-Integrated Framework (2013)*. Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2018.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item is incorporated by reference to the information set forth in the sections titled “Nominees for Election as Directors,” “Information About Our Executive Officers,” “Directors Continuing in Office,” “Section 16(a) Beneficial Ownership Reporting Compliance,” “Code of Business Conduct and Ethics” and “Information about the Board of Directors and Corporate Governance - Audit Committee” in our Proxy Statement.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference to the information set forth in the sections titled “Executive Compensation,” “Director Compensation” and “Information about the Board of Directors and Corporate Governance - Compensation Committee Interlocks and Insider Participation” in our Proxy Statement.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated by reference to the information set forth in the sections titled “Securities Authorized for Issuance under Equity Compensation Plans” and “Security Ownership of Certain Beneficial Owners and Management” in our Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated by reference to the information set forth in the sections titled “Board of Directors’ Independence” and “Transactions with Related Persons” in our Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated by reference to the information set forth in the section titled “Independent Registered Public Accounting Firm Fees and Services” in our Proxy Statement.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

The financial statement schedules and exhibits filed as part of this Annual Report on Form 10-K are as follows:

(a)(1) Financial Statements

See “Index to Consolidated Financial Statements” beginning on page F-1 of this report.

(a)(2) Financial Statement Schedules

Financial statement schedules have been omitted because the required information is not present, or not present in amounts sufficient to require submission of the schedules, or because the required information is provided in the financial statements or notes thereto.

(a)(3) Exhibits

The exhibits required to be filed as part of this report are listed in the Exhibit Index attached hereto and are incorporated herein by reference.

ITEM 16. FORM 10-K SUMMARY

None.

EXHIBIT INDEX

<u>EXHIBIT NO.</u>	<u>EXHIBIT DESCRIPTION</u>
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on October 31, 2013).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on October 31, 2013).
4.1	Exchange and Termination Agreement, dated as of July 23, 2018, by and among Aerie Pharmaceuticals, Inc., Deerfield Private Design Fund III, L.P., Deerfield Partners, L.P. and Deerfield Special Situations Fund, L.P. (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on July 23, 2018).
4.2	Registration Rights Agreement, dated as of July 23, 2018, by and among Aerie Pharmaceuticals, Inc., Deerfield Private Design Fund III, L.P., Deerfield Partners, L.P. and Deerfield Special Situations Fund, L.P. (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on July 23, 2018).
10.1	Form of Aerie Pharmaceuticals, Inc. Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
10.2	Aerie Pharmaceuticals, Inc. Second Amended and Restated Omnibus Incentive Plan (incorporated by reference to the appendix to the Registrant's Definitive Proxy Statement on Schedule 14A (File No. 001-36152) filed on April 27, 2018).
10.3	Form of Aerie Pharmaceuticals, Inc. Incentive Stock Option Agreement (Cliff Vesting) (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on February 24, 2015).
10.4	Form of Aerie Pharmaceuticals, Inc. Incentive Stock Option Agreement (Monthly Vesting) (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on February 24, 2015).
10.5	Form of Aerie Pharmaceuticals, Inc. Restricted Stock Agreement (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on February 24, 2015).
10.6	Form of Aerie Pharmaceuticals, Inc. Incentive Stock Option Agreement (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on March 19, 2014).
10.7	Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan, dated as of July 13, 2005 (incorporated by reference to Exhibit 10.5 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
10.8	First Amendment of Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan, dated as of February 19, 2008 (incorporated by reference to Exhibit 10.6 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
10.9	Second Amendment of Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan, dated as of December 3, 2009 (incorporated by reference to Exhibit 10.7 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
10.10	Third Amendment of Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan, dated as of February 23, 2011 (incorporated by reference to Exhibit 10.8 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
10.11	Fourth Amendment of Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan, dated as of August 9, 2013 (incorporated by reference to Exhibit 10.9 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
10.12	Fifth Amendment of Aerie Pharmaceuticals, Inc. 2005 Stock Option Plan, dated as of September 16, 2013 (incorporated by reference to Exhibit 10.10 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).

- 10.13 Form of Indemnification Agreement for officers and directors (incorporated by reference to Exhibit 10.19 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 21, 2013).
- 10.14 Employment Agreement, dated as of September 20, 2013, by and between Aerie Pharmaceuticals, Inc. and Vicente Anido, Jr., Ph.D. (incorporated by reference to Exhibit 10.18 to the Registrant's Form S-1 Registration Statement (File No. 333-191219) filed on October 3, 2013).
- 10.15 Amended and Restated Employment Agreement, dated July 25, 2017, by and between Aerie Pharmaceuticals, Inc. and Vicente Anido, Jr., Ph.D. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on July 26, 2017).
- 10.16 Amended and Restated Employment Agreement, dated as of December 18, 2013, between Aerie Pharmaceuticals, Inc. and Thomas Mitro (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on December 20, 2013).
- 10.16.1 Amendment to Amended and Restated Employment Agreement, dated as of March 6, 2017, by and between Aerie Pharmaceuticals, Inc. and Thomas Mitro (incorporated by reference to Exhibit 10.16.1 to the Registrant's Annual Report on Form 10-K (File No. 001-36152) filed on March 9, 2017).
- 10.17 Amended and Restated Employment Agreement, dated as of December 18, 2013, between Aerie Pharmaceuticals, Inc. and Richard Rubino (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on December 20, 2013).
- 10.17.1 Amendment to Amended and Restated Employment Agreement, dated as of March 6, 2017, by and between Aerie Pharmaceuticals, Inc. and Richard Rubino (incorporated by reference to Exhibit 10.17.1 to the Registrant's Annual Report on Form 10-K (File No. 001-36152) filed on March 9, 2017).
- 10.18 Employment Agreement, dated as of December 18, 2013, between Aerie Pharmaceuticals, Inc. and Casey Kopczynski (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on December 20, 2013).
- 10.18.1 Amendment to Employment Agreement, dated as of March 6, 2017, by and between Aerie Pharmaceuticals, Inc. and Casey Kopczynski (incorporated by reference to Exhibit 10.18.1 to the Registrant's Annual Report on Form 10-K (File No. 001-36152) filed on March 9, 2017).
- 10.19 Aerie Pharmaceuticals, Inc. Second Amended & Restated Inducement Award Plan (incorporated by reference to Exhibit 4.2 to the Registrant's Form S-8 Registration Statement (File No. 333-223364) filed on March 1, 2018).
- 10.20 Form of Aerie Pharmaceuticals, Inc. Inducement Award Plan Nonqualified Stock Option Agreement (incorporated by reference to Exhibit 10.20 to the Registrant's Annual Report on Form 10-K (File No. 001-36152) filed on March 9, 2017).
- 10.21 Form of Aerie Pharmaceuticals, Inc. Inducement Award Plan Restricted Stock Agreement (incorporated by reference to Exhibit 10.21 to the Registrant's Annual Report on Form 10-K (File No. 001-36152) filed on March 9, 2017).
- 10.22 Employment Agreement, dated as of January 19, 2018, by and between Aerie Pharmaceuticals, Inc. and John LaRocca (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36152) filed on May 9, 2018).
- 10.23 Credit Agreement, dated as of July 23, 2018, by and among Aerie Pharmaceuticals, Inc., Aerie Distribution, Inc., the other Loan Parties (as defined therein) party thereto from time to time, Deerfield Partners, L.P., Deerfield Special Situations Fund, L.P. and Deerfield Private Design Fund III, L.P., as lenders, and Deerfield Private Design Fund III, L.P., as agent for itself and the lenders party thereto from time to time (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on July 23, 2018).
- 10.24 Guaranty and Security Agreement, dated as of July 23, 2018, by and among Aerie Pharmaceuticals, Inc., the other Grantors and Guarantors (each as defined therein) party thereto from time to time, and Deerfield Private Design Fund III, L.P., as agent (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-36152) filed on July 23, 2018).

10.25	First Amendment to Credit Agreement, dated August 7, 2018, by and among Aerie Pharmaceuticals, Inc., the guarantors party thereto, the lenders party thereto, and Deerfield Private Design Fund III, L.P., as agent (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 10-Q (File No. 001-36152) filed on August 9, 2018).
10.26†	Contract Manufacturing Supply Agreement, dated as of December 9, 2014, by and between Bausch & Lomb Incorporated and Aerie Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 10-Q (File No. 001-36152) filed on November 7, 2018).
10.27†	First Amendment to Contract Manufacturing Supply Agreement, dated as of May 31, 2018, by and between Bausch & Lomb Incorporated, Aerie Pharmaceuticals, Inc. and Aerie Distribution Incorporated (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 10-Q (File No. 001-36152) filed on November 7, 2018).
10.28†	Second Amendment to Contract Manufacturing Supply Agreement, dated as of August 15, 2018, by and between Bausch & Lomb Incorporated, Aerie Pharmaceuticals, Inc. and Aerie Distribution Incorporated (incorporated by reference to Exhibit 10.6 to the Registrant's Current Report on Form 10-Q (File No. 001-36152) filed on November 7, 2018).
10.29†	Manufacture and Supply Agreement, dated as of January 1, 2018, by and between Cayman Chemical Company, Incorporated and Aerie Distribution, Incorporated (incorporated by reference to Exhibit 10.7 to the Registrant's Current Report on Form 10-Q (File No. 001-36152) filed on November 7, 2018).
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Annual Report on Form 10-K (File No. 001-36152) filed on March 9, 2017).
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
31.1*	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a)
31.2*	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a)
32.1***	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2***	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS**	XBRL Instance Document.
101.SCH**	XBRL Taxonomy Extension Schema Document.
101.CAL**	XBRL Taxonomy Extension Calculation Linkbase Document.
101.LAB**	XBRL Taxonomy Extension Label Linkbase Database.
101.PRE**	XBRL Taxonomy Extension Presentation Linkbase Document.
101.DEF**	XBRL Taxonomy Extension Definition Linkbase Document.

† Certain portions of this exhibit have been omitted and separately filed with the SEC pursuant to a request for confidential treatment which has been granted by the SEC.

* Filed herewith.

** Attached as Exhibit 101 to this report are the following formatted in XBRL (Extensible Business Reporting Language):

(i) Consolidated Balance Sheets at December 31, 2018 and 2017, (ii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2018, 2017 and 2016 (iii) Consolidated Statements of Stockholders' Equity for the years ended December 31, 2018, 2017 and 2016 (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2018, 2017 and 2016 and (v) Notes to Consolidated Financial Statements.

*** Furnished herewith.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AERIE PHARMACEUTICALS, INC.

Date: March 1, 2019

By: /s/ VICENTE ANIDO, JR., PH.D.
 Vicente Anido, Jr., Ph.D.
 Chief Executive Officer, Chairman of the Board

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons in the capacities and on the dates indicated.

<u>SIGNATURE</u>	<u>TITLE</u>	<u>DATE</u>
<u>/s/ VICENTE ANIDO, JR., PH.D.</u> Vicente Anido, Jr., Ph.D.	Chief Executive Officer, Chairman of the Board (Principal Executive Officer)	March 1, 2019
<u>/s/ RICHARD J. RUBINO</u> Richard J. Rubino	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 1, 2019
<u>/s/ GERALD D. CAGLE, PH.D.</u> Gerald D. Cagle, Ph.D.	Director	March 1, 2019
<u>/s/ RICHARD CROARKIN</u> Richard Croarkin	Director	March 1, 2019
<u>/s/ MECHEL M. DU TOIT</u> Mechiel M. du Toit	Director	March 1, 2019
<u>/s/ MURRAY A. GOLDBERG</u> Murray A. Goldberg	Director	March 1, 2019
<u>/s/ DAVID W. GRYSKA</u> David W. Gryska	Director	March 1, 2019
<u>/s/ BENJAMIN F. MCGRAW III, PHARM. D.</u> Benjamin F. McGraw III, Pharm. D.	Director	March 1, 2019
<u>/s/ JULIE MCHUGH</u> Julie McHugh	Director	March 1, 2019

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AERIE PHARMACEUTICALS, INC.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Aerie Pharmaceuticals, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Aerie Pharmaceuticals, Inc. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, of stockholders’ equity and of cash flows for each of the three years in the period ended December 31, 2018, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PricewaterhouseCoopers LLP

Florham Park, New Jersey

March 1, 2019

We have served as the Company's auditor since 2011.

AERIE PHARMACEUTICALS, INC.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	DECEMBER 31,	
	2018	2017
Assets		
Current assets		
Cash and cash equivalents	\$ 202,818	\$ 197,569
Short-term investments	—	52,086
Accounts receivable, net	2,715	—
Inventory	10,112	—
Prepaid expenses and other current assets	4,530	4,487
Total current assets	220,175	254,142
Property, plant and equipment, net	60,525	31,932
Other assets	4,344	4,202
Total assets	<u>\$ 285,044</u>	<u>\$ 290,276</u>
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	\$ 12,403	\$ 6,245
Accrued expenses and other current liabilities	38,381	18,939
Total current liabilities	50,784	25,184
Convertible notes, net	—	123,845
Other non-current liabilities	6,454	5,648
Total liabilities	57,238	154,677
Commitments and contingencies (Note 13)		
Stockholders' equity		
Preferred stock, \$0.001 par value; 15,000,000 shares authorized as of December 31, 2018 and December 31, 2017; None issued and outstanding	—	—
Common stock, \$0.001 par value; 150,000,000 shares authorized as of December 31, 2018 and December 31, 2017; 45,478,883 and 36,947,637 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively	45	37
Additional paid-in capital	924,180	597,318
Accumulated other comprehensive loss	—	(28)
Accumulated deficit	(696,419)	(461,728)
Total stockholders' equity	227,806	135,599
Total liabilities and stockholders' equity	<u>\$ 285,044</u>	<u>\$ 290,276</u>

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

AERIE PHARMACEUTICALS, INC.

Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	YEAR ENDED DECEMBER 31,		
	2018	2017	2016
Product revenues, net	\$ 24,181	\$ —	\$ —
Total revenues, net	24,181	—	—
Costs and expenses:			
Cost of goods sold	641	—	—
Selling, general and administrative	120,614	56,905	34,706
Pre-approval commercial manufacturing	26,545	16,710	9,772
Research and development	86,123	72,078	52,394
Total costs and expenses	233,923	145,693	96,872
Loss from operations	(209,742)	(145,693)	(96,872)
Other income (expense), net	(22,824)	(1,170)	(1,994)
Loss before income taxes	(232,566)	(146,863)	(98,866)
Income tax expense (benefit)	3	(1,758)	193
Net loss	\$ (232,569)	\$ (145,105)	\$ (99,059)
Net loss per common share—basic and diluted	\$ (5.58)	\$ (4.11)	\$ (3.40)
Weighted average number of common shares outstanding—basic and diluted	41,663,958	35,324,472	29,135,583
Net loss	\$ (232,569)	\$ (145,105)	\$ (99,059)
Unrealized gain on available-for-sale investments	28	40	111
Comprehensive loss	\$ (232,541)	\$ (145,065)	\$ (98,948)

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

AERIE PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE LOSS	ACCUMULATED DEFICIT	TOTAL
	SHARES	AMOUNT				
Balances at December 31, 2015	26,458,495	\$ 26	\$ 236,492	\$ (179)	\$ (217,564)	\$ 18,775
Issuance of common stock, net of discounts, commissions and expenses of \$5,963	6,721,529	7	167,158	—	—	167,165
Issuance of common stock upon exercise of stock purchase rights	75,205	—	1,120	—	—	1,120
Issuance of common stock upon exercise of stock options	149,186	—	591	—	—	591
Issuance of common stock for restricted stock awards, net	54,192	—	(153)	—	—	(153)
Stock-based compensation	—	—	16,794	—	—	16,794
Other comprehensive income	—	—	—	111	—	111
Net loss	—	—	—	—	(99,059)	(99,059)
Balances at December 31, 2016	33,458,607	33	422,002	(68)	(316,623)	105,344
Issuance of common stock, net of discounts, commissions and expenses of \$3,458	2,506,387	2	133,810	—	—	133,812
Issuance of common stock upon exercise of stock purchase rights	27,953	—	1,050	—	—	1,050
Issuance of common stock upon exercise of stock options	201,592	1	827	—	—	828
Issuance of common stock for restricted stock awards, net	489,952	1	(751)	—	—	(750)
Shares issued for asset acquisition	263,146	—	14,302	—	—	14,302
Stock-based compensation	—	—	26,078	—	—	26,078
Other comprehensive income	—	—	—	40	—	40
Net loss	—	—	—	—	(145,105)	(145,105)
Balances at December 31, 2017	36,947,637	37	597,318	(28)	(461,728)	135,599
Cumulative effect adjustment from adoption of ASU 2016-16	—	—	—	—	(2,122)	(2,122)
Issuance of common stock, net of commissions and expenses of \$1,345	2,313,824	2	136,443	—	—	136,445
Issuance of common stock upon exercise of stock purchase rights	34,193	—	1,401	—	—	1,401
Issuance of common stock upon exercise of stock options and warrants	597,777	1	4,250	—	—	4,251
Issuance of common stock for restricted stock awards, net	216,005	—	(2,172)	—	—	(2,172)
Issuance of shares upon conversion of 2014 Convertible Notes	5,369,447	5	148,078	—	—	148,083
Stock-based compensation	—	—	38,862	—	—	38,862
Other comprehensive income	—	—	—	28	—	28
Net loss	—	—	—	—	(232,569)	(232,569)
Balances at December 31, 2018	45,478,883	\$ 45	\$ 924,180	\$ —	\$ (696,419)	\$ 227,806

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

AERIE PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

(in thousands)

	YEAR ENDED DECEMBER 31,		
	2018	2017	2016
Cash flows from operating activities			
Net loss	\$ (232,569)	\$ (145,105)	\$ (99,059)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation	2,442	1,410	970
Amortization of debt issuance costs and fees	1,577	306	303
Amortization and accretion of premium or discount on investments, net	69	9	525
Acquisition of assets expensed to research and development	—	24,802	—
Stock-based compensation	38,728	26,078	16,794
Induced conversion of convertible notes	24,059	—	—
Unrealized foreign exchange (gain) loss	(270)	601	—
Changes in operating assets and liabilities			
Accounts receivable, net	(2,715)	—	—
Inventory	(9,689)	—	—
Prepaid, current and other assets	(791)	(2,239)	(1,852)
Accounts payable, accrued expenses and other current liabilities	26,583	925	2,479
Net cash used in operating activities	<u>(152,576)</u>	<u>(93,213)</u>	<u>(79,840)</u>
Cash flows from investing activities			
Acquisition of assets from Envisia	—	(10,500)	—
Purchase of available-for-sale investments	(56,195)	(104,490)	(35,169)
Proceeds from sales and maturities of investments	108,297	88,153	58,346
Purchase of property, plant and equipment	(31,313)	(15,970)	(5,077)
Net cash provided by (used in) investing activities	<u>20,789</u>	<u>(42,807)</u>	<u>18,100</u>
Cash flows from financing activities			
Proceeds from sale of common stock, net	135,972	134,215	167,383
Proceeds related to issuance of stock for stock-based compensation arrangements, net	3,630	1,429	1,242
Payments of debt issuance costs	(1,883)	—	—
Other financing	(683)	—	—
Net cash provided by financing activities	<u>137,036</u>	<u>135,644</u>	<u>168,625</u>
Net change in cash and cash equivalents	<u>5,249</u>	<u>(376)</u>	<u>106,885</u>
Cash and cash equivalents, at beginning of period	<u>197,569</u>	<u>197,945</u>	<u>91,060</u>
Cash and cash equivalents, at end of period	<u>\$ 202,818</u>	<u>\$ 197,569</u>	<u>\$ 197,945</u>
Supplemental disclosures			
Cash paid for interest	\$ 1,774	\$ 2,188	\$ 2,192
Cash paid for income taxes	\$ —	\$ —	\$ 1,790
Non-cash investing and financing activities:			
Conversion of convertible notes to common stock (Note 9)	\$ 148,078	\$ —	\$ —
Equity issued for Envisia Asset Acquisition	\$ —	\$ 14,302	\$ —
Purchases of property, plant and equipment	\$ 3,526	\$ 4,176	\$ 482
Acquisition of capital lease obligation	\$ —	\$ 689	\$ —
Deferred costs from the sale of common stock	\$ —	\$ 403	\$ 70
Build-to-suit lease transaction (Note 7)			

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

AERIE PHARMACEUTICALS, INC.

Notes to the Consolidated Financial Statements

1. The Company

Aerie Pharmaceuticals, Inc. (“Aerie”), with its wholly-owned subsidiaries, Aerie Distribution, Inc., Aerie Pharmaceuticals Limited and Aerie Pharmaceuticals Ireland Limited (“Aerie Distribution,” “Aerie Limited” and “Aerie Ireland Limited,” respectively, together with Aerie, the “Company”), is an ophthalmic pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with open-angle glaucoma, retinal diseases and other diseases of the eye. The Company has its principal executive offices in Durham, North Carolina, and operates as one business segment.

The Company has a U.S. Food and Drug Administration (“FDA”) approved product, Rhopressa[®] (netarsudil ophthalmic solution) 0.02% (“Rhopressa[®]”), and an advanced-stage product candidate, Rocklatan[™] (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% (“Rocklatan[™]”), previously referred to as Roclatan[™], both designed to reduce elevated intraocular pressure (“IOP”) in patients with open-angle glaucoma or ocular hypertension. The Company is commercializing Rhopressa[®] and intends to commercialize Rocklatan[™], if approved, on its own in North American markets. The Company’s strategy also includes pursuing regulatory approval for Rhopressa[®] and Rocklatan[™] in Europe and Japan on its own, though the products may be named differently in those respective regions.

Rhopressa[®] is a once-daily eye drop designed to reduce elevated IOP in patients with open-angle glaucoma or ocular hypertension that received FDA approval on December 18, 2017. The Company launched Rhopressa[®] in the United States at the end of April 2018. On October 9, 2018, the Company announced that the European Medicines Agency (“EMA”) accepted for review the marketing authorization application (“MAA”) for Rhopressa[®], which will be marketed under the name Rhokiinsa[®] in Europe, if approved. Additionally, the Company has completed a Phase 1 clinical trial and a successful pilot Phase 2 clinical study in the United States on Japanese and Japanese-American subjects, which were designed to support meeting the requirements of Japan’s Pharmaceuticals and Medical Devices Agency for potential regulatory submission of Rhopressa[®] in Japan. The Company is also planning to initiate a Phase 2 clinical trial on Japanese patients in Japan by the end of the first quarter of 2019 to support subsequent Phase 3 registration trials that are also expected to be conducted in Japan under its direction.

The Company’s advanced-stage product candidate, Rocklatan[™], is a once-daily fixed-dose combination of Rhopressa[®] and latanoprost. The Company submitted a New Drug Application (“NDA”) to the FDA in May 2018. In July 2018, the Company announced that the NDA was accepted for review by the FDA and the Prescription Drug User Fee Act goal date was set for March 14, 2019, which represents a ten-month review. In Europe, the Company is currently conducting a Phase 3 trial, named Mercury 3, comparing Rocklatan[™] to Ganfort[®], a fixed-dose combination product marketed in Europe of bimatoprost (a prostaglandin analog) and timolol (a beta blocker). If successful, Mercury 3 is expected to improve its commercialization prospects in Europe. Mercury 3 is not necessary for approval in the United States. The Company plans to submit an MAA with the EMA in early 2020 for Rocklatan[™], if the EMA has approved Rhokiinsa[®] by such time. Rocklatan[™] will be marketed under the name Roclanda[™] in Europe, if approved.

The Company is also focused on furthering the development of its preclinical molecules and technologies focused on retinal diseases, particularly AR-13503 and AR-1105. Through business development activities, discussed further below, the Company has acquired worldwide ophthalmic rights to a bio-erodible polymer technology from DSM, a global science-based company headquartered in the Netherlands, and PRINT[®] implant manufacturing technology from Envisia Therapeutics Inc. (“Envisia”), with which the Company has created a sustained-release ophthalmology platform. Using this technology, the Company is currently developing two preclinical sustained-release implants, AR-13503 and AR-1105, both of which are expected to commence clinical trials in 2019.

In July 2017, the Company entered into a collaborative research, development and licensing agreement with DSM, which included an option to license DSM’s bio-erodible polymer implant technology for sustained delivery of certain Aerie compounds to treat ophthalmic diseases. This technology uses polyesteramide polymers to produce an injectable, thin fiber that is minute in size.

On August 1, 2018, the Company entered into an Amended and Restated Collaborative Research, Development, and License Agreement with DSM (the “Collaboration Agreement”), which provides for (i) a worldwide exclusive license for all ophthalmic indications to DSM’s polyesteramide polymer technology, (ii) continuation of the collaborative research initiatives through the end of 2020, including the transfer of DSM’s formulation technology to Aerie during that time and (iii) access to a

preclinical latanoprost implant. Aerie paid \$6.0 million to DSM upon execution of the Collaboration Agreement, with an additional \$9.0 million payable to DSM through the end of 2020. As a result, \$9.6 million related to the expanded collaboration agreement with DSM was expensed to research and development expense during the year ended December 31, 2018, which included the upfront payment of \$6.0 million. The Collaboration Agreement includes contingent payments of up to \$75.0 million that may be due to DSM upon the achievement of certain development and regulatory milestones. In addition, pursuant to the Collaboration Agreement, a \$3.0 million milestone payment was made during the year ended December 31, 2018 upon the completion of certain manufacturing technology transfer activities. Aerie would also pay royalties to DSM when products are commercialized under this Collaboration Agreement, if any.

In October 2017, the Company entered into an Asset Purchase Agreement (the “Agreement”) with Envisia to acquire the rights to use PRINT[®] technology in ophthalmology, as well as rights relating to a preclinical dexamethasone steroid implant for the potential treatment of retinal vein occlusion and diabetic macular edema that utilizes the PRINT[®] technology, referred to as AR-1105. Under the terms of the Agreement, the Company (a) made an upfront cash payment of \$10.5 million and issued 263,146 shares of Aerie’s common stock valued at approximately \$14.3 million and (b) agreed to make potential milestone payments of up to an aggregate of \$45.0 million, contingent upon the achievement of certain product regulatory approvals. Under the provisions of Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Topic 805: *Business Combinations* (“ASC Topic 805”), including the provisions of Accounting Standards Update (“ASU”) 2017-01 (see Note 2), the Company accounted for the transaction as an asset acquisition rather than a business combination, and expensed \$24.8 million of acquired in-process research and development (“IPR&D”) to research and development in the consolidated statement of operations and comprehensive loss during the three months ended December 31, 2017. In addition, any milestone payments will be recognized only once the contingency is resolved and such amounts are payable.

The Company launched Rhopressa[®] in the United States in April 2018 and commenced generating product revenues in the second quarter of 2018. The Company’s activities prior to the commercial launch of Rhopressa[®] had primarily consisted of developing product candidates, raising capital and performing research and development activities. The Company has incurred losses and experienced negative operating cash flows since inception. The Company had previously funded its operations primarily through the sale of equity securities (Note 11) and issuance of convertible notes (Note 9) prior to generating product revenues.

If the Company does not successfully commercialize Rhopressa[®], Rocklatan[™] or any future product candidates, it may be unable to achieve profitability. Accordingly, the Company may be required to draw down on the \$100 million senior secured delayed draw term loan facility (the “credit facility”) that was entered into in July 2018, or to obtain further funding through public or private debt or equity offerings, or other arrangements. Adequate additional funding may not be available to the Company on acceptable terms, or at all. If the Company is unable to raise capital when needed or on acceptable terms, it may be forced to delay, reduce or eliminate its research and development programs or commercialization and manufacturing efforts.

2. Significant Accounting Policies

Basis of Presentation and Consolidation

The Company’s consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“U.S. GAAP”). The consolidated financial statements include the accounts of Aerie and its wholly-owned subsidiaries. All intercompany accounts, transactions and profits have been eliminated in consolidation. Certain reclassifications have been made to prior year amounts to conform to the current year presentation.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of income and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, inventories, accrued expenses, fair value measurements, acquisitions and stock-based compensation. Actual results could differ from the Company’s estimates.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business as one operating segment.

Concentration of Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist of cash, cash equivalents and investments. The Company's cash and cash equivalents, which include short-term highly liquid investments with original maturities of three months or less, are held at several financial institutions and at times may exceed insured limits. The Company has placed these funds in high quality institutions to minimize risk relating to exceeding insured limits. The Company's investment policy permits investments in U.S. federal government and federal agency securities, corporate bonds or commercial paper, money market instruments, and certain qualifying money market mutual funds, and places restrictions on credit ratings, maturities, and concentration by type and issuer. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash, cash equivalents and investments to the extent recorded on the consolidated balance sheet.

The Company relies on its third-party manufacturers to produce the active pharmaceutical ingredient ("API") and final drug product for Rhopressa[®] and Rocklatan[™] and may rely on third-party manufacturers for its current and future product candidates. The Company is in the process of adding an additional API contract manufacturer and an additional Rhopressa[®] drug product contract manufacturer, both of which are expected to begin to supply commercial materials in the first half of 2019. In addition, the Company is in the process of establishing its own manufacturing plant in Athlone, Ireland, for future commercial production of Rhopressa[®] and, if approved, Rocklatan[™], Rhokiinsa[®] and Roclanda[™]. Commercial supply from the plant is expected to be available in early 2020.

Cash Equivalents

The Company's cash and cash equivalents are held principally at several financial institutions and at times may exceed insured limits. The Company has placed these funds in high quality institutions in order to minimize risk relating to exceeding insured limits.

Inventories

Prior to the date the Company obtains regulatory approval for its product candidates, manufacturing costs related to commercial production are expensed as pre-approval commercial manufacturing expense. Once regulatory approval is obtained, the Company capitalizes such costs as inventory. Inventories are stated at the lower of cost or net realizable value. The Company determines the cost of inventory using the first-in, first-out ("FIFO") method. The Company analyzes its inventory levels at least quarterly and writes down inventory that is expected to expire prior to being sold, inventory in excess of expected sales requirements and inventory that fails to meet commercial sale specifications, with a corresponding charge to cost of goods sold. The determination of whether inventory costs will be realizable requires estimates by management of future expected inventory requirements based on sales forecasts. If actual net realizable value is less than the estimated amount or if actual market conditions are less favorable than the Company's projections, additional inventory write-downs may be required. Charges for inventory write-downs are not reversed if it is later determined that the product is saleable.

Property, Plant and Equipment, Net

Property, plant and equipment is recorded at historical cost. Depreciation is calculated using the straight-line method over the estimated useful lives of the related assets. Construction-in-progress reflects amounts incurred for property, plant or equipment construction or improvements that have not been yet placed in service and are not depreciated or amortized, which primarily relates to the build-out of the Company's manufacturing plant in Ireland. Repairs and maintenance are expensed when incurred. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are removed from the accounts, and any resulting gain or loss is included in the determination of net loss.

Estimated useful lives by major asset category are as follows:

Manufacturing equipment	10 years
Laboratory equipment	7 years
Furniture and fixtures	5 years
Software, computer and other equipment	3 years
Leasehold improvements	Lower of estimated useful life or term of lease

Impairment of Long-Lived Assets

The Company reviews its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by a comparison of the carrying amount of an asset or asset group to estimated undiscounted future cash flows expected to be generated by the asset or asset group. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized for the amount by which the carrying amount of the asset exceeds the fair value of the asset. For the years ended December 31, 2018, 2017 and 2016, no such impairment losses have been recorded by the Company.

Acquisitions

The Company evaluates acquisitions to determine whether the acquisition is a business combination or an acquisition of assets under ASC Topic 805. Business combinations are accounted for using the acquisition method of accounting, whereby assets acquired and liabilities assumed are recorded as of the acquisition date at their respective fair values and excess of the fair value of the consideration transferred over the fair value of the net assets acquired is recorded as goodwill. In an asset acquisition that does not constitute a business, no goodwill is recognized, and the net assets acquired are generally recorded at cost. Significant judgment is required in estimating the fair value of intangible assets and in a determination of whether an acquisition is a business combination or an acquisition of assets. The fair value estimates are based on available historical information and on future expectations and assumptions deemed reasonable by management, but are inherently uncertain.

The consolidated financial statements as of and for the year ended December 31, 2017 include the impact of the acquisition of assets from Envisia (see Note 1 for additional information).

Revenue Recognition

Effective January 1, 2018, the Company adopted Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Topic 606, Revenue from Contracts with Customers (“ASC Topic 606”). The Company did not generate any revenue prior to the three months ended June 30, 2018, and therefore the adoption of ASC Topic 606 did not have an impact on the Company’s financial statements for any prior periods or upon adoption. In accordance with ASC Topic 606, the Company recognizes revenue when the customer obtains control of a promised good or service, in an amount that reflects the consideration that the Company expects to receive in exchange for the good or service. The reported results for the year ended December 31, 2018 reflect the application of ASC Topic 606.

The Company’s net product revenues are generated through sales of Rhopressa[®], which was approved by the FDA in December 2017 and was commercially launched in the United States on April 30, 2018. See Note 3 for additional information.

Research and Development Costs

Research and development costs are charged to expense as incurred and include, but are not limited to:

- employee-related expenses including salaries, benefits, travel and stock-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations (“CROs”), contract manufacturing organizations and service providers that assist in conducting clinical and preclinical studies;
- costs associated with any collaboration arrangements, licenses or acquisitions of preclinical molecules, product candidates or technologies;
- costs associated with preclinical activities and development activities;
- costs associated with regulatory operations; and

- depreciation expense for assets used in research and development activities.

Costs for certain development activities, such as clinical studies, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the consolidated financial statements as prepaid expenses or accrued expenses as deemed appropriate. No material adjustments to these estimates have been recorded in these consolidated financial statements.

Research and development costs also include the cost of IPR&D projects acquired as part of an asset acquisition that have no alternative future use. Milestone payments due to third parties in connection with research and development activities prior to regulatory approval are expensed as incurred, while milestone payments due to third parties upon, or subsequent to, regulatory approval are capitalized and amortized over the estimate useful life.

Stock-Based Compensation

Stock-based compensation for awards granted to employees and non-employees is measured at grant date, based on the estimated fair value of the award. The Company estimates the fair value of options to purchase common stock and stock appreciation rights (“SARs”) using a Black-Scholes option pricing model. The Black-Scholes option pricing model utilizes assumptions including expected term, volatility, a risk-free interest rate and an expected dividend yield. The Company utilized the guidance set forth in the Securities and Exchange Commission (“SEC”) Staff Accounting Bulletin 107, *Share-Based Payment* (“SAB 107”), to determine the expected term of options, as it does not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. The simplified method utilizes the midpoint between the vesting date and the maximum contractual expiration date as the expected term. Volatility is based on the historical volatility of the Company as well as several public entities that are similar to the Company. The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected term. The Company uses an expected dividend yield of zero as it does not expect to pay cash dividends for the foreseeable future. Upon issuance and at each reporting period, the fair value of each SARs award is estimated using the Black-Scholes option pricing model and is marked to market through stock-based compensation expense. SARs are liability-based awards as they may only be settled in cash.

The fair value of restricted stock awards (“RSAs”), including restricted stock awards with non-market performance and service conditions (“PSAs”) is determined based on the fair value of Aerie’s common stock on the date of grant. Compensation expense related to RSAs is recognized ratably over the vesting period. As the PSAs have multiple performance conditions, compensation expense is recognized for each vesting tranche over the respective requisite service period of each tranche if and when the Company’s management deems it probable that the performance conditions will be satisfied. Stock-based compensation related to stock options, RSAs and PSAs is expensed on a straight-line basis over the relevant vesting period, although the Company may recognize a cumulative true-up adjustment related to PSAs once a condition becomes probable of being satisfied if the related service period had commenced in a prior period. All stock-based compensation expense is recorded between selling, general and administrative, pre-approval commercial manufacturing and research and development costs in the consolidated statements of operations and comprehensive loss based upon the underlying employees’ roles within the Company. The Company accounts for forfeitures as they occur.

Investments

The Company determines the appropriate classification of its investments in debt and equity securities at the time of purchase. The Company’s investments are comprised of certificates of deposit, commercial paper, corporate bonds and government agency securities that are classified as available-for-sale in accordance with ASC Topic 320, *Investments—Debt and Equity Securities*. The Company classifies investments available to fund current operations as current assets on its consolidated balance sheets. Investments are classified as long-term assets on the consolidated balance sheets if (i) the Company has the intent and ability to hold the investments for a period of at least one year and (ii) the contractual maturity date of the investments is greater than one year.

Available-for-sale investments in debt securities are recorded at fair value, with unrealized gains or losses included in comprehensive loss on the consolidated statements of operations and comprehensive loss and in accumulated other comprehensive loss on the consolidated balance sheets. Realized gains and losses, interest income earned on the Company’s cash, cash equivalents and investments, and amortization or accretion of discounts and premiums on investments are included within other income (expense), net. Interest income was \$3.4 million, \$1.8 million and \$0.6 million for the years ended December 31, 2018, 2017 and 2016, respectively. Realized gains and losses are determined using the specific

identification method and are included as a component of other income (expense), net. Realized gains or losses were immaterial for the years ended December 31, 2018, 2017 and 2016.

The Company reviews investments in debt securities for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. The Company did not recognize any impairments on its investments during the years ended December 31, 2018, 2017 or 2016.

Fair Value Measurements

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

- Level 1—Unadjusted quoted prices in active, accessible markets for identical assets or liabilities.
- Level 2—Other inputs that are directly or indirectly observable in the marketplace.
- Level 3—Unobservable inputs that are supported by little or no market activity.

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

There were no transfers between the different levels of the fair value hierarchy in 2018 or in 2017.

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive loss. Other comprehensive loss includes changes in stockholders' equity that are excluded from net income (loss), specifically changes in unrealized gains and losses on the Company's available-for-sale securities.

Income Taxes

Deferred tax assets or liabilities are recorded for temporary differences between financial statement and tax basis of assets and liabilities, using enacted rates in effect for the year in which the differences are expected to reverse. A valuation allowance is recorded if it is more likely than not that a deferred tax asset will not be realized. The Company has provided a full valuation allowance on its deferred tax assets that consist of federal and state net operating losses ("NOLs"), stock-based compensation and tax credits as of December 31, 2018 and 2017 (Note 10). The Company reduced its valuation allowance during the year ended December 31, 2017 for federal alternative minimum tax ("AMT") credit carryforwards that became fully refundable under the Tax Act (defined herein). See Note 10 for additional information.

The Company recognizes the impact of an uncertain tax position in the consolidated financial statements only if it is more likely than not that the tax position will be sustained upon examination by the taxing authorities. The Company's policy is to record interest and penalties on uncertain tax positions as income tax expense. The Company did not recognize interest or penalties on uncertain tax positions for the years ended December 31, 2018, 2017 or 2016. As of December 31, 2018 and 2017, the Company had no uncertain tax positions.

Adoption of New Accounting Standards

In August 2018, the FASB issued Accounting Standards Update ("ASU") 2018-15, *Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, which amends ASC 350-40, *Internal-Use Software*, to include in its scope implementation costs of a cloud computing arrangement that is a service contract. Consequently, the accounting for costs incurred to implement a cloud computing arrangement that is a service arrangement, is aligned with the guidance on capitalizing costs associated with developing or obtaining internal-use software. This ASU is effective for the Company beginning January 1, 2019 and early adoption is permitted. The Company elected to early adopt this standard during the third quarter of 2018, which did not have a material impact on its consolidated financial statements and disclosures.

In March 2018, the FASB issued ASU 2018-05, *Income Taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118* (“SAB 118”) (“ASU 2018-05”), which adds guidance to clarify the treatment of income taxes based on changes enacted in December 2017 in H.R. 1 (referred to herein as the “Tax Act”). ASU 2018-05 incorporates references in ASC Topic 740 to SAB 118, which was issued in December 2017, to address the application of U.S. GAAP in situations when a registrant may not have the necessary information available in reasonable detail to complete the accounting for certain income tax effects. The guidance became effective immediately upon the enactment of the Tax Act in accordance with U.S. GAAP which requires deferred tax assets and liabilities to be revalued during the period in which new tax legislation is enacted. The Company’s final impact assessment on the consolidated financial statements did not materially change from its initial estimates.

In May 2017, the FASB issued ASU 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting* (“ASU 2017-09”), which clarifies when changes to the terms or conditions of share-based payment awards must be accounted for as modifications. Under ASU 2017-09, an entity will not apply modification accounting to a share-based payment award if the award’s fair value, vesting conditions and classification as an equity or liability instrument are the same immediately before and after the change. ASU 2017-09 will be applied prospectively to awards modified on or after the adoption date. The guidance became effective for the Company beginning on January 1, 2018. The impact of the adoption of this guidance on its consolidated financial statements would be dependent on future modifications to share-based payment awards, if any.

In October 2016, the FASB issued ASU 2016-16, *Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory* (“ASU 2016-16”), which eliminates the exception to the principle in ASC Topic 740, *Income Taxes*, that generally requires comprehensive recognition of current and deferred income taxes for all intra-entity sales of assets other than inventory. As a result, a reporting entity would recognize the tax expense from the sale of the asset in the seller’s tax jurisdiction when the transfer occurs, even though the pre-tax effects of that transaction are eliminated in consolidation. This ASU became effective for the Company on January 1, 2018 and was required to be applied on a modified retrospective basis through a cumulative-effect adjustment directly to accumulated deficit as of the beginning of the period of adoption. At December 31, 2017, the Company had \$2.1 million of income tax effects deferred from past intercompany transactions that were recorded as prepaid assets within other assets, net, at December 31, 2017 that were adjusted through accumulated deficit as of January 1, 2018.

In January 2016, the FASB issued ASU 2016-01, *Financial Instruments-Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities* (“ASU 2016-01”), which provides guidance related to the accounting for equity investments, financial liabilities under the fair value option and the presentation and disclosure requirements for financial instruments. The guidance became effective for the Company beginning on January 1, 2018 and prescribes different transition methods for the various provisions. The adoption of ASU 2016-01 did not have a material impact on its consolidated financial statements and disclosures.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)* (“ASU 2014-09”). The standard states that an entity should recognize revenue based on the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The FASB subsequently issued amendments to ASU 2014-09 that had the same effective date of January 1, 2018. The Company did not generate any revenue prior to the three months ended June 30, 2018, and therefore the adoption of ASC Topic 606 did not have an impact on the Company’s financial statements for any prior periods or upon adoption. Revenue from sales of Rhopressa[®], as well as any other future revenue arrangements, are and will be recognized under the provisions of ASC Topic 606.

In January 2017, the FASB issued ASU 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business*. The new standard clarifies the definition of a business and provides a screen to determine when an integrated set of assets and activities is not a business. The screen requires that when substantially all of the fair value of the gross assets acquired, or disposed of, is concentrated in a single identifiable asset or a group of similar identifiable assets, the set is not a business. The new standard was effective for the Company beginning on January 1, 2018; however, Aerie elected to early adopt this standard as of July 1, 2017. Under this guidance, the October 4, 2017 transaction to acquire assets from Envisia was determined to meet the criteria of an asset acquisition rather than a business combination resulting in a \$24.8 million charge to research and development expense on the consolidated statement of operations and comprehensive loss in the three months ended December 31, 2017. See Note 1 for additional information.

Recently Issued Accounting Standards

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820-10): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* (“ASU 2018-13”), which changes the fair value measurement disclosure requirements of ASC Topic 820, *Fair Value Measurements and Disclosures*. Under this ASU, certain disclosure

requirements for fair value measurements are eliminated, amended or added. These changes aim to improve the overall usefulness of disclosures to financial statement users and reduce unnecessary costs to companies when preparing the disclosures. The guidance is effective for the Company beginning on January 1, 2020 and prescribes different transition methods for the various provisions. The Company does not expect the adoption of ASU 2018-13 to have a material impact on its consolidated financial statements and disclosures.

In June 2018, the FASB issued ASU 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* (“ASU 2018-07”), which expands the scope of ASC Topic 718, *Compensation-Stock Compensation* to include share-based payments issued to non-employees for goods or services. Consequently, the accounting for share-based payments to non-employees and employees will be substantially aligned. This ASU is effective for the Company beginning January 1, 2019, including interim periods within that fiscal year, but early adoption is permitted. The Company does not expect the adoption of ASU 2018-07 to have a material impact on its consolidated financial statements and disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”), which requires that financial assets measured at amortized cost be presented at the net amount expected to be collected. Currently, U.S. GAAP delays recognition of the full amount of credit losses until the loss is probable of occurring. Under this ASU, the income statement will reflect an entity’s current estimate of all expected credit losses. The measurement of expected credit losses will be based upon historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount. Credit losses relating to available-for-sale debt securities will be recorded through an allowance for credit losses rather than as a direct write-down of the security. In November 2018, the FASB issued ASU No. 2018-19, *Codification Improvements to Topic 326, Financial Instruments—Credit Losses* (“ASU 2018-19”), which clarifies that receivables from operating leases are accounted for using the lease guidance and not as financial instruments. The guidance is effective for the Company beginning on January 1, 2020, with early adoption permitted beginning on January 1, 2019. The new guidance prescribes different transition methods for the various provisions. The Company does not expect the adoption of ASU 2016-13 or ASU 2018-19 to have a material impact on its consolidated financial statements and disclosures.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)* (“ASU 2016-02”), which requires lessees to recognize a right of use asset and related lease liability for those leases classified as operating leases at the commencement date and for those leases that have lease terms of more than 12 months. In July 2018, the FASB issued both ASU 2018-10, *Codification Improvements to Topic 842, Leases* (“ASU 2018-10”) and ASU 2018-11, *Leases (Topic 842)-Targeted Improvements* (“ASU 2018-11”), which provides additional guidance or clarifications affecting certain aspects of ASU 2016-02 and certain practical expedients. Further, the updated guidance allows an additional transition method to apply the new leases standard at the adoption date, as compared to the beginning of the earliest period presented, and recognize a cumulative-effect adjustment to the beginning balance of retained earnings in the period of adoption. ASU 2016-02, ASU 2018-10 and ASU 2018-11 were effective for the Company beginning on January 1, 2019, and all annual and interim periods thereafter. The Company has elected the transition method described in ASU 2018-11 at the adoption date of January 1, 2019. The Company is currently finalizing its evaluation of the impact of ASU 2016-02, ASU 2018-10 and ASU 2018-11 on its consolidated financial statements and disclosures related to its existing operating leases and a lease space for which the Company has historically applied build-to-suit accounting. The Company will recognize a right of use asset and corresponding lease liability related to its operating leases as of the date of adoption. The Company is also in process of finalizing its processes and internal controls required to comply with the new lease accounting and disclosure requirements set by the new standard on an ongoing basis.

Net Loss per Common Share

Basic net loss per common share (“Basic EPS”) is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration for potentially dilutive securities with the exception of warrants for common stock with a \$0.05 exercise price, which are exercisable for nominal consideration and are therefore included in the calculation of the weighted-average number of shares of common stock as common stock equivalents. Diluted net loss per share (“Diluted EPS”) gives effect to all dilutive potential shares of common stock outstanding during this period. For Diluted EPS, net loss used in calculating Basic EPS may be adjusted for certain items related to the dilutive securities.

For all periods presented, Aerie’s potential common stock equivalents have been excluded from the computation of Diluted EPS as their inclusion would have had an anti-dilutive effect.

The potential common stock equivalents that have been excluded from the computation of Diluted EPS consist of the following:

	DECEMBER 31,		
	2018	2017	2016
2014 Convertible Notes	—	5,040,323	5,040,323
Outstanding stock options	6,935,119	6,457,343	5,255,930
Stock purchase warrants	154,500	157,500	157,500
Nonvested restricted stock awards	572,706	447,049	164,194

3. Revenue Recognition

In accordance with ASC Topic 606, the Company recognizes revenues when its customers obtain control of its product in an amount that reflects the consideration it expects to receive from its customers in exchange for that product. To determine revenue recognition for contracts that are determined to be in scope of ASC Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies the performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. Once the contract is determined to be within the scope of ASC Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when such performance obligation is satisfied. Shipping and handling costs related to the Company's product sales are included in selling, general and administrative expenses.

Net product revenues for the year ended December 31, 2018 were derived from sales of Rhopressa[®] in the United States to customers, which include a limited number of national and select regional wholesalers (the "Distributors"). These Distributors subsequently resell the product, primarily to retail pharmacies that dispense the product to patients. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that would have been recognized is one year or less or the amount is immaterial. The product that is ultimately used by patients is generally covered by third-party payers, such as government or private healthcare insurers and pharmacy benefit managers ("Third-party Payers") and may be subject to rebates and discounts payable directly to those Third-party Payers.

Product revenue is recorded net of trade discounts, allowances, rebates, chargebacks, estimated returns and other incentives, discussed below. These reserves are classified as either reductions of accounts receivable or as current liabilities. Amounts billed or invoiced are included in accounts receivable, net on the consolidated balance sheet. The Company did not have any contract assets (unbilled receivables) at December 31, 2018, as customer invoicing generally occurs before or at the time of revenue recognition. The Company did not have any contract liabilities at December 31, 2018, as the Company did not receive payments in advance of fulfilling its performance obligations to its customers.

Net product revenue is typically recognized when Distributors obtain control of the Company's product, which occurs at a point in time, typically upon delivery of Rhopressa[®] to the Distributors. For the year ended December 31, 2018, three Distributors accounted for 33.9%, 33.3% and 29.7% of total revenues, respectively. The Company evaluates the creditworthiness of each of its Distributors to determine whether it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur. The Company does not assess whether a contract has a significant financing component if the expectation is such that the period between the transfer of the promised goods to the customer and the receipt of payment will be less than one year. Standard credit terms do not exceed 75 days.

The Company calculates its net product revenue based on the wholesale acquisition cost that the Company charges its Distributors for Rhopressa[®] less provisions for (i) trade discounts and allowances, such as discounts for prompt payment and Distributor fees, (ii) estimated rebates to Third-party Payers, estimated payments for Medicare Part D prescription drug program coverage gap (commonly called the "donut hole"), patient co-pay program coupon utilization, chargebacks and other discount programs and (iii) reserves for expected product returns. The estimates of reserves established for variable consideration reflect current contractual and statutory requirements, known market events and trends, industry data and forecasted customer mix. Provisions for revenue reserves reduced product revenues by \$19.6 million in aggregate for the year ended December 31, 2018. The transaction price may be subject to constraint and is included in the net product revenues only to the extent that it is probable that a significant reversal of the amount of the cumulative revenues recognized will not occur in a future period. Actual amounts may ultimately differ from these estimates. If actual results vary, estimates may be adjusted in the period such change in estimate becomes known, which could have an impact on earnings in the period of adjustment.

Trade Discounts and Allowances: The Company generally provides discounts on sales of Rhopressa[®] to its Distributors for prompt payment and pays fees for distribution services and for certain data that Distributors provide to the Company. The Company expects its Distributors to earn these discounts and fees, and accordingly deducts the full amount of these discounts and fees from its gross product revenues at the time such revenues are recognized.

Rebates, Chargebacks and Other Discounts: The Company contracts with Third-party Payers for coverage and reimbursement of Rhopressa[®]. The Company estimates the rebates and chargebacks it expects to be obligated to provide to Third-party Payers and deducts these estimated amounts from its gross product revenue at the time the revenue is recognized. The Company estimates the rebates and chargebacks that it expects to be obligated to provide to Third-party Payers based upon (i) the Company's contracts and negotiations with these Third-party Payers, (ii) estimates regarding the payer mix for Rhopressa[®] and (iii) historical industry information regarding the payer mix for comparable pharmaceutical products and product portfolios. Other discounts include the Company's co-pay assistance coupon programs for commercially-insured patients meeting certain eligibility requirements. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to pay associated with product that has been recognized as revenue.

Product Returns: The Company estimates the amount of Rhopressa[®] that will be returned and deducts these estimated amounts from its gross revenue at the time the revenue is recognized. The Company currently estimates product returns based on historical industry information regarding rates for comparable pharmaceutical products and product portfolios, the estimated remaining shelf life of Rhopressa[®] shipped to Distributors, and contractual agreements with the Company's Distributors intended to limit the amount of inventory they maintain. Reporting from the Distributors includes Distributor sales and inventory held by Distributors, which provides the Company with visibility into the distribution channel to determine when product would be eligible to be returned.

4. Investments

Cash and cash equivalents as of December 31, 2018 included the following:

(in thousands)	AMORTIZED COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	FAIR VALUE
Cash and cash equivalents:				
Cash and money market funds	\$ 202,818	\$ —	\$ —	\$ 202,818
Total cash and cash equivalents	<u>\$ 202,818</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 202,818</u>

Cash, cash equivalents and investments as of December 31, 2017 included the following:

(in thousands)	AMORTIZED COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	FAIR VALUE
Cash and cash equivalents:				
Cash and money market funds	\$ 197,569	\$ —	\$ —	\$ 197,569
Total cash and cash equivalents	<u>\$ 197,569</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 197,569</u>
Investments:				
Commercial paper	\$ 30,883	\$ —	\$ —	\$ 30,883
Corporate bonds	21,231	—	(28)	21,203
Total investments	<u>\$ 52,114</u>	<u>\$ —</u>	<u>\$ (28)</u>	<u>\$ 52,086</u>
Total cash, cash equivalents and investments	<u>\$ 249,683</u>	<u>\$ —</u>	<u>\$ (28)</u>	<u>\$ 249,655</u>

5. Fair Value Measurements

The following tables summarize the fair value of financial assets and liabilities that are measured at fair value and the classification by level of input within the fair value hierarchy:

FAIR VALUE MEASUREMENTS AS OF				
DECEMBER 31, 2018				
(in thousands)	LEVEL 1	LEVEL 2	LEVEL 3	TOTAL
Cash and cash equivalents:				
Cash and money market funds	\$ 202,818	\$ —	\$ —	\$ 202,818
Total cash and cash equivalents:	<u>\$ 202,818</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 202,818</u>

FAIR VALUE MEASUREMENTS AS OF				
DECEMBER 31, 2017				
(in thousands)	LEVEL 1	LEVEL 2	LEVEL 3	TOTAL
Cash and cash equivalents:				
Cash and money market funds	\$ 197,569	\$ —	\$ —	\$ 197,569
Total cash and cash equivalents:	<u>\$ 197,569</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 197,569</u>
Investments:				
Commercial paper	\$ —	\$ 30,883	\$ —	\$ 30,883
Corporate bonds	—	21,203	—	21,203
Total investments	<u>\$ —</u>	<u>\$ 52,086</u>	<u>\$ —</u>	<u>\$ 52,086</u>
Total cash, cash equivalents and investments:	<u>\$ 197,569</u>	<u>\$ 52,086</u>	<u>\$ —</u>	<u>\$ 249,655</u>

6. Inventory

Inventory consists of the following:

(in thousands)	DECEMBER 31, 2018
Raw materials	\$ 836
Work-in-process	6,885
Finished goods	2,391
Total inventory	<u>\$ 10,112</u>

The Company commenced capitalizing inventory for Rhopressa[®] upon FDA approval of Rhopressa[®] on December 18, 2017. No inventory was produced from the FDA approval date through the end of 2017; therefore, no inventory was capitalized on the consolidated balance sheet as of December 31, 2017.

7. Property, Plant and Equipment, Net

Property, plant and equipment, net consists of the following:

(in thousands)	DECEMBER 31,	
	2018	2017
Manufacturing equipment	\$ 2,366	\$ 2,082
Laboratory equipment	6,038	3,602
Furniture and fixtures	1,815	1,209
Software, computer and other equipment	2,702	1,932
Leasehold improvements	4,072	1,887
Construction-in-progress	49,057	24,228
Property, plant and equipment	66,050	34,940
Less: Accumulated depreciation	(5,525)	(3,008)
Property, plant and equipment, net	\$ 60,525	\$ 31,932

Depreciation expense was \$2.4 million, \$1.4 million and \$1.0 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Manufacturing Plant Build-Out

In January 2017, the Company entered into a Euro-denominated lease agreement, expiring in September 2037, for a new manufacturing plant in Athlone, Ireland, under which the Company is leasing approximately 30,000 square feet of interior floor space for build-out. The Company is permitted to terminate the lease beginning in September 2027.

Minimum expected lease payments were as follows at December 31, 2018 ^(a):

(in thousands)		
2019	\$	250
2020		250
2021		250
2022		259
2023		286
2024 and thereafter		1,219
Total minimum lease payments ^(b)	\$	2,514

(a) Uses foreign exchange rates in effect at December 31, 2018.

(b) This represents the obligation through the minimum lease term of September 2027. If the Company utilizes the leased space through the full term of the lease, expiring in September 2037, the total rental payments would be \$5.9 million.

The Company is not the legal owner of the leased space. However, in accordance with ASC Topic 840, *Leases*, the Company is deemed to be the owner of the leased space, including the building shell, during the construction period because of the Company's expected level of direct financial and operational involvement in the substantial tenant improvements required. As a result, the Company capitalized approximately \$4.2 million as a build-to-suit asset within property, plant and equipment, net and recognized a corresponding build-to-suit facility lease obligation as a liability on its consolidated balance sheets equal to the estimated replacement cost of the building at the inception of the lease.

Lease payments made under the lease will be allocated to interest expense and the build-to-suit facility lease obligation based on the implicit rate of the build-to-suit facility lease obligation. The build-to-suit facility lease obligation was approximately \$4.5 million as of December 31, 2018, of which \$0.2 million was classified as other current liabilities as of December 31, 2018. The build-to-suit facility lease obligation was approximately \$5.7 million as of December 31, 2017, of which \$0.3 million was classified as other current liabilities as of December 31, 2017. The lease obligation is denominated in Euros and is remeasured to U.S. dollars at the balance sheet date with any foreign exchange gain or loss recognized within other income (expense), net on the consolidated statements of operations and comprehensive loss. Unrealized foreign currency gain related to the remeasurement of the build-to-suit facility lease obligation for the year ended December 31, 2018 was \$0.2

million. The Company had an unrealized foreign currency loss related to the measurement of the lease obligation of \$0.6 million for the year ended December 31, 2017.

Additionally, construction costs incurred as part of the build-out and tenant improvements are also capitalized within property, plant and equipment, net. Costs of approximately \$24.8 million have been capitalized during the year ended December 31, 2018, related to both equipment purchases and the build-out of the facility. Once these costs are no longer considered construction-in-progress they will be moved to the respective asset category within property, plant and equipment and will begin depreciating.

8. Accrued Expenses & Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

(in thousands)	DECEMBER 31,	
	2018	2017
Accrued expenses and other current liabilities:		
Accrued compensation and benefits	\$ 10,438	\$ 7,886
Accrued consulting and professional fees	3,927	3,841
Accrued research and development ⁽¹⁾	7,503	1,855
Accrued revenue reserves	10,155	—
Accrued other ⁽²⁾	6,358	5,357
Total accrued expenses and other current liabilities	\$ 38,381	\$ 18,939

- (1) Comprised of accruals related to fees for investigative sites, contract research organizations, contract manufacturing organizations and other service providers that assist in conducting preclinical research studies and clinical trials.
- (2) Comprised of accruals related to commercial manufacturing activities for the Company's product candidates prior to the receipt of regulatory approval, as well as other business-related expenses.

9. Debt

2014 Convertible Notes

In September 2014, the Company issued \$125.0 million aggregate principal amount of the 2014 Convertible Notes to Deerfield Partners, L.P., Deerfield International Master Fund, L.P., Deerfield Private Design Fund III, L.P., Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., collectively with their transferees, "Deerfield." The 2014 Convertible Notes were issued pursuant to a note purchase agreement (as amended and supplemented from time to time, the "Note Purchase Agreement"), dated as of September 8, 2014, among Aerie and the Deerfield entities party thereto.

The 2014 Convertible Notes were scheduled to mature on the seventh anniversary from the date of issuance, unless earlier converted. The 2014 Convertible Notes were convertible at any time at the option of Deerfield, in whole or in part, into shares of common stock. In July 2018, Deerfield converted the entire outstanding principal amount of the 2014 Convertible Notes into shares of Aerie common stock.

The 2014 Convertible Notes bore interest at a rate of 1.75% per annum payable quarterly in arrears on the first business day of each January, April, July and October. The Company recorded the 2014 Convertible Notes as long-term debt at face value less \$2.1 million in debt discount and issuance costs incurred at the time of the transaction, which were being amortized to interest expense using the effective interest method through the conversion of the 2014 Convertible Notes.

The table below summarizes the carrying value of the 2014 Convertible Notes as of December 31, 2017:

(in thousands)	DECEMBER 31,	
	2017	
Gross proceeds	\$	125,000
Unamortized debt discount and issuance costs		(1,155)
Carrying value		\$123,845

Conversion of 2014 Convertible Notes

On July 23, 2018, Aerie entered into an Exchange and Termination Agreement (the “Exchange and Termination Agreement”) with Deerfield Private Design Fund III, L.P., Deerfield Partners, L.P. and Deerfield Special Situations Fund, L.P. (collectively, the “Holders”). Pursuant to the Exchange and Termination Agreement, (i) the Holders converted the entire outstanding principal amount of the 2014 Convertible Notes into 5,040,323 shares of Aerie common stock (the “Conversion Shares”) in accordance with the terms of the 2014 Convertible Notes, which was recognized in stockholders’ equity, (ii) Aerie issued the Conversion Shares, and (iii) Aerie paid accrued and unpaid interest on the Convertible Notes through July 23, 2018.

In addition, as mutually agreed to with the Holders in order to complete the conversion on the date of the Exchange and Termination Agreement, Aerie issued an additional 329,124 shares of Aerie common stock (the “Additional Shares”) to the Holders. Aerie expensed the value of the Additional Shares in the amount of \$24.1 million to other expense during the year ended December 31, 2018.

Entry into Credit Facility

On July 23, 2018, Aerie entered into a credit agreement (as amended on August 7, 2018) with certain entities affiliated with Deerfield Management Company L.P. providing for a \$100 million credit facility. The credit facility includes fees upon drawdown of 1.75% of amounts drawn, an 8.625% annual interest rate on drawn amounts, and annual fees on undrawn amounts of 1.5%. There is also an exit fee of \$1.5 million payable upon termination of the credit facility (whether at maturity or otherwise). The allowable draw period ends two years from the effective date of the credit facility. Fees on undrawn amounts are not payable until July 23, 2020, and no principal payments will be due on drawn amounts, if any, until July 23, 2020. The credit facility matures on July 23, 2024 in respect of any drawn amounts. The credit facility includes affirmative and negative covenants and prepayment terms. No funds were drawn at closing or as of December 31, 2018.

Interest expense was \$2.5 million for the year ended December 31, 2018, and included amortization of debt discount and issuance costs related to the 2014 Convertible Notes through the date of conversion as well as issuance costs and fees related to the credit facility. Interest expense was \$2.4 million and \$2.5 million for the years ended December 31, 2017 and 2016, respectively, which included amortization of debt discount and issuance costs related to the 2014 Convertible Notes.

10. Income Taxes

The provision for income taxes is based on net loss before income taxes as follows:

(in thousands)	DECEMBER 31,		
	2018	2017	2016
Net loss before income taxes:			
United States	\$ (203,230)	\$ (133,113)	\$ (88,123)
Other	(29,336)	(13,750)	(10,743)
Net loss before income taxes	\$ (232,566)	\$ (146,863)	\$ (98,866)

The components of the provision for income taxes are as follows:

(in thousands, except percentages)	DECEMBER 31,		
	2018	2017	2016
Provision for income taxes:			
Current:			
United States	\$ 3	\$ (24)	\$ 193
Other	—	—	—
Total	\$ 3	\$ (24)	\$ 193
Deferred:			
United States	\$ —	\$ (1,734)	\$ —
Other	—	—	—
Total	—	(1,734)	—
Provision for income taxes	\$ 3	\$ (1,758)	\$ 193
Effective tax rate	—%	1.20%	(0.19)%

Significant components of the Company's net deferred income tax assets as of December 31, 2018 and 2017 consist of the following:

(in thousands)	DECEMBER 31,	
	2018	2017
Net deferred tax assets:		
Net operating loss carryforwards	\$ 112,375	\$ 58,172
Stock-based compensation	17,734	13,681
U.S. tax credit carryforwards	5,996	4,182
Envisia asset acquisition	5,888	7,107
Other assets	2,857	591
Other liabilities	(1,535)	(349)
Valuation allowance	(143,315)	(83,384)
Total net deferred income taxes	\$ —	\$ —

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2018, 2017 and 2016 is as follows:

	DECEMBER 31,		
	2018	2017	2016
U.S. federal tax rate	21.00 %	35.00 %	35.00 %
Impact of federal tax legislation	— %	25.82 %	— %
State income taxes, net of federal benefit	4.56 %	7.71 %	5.34 %
Non-taxable foreign loss	0.09 %	(0.51)%	(2.69)%
Stock-based compensation	1.97 %	(0.02)%	(1.46)%
Other	(1.13)%	(2.19)%	(0.18)%
Change in valuation allowance	(26.49)%	(64.61)%	(36.20)%
Effective tax rate	— %	1.20 %	(0.19)%

In December 2017, the Tax Act was signed into law and enacted significant changes to the Internal Revenue Code of 1986, as amended. This tax legislation, among other changes, reduced the federal corporate income tax rate from 35% to 21% effective January 1, 2018. Under U.S. GAAP, deferred tax assets and liabilities are required to be revalued during the period in which the new tax legislation is enacted. Therefore, the deferred tax assets and liabilities were remeasured as of December 31, 2017, resulting in a reduction of the deferred tax asset balance and corresponding valuation allowance of \$34.2 million due to the enacted changes in tax rate. The Tax Act also repealed the corporate AMT for tax years beginning after December 31, 2017, and provides that existing AMT credit carryovers are refundable in tax years beginning after December 31, 2017. The Company has approximately \$1.7 million of AMT credit carryovers that are expected to be fully refunded between 2019 and 2022, of which \$0.3 million is recorded as a current receivable with the remainder recorded as a non-current receivable within other assets on the consolidated balance sheet as of December 31, 2018. The Company reduced the valuation allowance on its deferred tax assets by \$1.7 million and recognized an income tax benefit of the same amount during the year ended December 31, 2017 related to these federal AMT credit carryforwards.

At December 31, 2018, the Company had federal and state NOL carryforwards of approximately \$387.7 million and \$411.2 million, respectively. If not utilized, federal NOLs that arose prior to 2018 and state NOLs will begin to expire at various dates beginning in 2031 and 2024, respectively. Federal NOLs that arose on or after January 1, 2018 can be carried forward indefinitely against future income, but can only be used to offset a maximum of 80% of the Company's federal taxable income in any year. As of December 31, 2018, the Company also had foreign NOL carryforwards of \$44.1 million, which are available solely to offset taxable income of its foreign subsidiaries, subject to any applicable limitations under foreign law.

Federal NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities.

Realization of future tax benefits is dependent on the Company's ability to generate sufficient taxable income within the carryforward period. The Company provides a valuation allowance when it is more likely than not that deferred tax assets will not be realized. Due to the Company's history of operating losses and lack of available evidence supporting future taxable income, the Company maintains a valuation allowance on all of its deferred tax assets as of December 31, 2018. The increase in valuation allowance as of December 31, 2018 as compared to December 31, 2017 was primarily the result of the increase in NOL carryforwards.

The Company files income tax returns in the United States, Ireland and Malta. The federal and state income tax returns are open under the statute of limitations subject to tax examinations for the tax years ended December 31, 2014 through December 31, 2018. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the IRS or state tax authorities to the extent utilized in a future period.

11. Stockholders' Equity

During the year ended December 31, 2018, the Company received net proceeds of approximately \$136.4 million through the issue and sale of Aerie's common stock pursuant to an "at-the-market" sales agreements ("ATMs") that commenced in

December 2017 and pursuant to an underwriting agreement, dated January 23, 2018, relating to the registered public offering of approximately 1.3 million shares of Aerie's common stock.

During the year ended December 31, 2017, Aerie issued and sold approximately 1.1 million shares of common stock under ATMs entered into in May 2017 and December 2017, and received net proceeds of approximately \$61.1 million, after deducting fees and expenses. The Company also entered into an underwriting agreement, dated May 25, 2017, relating to the registered public offering of approximately 1.4 million shares of Aerie's common stock at a price to the public of \$53.75 per share, and received net proceeds of approximately \$72.7 million, after deducting fees and expenses.

During the year ended December 31, 2016, Aerie issued and sold approximately 4.2 million shares of common stock under ATMs entered into in November 2015 and September 2016, and received net proceeds of approximately \$96.2 million, after deducting fees and expenses. The Company also entered into an underwriting agreement, dated September 15, 2016, relating to the registered public offering of approximately 2.5 million shares of Aerie's common stock at a price to the public of \$29.50, and received net proceeds of approximately \$71.0 million, after deducting fees and expenses.

Holders of common stock are entitled to dividends when and if declared by Aerie's Board of Directors subject to prior rights of the holders of any preferred stock. The holder of each share of common stock is entitled to one vote.

Warrants

As of December 31, 2018, the following equity-classified warrants were outstanding:

NUMBER OF UNDERLYING SHARES	EXERCISE PRICE PER SHARE	WARRANT EXPIRATION DATE
75,000	\$5.00	February 2019
75,000	\$5.00	November 2019
4,500	\$5.00	August 2020
223,482	\$0.05	December 2019

The warrants outstanding as of December 31, 2018 are all currently exercisable. As of December 31, 2018 and 2017, all outstanding warrants are classified as equity and are recorded within additional paid-in capital on the consolidated balance sheets. Subsequent to December 31, 2018, 75,000 warrants due to expire in February 2019 were exercised for shares of Aerie common stock.

12. Stock-based Compensation

Stock-based compensation expense for options granted, RSAs, PSAs and stock purchase rights are reflected in the consolidated statements of operations and comprehensive loss as follows:

(in thousands)	YEAR ENDED DECEMBER 31,		
	2018	2017	2016
Selling, general and administrative	\$ 26,432	\$ 18,613	\$ 12,567
Pre-approval commercial manufacturing	2,622	1,359	446
Research and development	9,674	6,106	3,781
Total	<u>\$ 38,728</u>	<u>\$ 26,078</u>	<u>\$ 16,794</u>

As of December 31, 2018, the Company had \$68.9 million of unrecognized compensation expense related to options outstanding under its equity plans. This expense is expected to be recognized over a weighted average period of 2.7 years as of December 31, 2018. As of December 31, 2018, the Company had \$17.6 million of unrecognized compensation expense, related to unvested RSAs, including PSAs. This cost is expected to be recognized over a weighted average period of 2.7 years as of December 31, 2018.

Equity Plans

The Company maintains three equity compensation plans, the 2005 Aerie Pharmaceutical Stock Plan (the “2005 Plan”), the 2013 Omnibus Incentive Plan (the “2013 Equity Plan”), which was amended and restated as the Aerie Pharmaceuticals, Inc. Second Amended and Restated Omnibus Incentive Plan (the “Second Amended and Restated Equity Plan”), as described below, and the Aerie Pharmaceuticals, Inc. Inducement Award Plan (the “Inducement Award Plan”), as described below. The 2005 Plan, the Second Amended and Restated Equity Plan and the Inducement Award Plan are referred to collectively as the “Plans.”

On October 30, 2013, the effective date of the 2013 Equity Plan, the 2005 Plan was frozen and no additional awards have been or will be made under the 2005 Plan. Any remaining shares available for future grant under the 2005 Plan were allocated to the 2013 Equity Plan. On April 10, 2015, Aerie’s stockholders approved the adoption of the Aerie Pharmaceuticals, Inc. Amended and Restated Omnibus Incentive Plan (“Amended and Restated Equity Plan”) and no additional awards have been or will be made under the 2013 Equity Plan. Any remaining shares available under the 2013 Equity Plan were allocated to the Amended and Restated Equity Plan.

On June 7, 2018, Aerie’s stockholders approved the adoption of the Second Amended and Restated Equity Plan to increase the number of shares issuable under the Plan by 4,500,000. The Second Amended and Restated Equity Plan provides for the granting of up to 10,229,068 equity awards in respect of common stock of Aerie, including equity awards that were previously available for issuance under the 2013 Equity Plan.

On December 7, 2016, Aerie’s Board of Directors approved the Inducement Award Plan which provides for the granting of up to 418,000 equity awards in respect of common stock of Aerie and was subsequently amended during the year ended December 31, 2017 to increase the equity awards that may be issued by an additional 874,500 shares. Awards granted under the Inducement Award Plan are intended to qualify as employment inducement awards under NASDAQ Listing Rule 5635(c)(4).

Options to Purchase Common Stock

Weighted average assumptions utilized in the fair value calculation for options to purchase common stock as of December 31, 2018, 2017 and 2016 are as follows:

	YEAR ENDED DECEMBER 31,		
	2018	2017	2016
Expected term (years)	6.0	6.0	6.0
Expected stock price volatility	78%	84%	84%
Risk-free interest rate	2.7%	2.0%	1.4%
Dividend yield	—%	—%	—%

The following table summarizes the stock option activity under the Plans:

	NUMBER OF SHARES	WEIGHTED AVERAGE EXERCISE PRICE	WEIGHTED AVERAGE REMAINING CONTRACTUAL LIFE (YEARS)	AGGREGATE INTRINSIC VALUE (000’s)
Options outstanding at December 31, 2017	6,457,343	\$ 22.15		
Granted	1,283,884	56.54		
Exercised	(616,248)	8.97		
Canceled	(189,860)	47.85		
Options outstanding at December 31, 2018	6,935,119	\$ 28.96	6.7	\$ 91,728
Options exercisable at December 31, 2018	4,720,178	\$ 19.86	5.8	\$ 86,357

The weighted-average fair values of all stock options granted for the years ended December 31, 2018, 2017 and 2016 was \$38.38, \$35.01 and \$14.48, respectively. The aggregate intrinsic value of options exercised for the years ended December 31, 2018, 2017 and 2016 was \$32.0 million, \$8.6 million and \$3.9 million, respectively. The intrinsic value is calculated as the difference between the fair market value at December 31, 2018 and the exercise price per share of the stock options. The fair market value per share of common stock as of December 31, 2018 was \$36.10.

The following table provides additional information about stock options that are outstanding and exercisable at December 31, 2018:

EXERCISE PRICE	OPTIONS OUTSTANDING	WEIGHTED AVERAGE REMAINING CONTRACTUAL LIFE (YEARS)	OPTIONS EXERCISABLE
\$0.20 - \$10.00	1,579,133	4.2	1,579,133
\$10.01 - \$20.00	923,137	6.9	701,818
\$20.01 - \$30.00	1,590,265	5.7	1,522,535
\$30.01 - \$45.00	968,272	7.9	519,509
\$45.01 - \$55.00	923,305	8.9	238,307
\$55.01 - \$73.10	951,007	9.2	158,876
	<u>6,935,119</u>		<u>4,720,178</u>

Restricted Stock Awards

The following table summarizes the RSA, including PSAs, activity under the Plans:

	NUMBER OF SHARES	WEIGHTED AVERAGE FAIR VALUE PER SHARE
Nonvested RSAs at December 31, 2017	447,049	\$ 41.08
Granted	266,514	56.00
Vested	(129,961)	39.28
Canceled	(10,896)	52.83
Nonvested RSAs at December 31, 2018	<u>572,706</u>	<u>\$ 48.18</u>

The vesting of the RSAs is time and service based with terms of 1 to 4 years. The total fair value of restricted stock vested during the years ended December 31, 2018, 2017 and 2016 was \$5.1 million, \$1.3 million and \$0.9 million, respectively. During the year ended December 31, 2017, the Company granted 98,817 RSAs with non-market performance conditions that vest upon the satisfaction of certain performance conditions and service conditions. During the year ended December 31, 2018, there were 19,764 PSAs that vested.

Stock Appreciation Rights

During the year ended December 31, 2018, the Company granted 112,000 cash-settled SARs awards at a weighted average exercise price of \$53.83. As of December 31, 2018, 91,000 SARs awards were outstanding and had a weighted average remaining contractual life of 4.3 years.

Holders of the SARs are entitled under the terms of the Plans to receive cash payments calculated based on the excess of Aerie's common stock price over the exercise price in their award; consequently, these awards are accounted for as liability-classified awards and the Company measures compensation cost based on their estimated fair value at each reporting date, net of actual forfeitures, if any.

Employee Stock Purchase Plan

The Company maintains the 2013 Employee Stock Purchase Plan (the "Purchase Plan") under which substantially all employees may purchase Aerie's common stock through payroll deductions and lump sum contributions at a price equal to 85% of the lower of the fair market values of the stock as of the beginning or the end of the offering periods. Employees may not purchase more than the fair value equivalent of \$25,000 of stock during any calendar year. The Purchase Plan provides for the issuance of up to 645,814 shares of Aerie's common stock.

13. Commitments and Contingencies

Lease Commitment Summary

The following table presents future minimum commitments of the Company due under non-cancelable operating leases with original or remaining terms in excess of one year as of December 31, 2018. The Company's operating lease obligations are primarily related to its principal executive office and research facility in Durham, North Carolina, and its corporate offices in Irvine, California, and Bedminster, New Jersey.

Minimum lease payments under operating leases were as follows at December 31, 2018:

(in thousands)	
2019	\$ 4,283
2020	4,855
2021	4,278
2022	1,643
2023	1,438
2024 and thereafter	6,698
Total minimum lease payments	<u>\$ 23,195</u>

Minimum expected lease payments related to the Company's manufacturing plant in Athlone, Ireland, are not reflected in the table above (see Note 7).

Rent expense amounted to \$3.5 million, \$2.0 million and \$1.4 million for the years ended December 31, 2018, 2017 and 2016, respectively, and is reflected in selling, general and administrative expenses, pre-approval commercial manufacturing and research and development expenses as determined by the underlying activities occurring at each of the Company's locations.

Milestone Payments

In association with the Envisia asset acquisition (see Note 1), contingent milestone payments of up to \$45.0 million may be due, subject to achievement of certain product regulatory approvals using the IPR&D assets acquired, if achieved within the 15-year milestone period. Further, the Collaboration Agreement with DSM (see Note 1) includes contingent payments of up to \$75 million that may be due to DSM upon the achievement of certain development and regulatory milestones. These contingent milestone payments are recognized only when the contingency is resolved (the milestone is achieved) and the consideration is paid or becomes payable.

Litigation

The Company may periodically become subject to legal proceedings and claims arising in connection with its business. The Company is not a party to any known litigation, is not aware of any material unasserted claims and does not have contingency reserves established for any litigation liabilities.

14. Segment Information

Aerie has one operating segment: the discovery, development and commercialization of pharmaceutical products that address unmet medical needs, focusing on open-angle glaucoma, retinal diseases and other diseases of the eye. The Company's business is managed by a single management team, which reports to the Chief Executive Officer.

The following table presents total long-lived assets by geographic location:

(in thousands)	DECEMBER 31,	
	2018	2017
United States	\$ 10,393	\$ 6,609
Ireland	50,132	25,323
Total long-lived assets	<u>\$ 60,525</u>	<u>\$ 31,932</u>

Included in the above table is \$4.2 million related to the value of the building leased for the Company's build-out of its manufacturing plant in Ireland, which was recognized with a corresponding financing obligation, as the Company was deemed to be the owner of the building during the construction period under U.S. GAAP.

15. Selected Quarterly Financial Data (Unaudited)

The following table presents selected unaudited quarterly financial information for the years ended December 31, 2018 and 2017. The results for any quarter are not necessarily indicative of future quarterly results and, accordingly, period to period comparisons should not be relied upon as an indication of future performance.

(in thousands, except per share amounts)	FOR THE QUARTER ENDED			
	DECEMBER 31,	SEPTEMBER 30,	JUNE 30,	MARCH 31,
2018				
Total revenues, net	\$ 14,456	\$ 7,302	\$ 2,423	\$ —
Total costs and expenses	\$ 66,381	\$ 68,640	\$ 58,107	\$ 40,795
Net loss	\$ (51,458)	\$ (85,388)	\$ (55,024)	\$ (40,699)
Net loss per common share—basic and diluted	\$ (1.14)	\$ (1.96)	\$ (1.40)	\$ (1.05)
	DECEMBER 31,	SEPTEMBER 30,	JUNE 30,	MARCH 31,
2017				
Operating expenses	\$ 60,314	\$ 32,182	\$ 27,768	\$ 25,429
Net loss	\$ (58,513)	\$ (32,372)	\$ (28,433)	\$ (25,787)
Net loss per common share—basic and diluted	\$ (1.60)	\$ (0.89)	\$ (0.82)	\$ (0.76)

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COMPANY OVERVIEW

We were incorporated under the laws of the State of Delaware in June 2005. Our headquarters location is at 4301 Emperor Blvd, Suite 400, Durham, NC 27703 and our telephone number is 919-237-5300. Our website address is www.aeriepharma.com.

Trademarks and trade names may be referred to herein without the ® and TM symbols. Such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. Aerie®, Rhopressa®, and Rhokiinsa® are registered trademarks of Aerie Pharmaceuticals, Inc. and we have applications pending from the U.S. Patent and Trademark Office for the registration of our trademarks Rocklatan™ and Roclanda™ and for other trademarks. All other trademarks, trade names and service marks are the property of their respective owners.

SENIOR EXECUTIVE TEAM

Vicente Anido, Jr., Ph.D.

*Chief Executive Officer and
Chairman of the Board*

Casey C. Kopczynski, Ph.D.

Chief Scientific Officer

John W. LaRocca

General Counsel

Kathleen McGinley

*Vice President, Human Resources
and Corporate Services*

Thomas A. Mitro

President and Chief Operating Officer

Richard J. Rubino

Chief Financial Officer

BOARD OF DIRECTORS

Vicente Anido, Jr., Ph.D.

*Chief Executive Officer and
Chairman of the Board of Aerie
Pharmaceuticals, Inc.*

*Former President, Chief Executive Officer
and Director of ISTA Pharmaceuticals,
Inc. (acquired by Bausch + Lomb, Inc.
in 2012)*

*Former President and Chief Executive
Officer of CombiChem, Inc.*

Gerald D. Cagle, Ph.D.

*Former Chief Operating Officer of
Cognoptix, Inc.*

*Former Senior Vice President of
Research & Development and
Chief Scientific Officer of Alcon
Laboratories Inc.*

Richard Croarkin

*Former Senior Vice President,
CFO, Corporate Strategy Officer
of Alcon, Inc.*

*Former Chief Financial Officer of
Nestle Health Science S.A.*

Mechiel (Michael) M. du Toit

*Chief Growth Officer of Publicis Health
Former President of Everyday Health, Inc.
Former Global Group President of
Publicis Healthcare Communications
Group*

Murray A. Goldberg

*Former Chief Financial Officer of Regeneron
Pharmaceuticals, Inc.*

David W. Gryska

*Former Chief Financial Officer and
Executive Vice President of Incyte Corp.*

Benjamin F. McGraw III, Pharm.D.

*Chairman and Chief Executive Officer
of TheraVida, Inc.
Chief Executive Officer of Auration
Biotech, Inc.*

Julie McHugh

*Former Chief Operating Officer of
Endo Health Solutions, Inc.
Former Chief Executive Officer of
Nora Therapeutics, Inc.*

COMPANY LOCATIONS

Headquarters

4301 Emperor Blvd, Suite 400
Durham, NC 27703
Tel. 919-237-5300

Other Offices

2030 Main Street, Suite 1500
Irvine, CA 92614

550 Hills Drive, 3rd Floor
Bedminster, NJ 07921

International

Aerie Pharmaceuticals Ireland Limited

Pembroke House
28-32 Pembroke Street Upper
Dublin 2, Ireland

Pacific Century Place 8F
1-11-1 Marunouchi, Chiyoda-ku, Tokyo

Manufacturing Facility

Aerie Pharmaceuticals Ireland Limited
Athlone Business & Technology Park
Garrycastle
Athlone, Co. Westmeath, Ireland

www.aeriepharma.com

Annual Meeting of Stockholders

The annual meeting of stockholders will be held on May 23, 2019, at 8:00 am Eastern Time at The St. Regis New York at Two East 55th Street, New York, NY 10022.



AERIE PHARMACEUTICALS

www.aeriepharma.com