AERIE PHARMACEUTICALS INC

FORM 8-K
(Current report filing)

Filed 03/17/16 for the Period Ending 03/17/16

Address 7020 KIT CREEK ROAD
          SUITE 270
          RESEARCH TRIANGLE PARK, NC, 27709
Telephone 919-313-9650
CIK 0001337553
Symbol AERI
SIC Code 2836 - Biological Products, (No Diagnostic Substances)
Industry Biotechnology & Medical Research
Sector Healthcare
Fiscal Year 12/31
FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 17, 2016

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

Delaware
(State or other jurisdiction
of incorporation)

001-36152
(Commission
File Number)

2030 Main Street, Suite 1500
Irvine, California 92614
(Address of principal executive offices) (Zip code)

Registrant's telephone number, including area code: (949) 526-8700

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
Item 7.01. Regulation FD Disclosure.

On March 17, 2016, Aerie Pharmaceuticals, Inc. (the “Company”) issued a press release announcing further details on the safety profile for Rhopressa™ QD. The Company previously reported interim topline 12-month safety and efficacy data on February 17, 2016 for Aerie’s second Phase 3 registration trial for Rhopressa™ QD, indicating that Rhopressa™ QD had a positive safety profile with sustained efficacy through the 12-month period. A copy of the press release is furnished as Exhibit 99.1 hereto and is hereby incorporated by reference into this Item 7.01.

On or after March 17, 2016, representatives of the Company may present to various investors the information described in the slides attached to this report as Exhibit 99.2 hereto, which is hereby incorporated by reference into this Item 7.01.

The information in this Item 7.01 (including Exhibits 99.1 and 99.2) is being furnished, not filed, pursuant to Regulation FD. Accordingly, the information in this Item 7.01 will not be incorporated by reference into any registration statement filed by the Company under the Securities Act of 1933, as amended, unless specifically identified therein as being incorporated therein by reference. The furnishing of the information in this Item 7.01 is not intended to, and does not, constitute a determination or admission by the Company that this information is material or complete, or that investors should consider this information before making an investment decision with respect to any security of the Company.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

The following exhibits relating to Item 7.01 shall be deemed to be furnished, and not filed:

99.2 Company Presentation dated March 17, 2016
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AERIE PHARMACEUTICALS, INC.

Date: March 17, 2016

By: /s/ Richard J. Rubino

Richard J. Rubino
Chief Financial Officer
<table>
<thead>
<tr>
<th>Exhibit</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.2</td>
<td>Company Presentation dated March 17, 2016</td>
</tr>
</tbody>
</table>
Aerie Pharmaceuticals Reports Update on Positive Safety Results for Rhopressa™ QD (netarsudil ophthalmic solution) 0.02%

Conference Call and Webcast with Accompanying Slides Today, March 17, at 5:00 p.m. ET

IRVINE, Calif., March 17, 2016 — (BUSINESS WIRE) — Aerie Pharmaceuticals, Inc. (NASDAQ:AERI), a clinical-stage pharmaceutical company focused on the discovery, development and commercialization of first-in-class glaucoma therapies, today reported an update including further details on the safety profile for Rhopressa™ QD, a novel once-daily eye drop being tested for its ability to lower intraocular pressure (IOP) in patients with glaucoma or ocular hypertension. The Company previously reported interim topline 12-month safety and efficacy data on February 17, 2016, for Aerie’s second Phase 3 registration trial for Rhopressa™ QD, indicating that Rhopressa™ QD had a positive safety profile with sustained efficacy through the 12-month period. The Company expects to submit the NDA for Rhopressa™ QD in the third quarter of 2016. Management will host a conference call and provide accompanying slides to discuss this update at 5:00 p.m. ET today.

Rhopressa™ QD Safety Update Highlights

- Detailed 90-day safety data from Rocket 1 and Rocket 2 for Rhopressa™ QD were shared with the FDA during the Pre-NDA meeting that was held in October of 2015.

- Based on the Rhopressa™ QD safety and efficacy data reviewed by the Company to date, and in consideration of the adverse event and efficacy profiles of other products currently in the market, the Company believes that product candidate Rhopressa™ QD continues to have significant potential.

- Patients with contraindications to timolol, or beta blockers in general, or otherwise presenting with cardiopulmonary issues, were excluded from both Rocket 1 and Rocket 2. Based on Centers for Disease Control and Prevention data from 2011 and 2014, an estimated 47% of the U.S. population older than 65 years of age has heart disease and chronic obstructive pulmonary disease, all of which are contraindications to timolol. 1,2

- Since it is not systemically absorbed, Rhopressa™ QD has not shown any drug-related systemic effects, nor has it generated any serious adverse events. Every other product in the adjunctive market for glaucoma and ocular hypertension has a history of drug-related systemic effects. Rhopressa™ is being positioned to compete in the adjunctive market, which represents approximately half of the prescription volume for glaucoma products in the U.S.

- The most prevalent adverse event for Rhopressa™ QD was conjunctival hyperemia, the large majority of which was considered mild. Fifty percent of Rhopressa™ QD patients experienced hyperemia at some point during the trial; however, only ten percent of the patients in the trial had hyperemia at each visit over the 12-month trial period.

1 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6146a2.htm

2 Summary Health Statistics: National Health Interview Survey, 2014
Other adverse events for Rhopressa ™ QD, including corneal deposits, conjunctival hemorrhages, blurry vision, and reduced visual acuity, all of which have been observed in safety data for other marketed products, were commonly sporadic or self-resolving for the 118 patients on Rhopressa ™ QD for the 12-month period in Rocket 2.

Physicians’ perspectives at the recent American Glaucoma Society Annual Meeting indicated a high level of interest in Rhopressa™ QD among glaucoma specialists due to its competitive efficacy, safety profile, once-daily dosing, adjunctive use with prostaglandins and novel mechanisms of action.

The slides posted to the Aerie website include an in-depth analysis, including images where applicable, of the Rhopressa ™ QD adverse events noted in the safety data.

"Consistent with what we previously reported, Rhopressa ™ QD continues to demonstrate a positive safety profile after our deeper dive into the safety data. We believe Rhopressa ™ , if approved, will be well-received by both ophthalmologists and the payer community. Our NDA filing remains on track for the third quarter of 2016," said Vicente Anido, Jr., Ph.D., Chief Executive Officer and Chairman at Aerie.

Dr. Anido continued, "When comparing the adverse event profile of Rhopressa ™ to the other market-leading products, along with the durable efficacy profile and mechanisms of action, we remain very excited about the prospects for Rhopressa ™ in the marketplace. The attributes of Rhopressa™ also confirm a very strong case for Roclatan™ which already showed a positive safety and efficacy profile in its Phase 2b trial."

Richard A. Lewis, M.D., Aerie’s Chief Medical Officer and a glaucoma specialist, stated, “Having attended the American Glaucoma Society meeting two weeks ago, it is clear to me that the ophthalmologists in the glaucoma community see Rhopressa ™ as an exciting new potential entrant in glaucoma therapy.”

Rhopressa™

Rhopressa ™ (netarsudil ophthalmic solution) 0.02% is a novel eye drop that we believe, if approved, would become the only once-daily product available that specifically targets the trabecular meshwork, the eye’s primary fluid drain and the diseased tissue responsible for elevated IOP in glaucoma. Preclinical results have demonstrated that Rhopressa ™ also lowers episcleral venous pressure, which contributes approximately half of IOP in healthy subjects. Further, Rhopressa ™ provides an additional mechanism that reduces fluid production in the eye and therefore lowers IOP. Biochemically, Rhopressa ™ is known to inhibit both Rho Kinase (ROCK) and norepinephrine transporter (NET). Recent preclinical studies have shown that Rhopressa ™ may have disease-modifying properties, including an anti-fibrotic effect on the trabecular meshwork and the potential to increase perfusion of the trabecular meshwork. Preclinical research is also currently underway to evaluate the potential neuroprotective benefits of Rhopressa ™. The representations above regarding the Rhopressa ™ mechanisms of action are the result of Aerie’s preclinical studies and clinical trials.

There are two Phase 3 registration trials (Rocket 2 and Rocket 1) for Rhopressa ™ required for NDA filing. Rocket 2 will be the pivotal trial and Rocket 1 will be supportive for the NDA filing that we expect to submit to the FDA in the third quarter of 2016. Rocket 2, the interim safety results of which are
discussed in this press release, is a 12-month trial which previously achieved its 90-day primary efficacy endpoint. For Rocket 2, the 90-day efficacy period included IOP measurements at week two, week six and day 90 at 8 am, 10 am and 4 pm. Thereafter, safety observations and IOP measurements were conducted at 8 am only at the end of months six, nine and twelve. Rocket 1, the results of which were initially reported in April 2015, was a 90-day efficacy trial that did not achieve its primary endpoint, but did achieve its pre-specified secondary endpoint. Rocket 3 is a 12-month safety-only study in Canada which is currently in progress but not needed for NDA filing. A fourth Phase 3 trial, Rocket 4, commenced in late September 2015, and is designed to provide adequate six-month safety data to meet regulatory filing requirements in Europe, and is also not required for the NDA filing in the U.S.

Conference Call / Web Cast Information

Aerie management will host a live conference call and webcast at 5:00 p.m. Eastern Time today to discuss an update to the Rhopressa™ Phase 3 twelve-month safety results from Rocket 2.

The live webcast and a replay may be accessed by visiting Aerie’s website at http://investors.aeriepharma.com. In addition, key data slides from the Rocket 2 safety study will be discussed on the conference call and are posted to Aerie’s website. Please connect to Aerie’s website at least 15 minutes prior to the live webcast to ensure adequate time for any software download that may be needed to access the webcast. Alternatively, please call 1-888-734-0328 (U.S.) or 1-678-894-3054 (international) to listen to the live conference call. The conference ID number for the live call is 74114965. Please dial in approximately 10 minutes prior to the call. Telephone replay will be available approximately two hours after the call. To access the replay, please call 1-855-859-2056 (U.S.) or 1-404-537-3406 (international). The conference ID number for the replay is 74114965. The telephone replay will be available until March 24, 2016.

About Aerie Pharmaceuticals, Inc.

Aerie is a clinical-stage pharmaceutical company focused on the discovery, development and commercialization of first-in-class therapies for the treatment of patients with glaucoma and other diseases of the eye. Aerie’s two lead product candidates are once-daily IOP-lowering therapies with novel mechanisms of action to treat patients with glaucoma and ocular hypertension. It is expected that the NDA filing for Rhopressa™ (netarsudil ophthalmic solution) 0.02% will take place in the third quarter of 2016. The second product candidate, Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%, which is a fixed dose combination of Rhopressa™ and widely prescribed PGA latanoprost, currently has one Phase 3 registration trial underway, named Mercury 1, with a second trial expected to commence in March 2016. If these trials are successful, a Roclatan™ NDA filing is expected to take place in the second half of 2017. Aerie also announced in 2015 its research collaborations with GrayBug, Inc. and Ramot at Tel Aviv University as it further builds its pipeline for future growth.

Forward-Looking Statements

This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. We may, in some cases, use terms such as “predicts,” “believes,” “potential,” “proposed,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “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 include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: the success, timing and cost of our ongoing and anticipated preclinical studies and clinical trials for our current product candidates, including statements
regarding the timing of initiation and completion of the studies and trials; our expectations regarding the clinical effectiveness of our product candidates and results of our clinical trials; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration or other regulatory authority approval of, or other action with respect to, our product candidates; our expectations regarding the commercialization of our product candidates; our expectations related to the use of proceeds from our initial public offering and the issuance and sale of our senior secured convertible notes and the issuance and sale of shares of our common stock in connection with our "at the market" sales agreements; our estimates regarding anticipated capital requirements and our needs for additional financing; the potential advantages of our product candidates; our plans to pursue development of our product candidates for additional indications and other therapeutic opportunities; our plans to explore possible uses of our existing proprietary compounds beyond glaucoma; our ability to protect our proprietary technology and enforce our intellectual property rights; and our expectations regarding strategic operations, including our ability to in-license or acquire additional ophthalmic products or product candidates. By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on regulatory approvals and economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. We discuss many of these risks in greater detail under the heading “Risk Factors” in the quarterly and annual reports that we file with the Securities and Exchange Commission (SEC). In particular, the preclinical research discussed in this press release 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 press release. In addition, the financial information presented above is preliminary, based solely on information available to us as of the date of this press release, and may differ materially from final 2015 financial results. Forward-looking statements are not guarantees of future performance and 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 press release. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update our forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

Contacts

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Media
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Source: Aerie Pharmaceuticals, Inc.
Update on Rhopressa™ QD (netarsudil ophthalmic solution) 0.02% and Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%
Important Information

Any discussion of the potential use or expected success of our product candidates is subject to our product candidates being approved by regulatory authorities.

The information in this presentation is current only as of its date and may have changed or may change in the future. We undertake no obligation to update this information in light of new information, future events or otherwise. We are not making any representation or warranty that the information in this presentation is accurate or complete.

Certain statements in this presentation are “forward-looking statements” within the meaning of the federal securities laws. Words such as “may,” “will,” “should,” “would,” “could,” “believe,” “expects,” “anticipates,” “plans,” “intends,” “estimates,” “targets,” “projects,” “potential” or similar expressions are intended to identify these forward-looking statements. These statements are based on the Company’s current plans and expectations. Known and unknown risks, uncertainties and other factors could cause actual results to differ materially from those contemplated by the statements. In evaluating these statements, you should specifically consider various factors that may cause our actual results to differ materially from any forward-looking statements. These risks and uncertainties are described more fully in the quarterly and annual reports that we file with the SEC, particularly in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” Such forward-looking statements only speak as of the date they are made. We undertake no obligation to publicly update or revise any forward-looking statements, whether because of new information, future events or otherwise, except as otherwise required by law.
Agenda

Overview

Rhopressa™ Safety and Efficacy

Roclatan™ Regulatory Perspective

AGS 2016 Physicians’ Perspective

Q & A
In a study of plasma drug concentration in six subjects, the systemic exposure to timolol was determined following twice daily administration of TIMOPTIC 0.5%. The mean peak plasma concentration following morning dosing was 0.46 ng/mL and following afternoon dosing was 0.35 ng/mL.

In these studies, TIMOPTIC was generally well tolerated and produced fewer and less severe side effects than either pilocarpine or epinephrine. A slight reduction of resting heart rate in some patients receiving.

TIMOPTIC (mean reduction 2.9 beats/minute standard deviation 10.2) was observed.

**CONTRAINDICATIONS**

- TIMOPTIC is contraindicated in patients with (1) bronchial asthma; (2) a history of bronchial asthma; (3) severe chronic obstructive pulmonary disease (see WARNINGS); (4) sinus bradycardia; (5) second or third degree atrioventricular block; (6) overt cardiac failure (see WARNINGS); (7) cardiogenic shock; or (8) hypersensitivity to any component of this product.

**Warnings**

- As with many topically applied ophthalmic drugs, this drug is absorbed systemically. The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate.
Additional Timolol Considerations

- Nelson-1986: Between September 1978 and December 1985, 450 case reports of serious respiratory and cardiovascular events and 32 case reports of death attributed to ophthalmic timolol were received by the United States Food and Drug Administration and the National Registry of Drug-Induced Ocular Side Effects.

- Based on Centers for Disease Control and Prevention data from 2011 and 2014, an estimated 47% of the population older than 65 years of age has heart disease and chronic obstructive pulmonary disease, all of which are contraindications to timolol.
Update on Rhopressa™ QD (netarsudil ophthalmic solution) 0.02%
FDA Pre-NDA Clinical Meeting (October ‘15) discussions:

- Minimum of 100 Rhopressa™ QD patients with 12 months of safety data needed for NDA filing

- Detailed 3-month safety data on Rhopressa™ QD were shared and discussed during the Pre-NDA meeting

- No requirement for Risk Management Plan
Rhopressa™ QD Safety Profile To Date

- There were no drug-related serious adverse events (SAEs)
- No new adverse events observed over the twelve-month period compared to three-month period
- There was no evidence of treatment-related systemic effects (e.g., clinical laboratory or haematology values, heart rate or blood pressure)
  - No systemic absorption (i.e. below level of detection)
- The most common adverse event was conjunctival hyperemia ~50%
- Other ocular AEs
  - AEs occurring in ~5-23% of patients included: corneal deposits, conjunctival hemorrhage, vision blurred and visual acuity reduced

**Data on File
Based on Rocket 2 3-Month Safety and 2 Interim 12-month safety**
The incidence of adverse events significantly decreased from the first 3 months to the final Month 12 visit:

- Conjunctival hyperemia, conjunctival hemorrhage, vision blurred, visual acuity reduced, eye pruritus and conjunctival edema

**Data on File**
Based on Rocket 2 3-Month Safety and Rocket 2 Interim 12-month safety
When Present, 80% of Rhopressa™ QD Hyperemia Graded as Mild

<table>
<thead>
<tr>
<th>Grade</th>
<th>Image</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td><img src="image" alt="None/Normal Image" /></td>
<td>None/Normal</td>
</tr>
<tr>
<td>1</td>
<td><img src="image" alt="Mild Image" /></td>
<td>Mild</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Moderate Image" /></td>
<td>Moderate</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Severe Image" /></td>
<td>Severe</td>
</tr>
</tbody>
</table>

For illustrative purposes only

**Data on File based on Rocket 2 Interim 12-month safety**
No Change in Mean Hyperemia Score Over Time (Interim Month 12)

Hyperemia severity:
0 = none
1 = mild
2 = moderate
3 = severe

- Hyperemia severity did not increase with continued dosing from month 3 to month 12
- Hyperemia was sporadic
  - Only 10% of patients had hyperemia at each study visit from week 2 to month 12

**Data on File based on Rocket 2 Interim 12-month safety**
Conjunctival Hemorrhage Using Biomicroscopy Evaluation

- Subconjunctival petechiae seen sporadically in Rhopressa™ Rocket studies
  - MedDRA coded to conjunctival hemorrhage
- No conjunctival hemorrhages noted at month 12 visit

**Data on File – an example of conjunctival hemorrhage courtesy of investigator from Rocket 2**
Corneal Deposits Are Asymptomatic And Did Not Affect Visual Acuity

- Corneal deposits (lipid microdeposits in the corneal epithelial layer) noted were:
  - Asymptomatic - Did not affect visual acuity
  - Only visible via biomicroscopy evaluation
  - ~75% resolved to date
    - ~30% resolved during continued Rhopressa™ dosing
  - Noted in Rhopressa™ and timolol subjects
  - Rhopressa™ corneal deposits due to phospholipidosis
  - Follow-up program in place

- Ophthalmologists are familiar with corneal deposits with other drugs such as Amiodarone

**Data on File – an example from Rocket 1 and 2 (courtesy of investigators)**
Cordarone (Amiodarone) Prescribing Information
FDA Phospholipidosis (PLD) workshop in 2010
- Adaptive process
- More than 290 PLD-inducing compounds in FDA database
- Over 50 marketed products across ~25 drug classes
Other Corneal Evaluations in the Rocket Studies

- NDA submission with endothelial cell counts for 100 treated patients plus a control group for at least 3 months
- No significant changes in corneal endothelial cell density or hexagonality (shape) using specular microscopy seen in Rhopressa™
- No other significant corneal findings (including guttatae-like finding) were reported in Rhopressa™

**Data on File Topline 3-Month and Interim 12-Month Rocket 2**
Visual Acuity Reduced Adverse Event: Infrequent, Sporadic and Self-Resolving

- Topline 3-month:
  - Only 2 (0.8%) Rhopressa™ patients had reduced visual acuity at more than 1 visit (with no change in severity)
  - Typically limited to one eye (both eyes are treated)

Incidence reduced over time:

<table>
<thead>
<tr>
<th></th>
<th>Topline 3-month:</th>
<th>Interim 12-month:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.4% for Rhopressa™, 1.6% for timolol</td>
<td>2.5% for Rhopressa™, 0.6% for timolol</td>
</tr>
</tbody>
</table>

**Data on File Topline 3-Month and Interim 12-Month Rocket 2**
## Reduced Visual Acuity in Other Registration Studies

### Brimonidine

**Visual Acuity**

*Compared to Baseline at Subject's Final Evaluation*

*Number of Subjects - All Subjects*

<table>
<thead>
<tr>
<th>Changes[a]</th>
<th>0.2% Bmi</th>
<th>0.5% Tim</th>
<th>P-value[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worse</td>
<td>13 (5.9%)</td>
<td>21 (9.5%)</td>
<td>0.158</td>
</tr>
<tr>
<td>No Change</td>
<td>208 (94.1%)</td>
<td>201 (90.5%)</td>
<td></td>
</tr>
<tr>
<td>Better</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>221</td>
<td>222</td>
<td></td>
</tr>
</tbody>
</table>

[a] Worse = decrease of 2 lines or more

For Rocket studies, no minimum decrease in lines was required for visual acuity adverse event reporting.
Vision Blurred Adverse Event:
Intermittent and Self-Resolving

- Topline 3-month:
  - Patient reported adverse event
  - 17 out of 18 Rhopressa™ patients reporting blurred vision had no reduced visual acuity at office visit

Incidence reduced over time:

<table>
<thead>
<tr>
<th></th>
<th>Rhopressa™</th>
<th>Timolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topline 3-month</td>
<td>7.2%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Interim 12-month</td>
<td>0.8%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

**Data on File
Based on Rocket 2 3-Month Safety and 2 Interim 12-month safety**
Systemic Safety: Rhopressa™

- There was no evidence of treatment-related systemic effects (e.g., clinical laboratory or haematology values, heart rate or blood pressure)
- No systemic absorption in prior PK study (i.e. below level of detection)

**Data on File
Based on Rocket 2 3-Month Safety and 2 Interim 12-month safety**
Systemic Safety: Warnings for Timolol Use
Systemic AEs Referenced in the timolol Label

WARNINGS
The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate.

Because timolol is the comparator in the Rocket studies, patients with known contraindication or hypersensitivity to timolol/Beta-blockers were excluded.

++Package Insert
Timolol Caused Statistically Significant Reduction in Heart Rate (Rocket 2)

- Timolol reduced mean heart rate by ~3 beats per minute (average across all patients)
- Despite all measures to exclude patients with possible negative sensitivity to beta-blockers

++Data on File Topline 3-Month Rocket 2
## Safety Profile for Other Approved Products

<table>
<thead>
<tr>
<th></th>
<th>Alphagan P</th>
<th>Lumigan</th>
<th>Travatan Z</th>
<th>Combigan</th>
<th>Simbrinza</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctival Hyperemia</td>
<td>10-20%</td>
<td>0.01% = 31%</td>
<td>0.03% = 45%</td>
<td>30-50%</td>
<td>5-15%</td>
</tr>
<tr>
<td>Conjunctival Hemorrhage</td>
<td>1-4%</td>
<td>1-4%</td>
<td>1-4%</td>
<td></td>
<td>1-4%</td>
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<tr>
<td>Vision Blurred</td>
<td>1-4%</td>
<td>1-4%</td>
<td>1-4%</td>
<td></td>
<td>3-5%</td>
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<tr>
<td>Lacrimation Increased</td>
<td>Tearing 1-4%</td>
<td>1-4%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Acuity Reduced</td>
<td>Visual disturbance 5-9%</td>
<td>1-4%</td>
<td>5-10%</td>
<td>Visual disturbance 1-5%</td>
<td></td>
</tr>
<tr>
<td>Eye Pruritus</td>
<td>10-20%</td>
<td>1-4%</td>
<td>5-10%</td>
<td>5-15%</td>
<td></td>
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<tr>
<td>Erythema of Eyelid</td>
<td>1-4%</td>
<td>1-4%</td>
<td></td>
<td>1-5%</td>
<td></td>
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<tr>
<td>Conjunctival Edema</td>
<td>1-4%</td>
<td>1-4%</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Other</td>
<td>Allergic Conjunct 10-20%</td>
<td>Burning 5-9%</td>
<td>Conjunct folliculosis 5-9%</td>
<td>Ocular Allergy 5-9%</td>
<td>Allergic reaction 1-4%</td>
</tr>
<tr>
<td></td>
<td>Iris pigmentation, periorbital tissues and eyelashes; Changes in eyelashes; Intraocular inflammation</td>
<td>Eye discomfort 5-10%</td>
<td>Foreign body 5-10%</td>
<td>Biepharitis 1-4%</td>
<td>Dropping eyelid sulcus</td>
</tr>
<tr>
<td></td>
<td>Allergic conjunct 5-15%</td>
<td>Burning / Stinging 5-15%</td>
<td>Conjunct folliculosis 5-15%</td>
<td>Asthonia 1-5%</td>
<td>Biepharitis 1-5%</td>
</tr>
<tr>
<td></td>
<td>Ocular allergy 10-30%</td>
<td>Fatigue/drowsiness 10-30%</td>
<td>Eye irritation 3-5%</td>
<td>Dysgeusia 3-5%</td>
<td>Dry mouth3-5%</td>
</tr>
</tbody>
</table>
Rhopressa™ On Target To File NDA

- Completed 90-day efficacy and 90-day safety for Rocket 2 and Rocket 1, which was shared with FDA, in October 2015
- The first 118 patients on Rhopressa™ QD completed the 12-month period
  - Adverse event profile in Month 12 similar to Month 3
  - Stable efficacy from Month 3 to Month 12
- On target to file NDA in Q3 2016

*Data on File. Based on Rocket 2 3-month and Interim 12-month data
Update on Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%
Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% Phase 2b Study Demonstrated Significant IOP-Lowering Therapy

- Achieved primary efficacy outcome of superiority over each of the components on day 29
- Mean diurnal IOP reduction on day 29 was approximately 2 mmHg better than latanoprost
- Achieved statistical superiority over the individual components at all time points
  - More efficacious than latanoprost by 1.6 – 3.2 mmHg
  - More efficacious than AR-13324 by 1.7 – 3.4 mmHg
- The main adverse event was hyperemia, or eye redness, reported in 40 percent of patients and scored as mild for the large majority of patients
- No systemic drug-related adverse events

Roclatan™ Phase 2b Safety Profile

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>PG324 0.02% q.d PM n=73</th>
<th>AR-13324 0.02% q.d PM n=78</th>
<th>Latanoprost q.d. PM n=73</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye Disorders</strong></td>
<td>43 (58.9%)</td>
<td>45 (57.7%)</td>
<td>19 (26.0%)</td>
</tr>
<tr>
<td>Conjunctival Hyperemia</td>
<td>29 (39.7%)</td>
<td>31 (39.7%)</td>
<td>10 (13.7%)</td>
</tr>
<tr>
<td>Conjunctival Hemorrhage</td>
<td>5 (6.8%)</td>
<td>5 (6.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Lacrimation Increased</td>
<td>4 (5.5%)</td>
<td>5 (6.4%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Eye Pruritus</td>
<td>4 (5.5%)</td>
<td>2 (2.6%)</td>
<td>2 (2.7%)</td>
</tr>
<tr>
<td><strong>Administration Site Conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instillation site erythema</td>
<td>14 (19.2%)</td>
<td>17 (21.8%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Instillation site pain</td>
<td>8 (11.0%)</td>
<td>4 (5.1%)</td>
<td>2 (2.7%)</td>
</tr>
</tbody>
</table>

Patients with known contraindications or hypersensitivity to latanoprost were excluded.
Fixed-Dose Combination

- Trial design follows FDA requirement for fixed-dose combination (FDC)
  - Superiority of combination over each individual component
  - Statistically significant difference at measured time points
  - Higher combo efficacy vs. components of at least ~1–3 mmHg, as previously accepted by FDA for product approval
  - Favorable safety profile

++Data on File. FDA guidance, presentations and sponsor meetings.
**SIMBRINZA® (FDC)**
approved April 2013

<table>
<thead>
<tr>
<th>IOP Lowering</th>
<th>1 to 3 mmHg greater than monotherapy with either 1% brinzolamide or 0.2% brimonidine tartrate (actual range was 0.8 mmHg greater than 1% brinzolamide or 0.2% brimonidine tartrate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs from Package Insert</td>
<td>The most frequently reported adverse reactions in patients treated with SIMBRINZA occurring in approximately 3 to 5% of patients in descending order of incidence were blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, eye allergy.</td>
</tr>
<tr>
<td></td>
<td>In clinical studies of brinzolamide ophthalmic suspension 1%, the most frequently reported adverse reactions reported in 5 to 10% of patients were blurred vision and bitter, sour or unusual taste. Adverse reactions occurring in 1 to 5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus and rhinitis.</td>
</tr>
<tr>
<td></td>
<td>In clinical studies of brimonidine tartrate 0.2%, adverse reactions occurring in approximately 10 to 30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus. Reactions occurring in approximately 3 to 9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain. The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness, syncope.</td>
</tr>
<tr>
<td>Warnings &amp; Precautions</td>
<td>Brimonidine tartrate, a component of SIMBRINZA, has a less than 5% mean decrease in blood pressure 2 hours after dosing in clinical studies; caution should be exercised in treating patients with severe cardiovascular disease.</td>
</tr>
<tr>
<td></td>
<td>Sulfonamide hypersensitivity reactions</td>
</tr>
<tr>
<td></td>
<td>Brimonidine tartrate, a component of SIMBRINZA, may potentiate syndromes associated with vascular insufficiency. SIMBRINZA should be used with caution in patients with depression, cerebral or coronary insufficiency.</td>
</tr>
</tbody>
</table>

++Package Insert
Market Research from the American Glaucoma Society Annual Meeting (March 2016)

- 30 Glaucoma specialists participated in 90-minute sessions
- Rhopressa™ pre-clinical and clinical data were presented
- Rhopressa™ data were compared to all products used as adjunctive therapy to prostaglandins (PGA):
  - MOAs
  - Efficacy
  - Safety
  - Ease of Use
Physicians’ Perspectives on Clinical Data

- **Glaucoma specialists were impressed with Rhopressa™ QD efficacy**
  - Rhopressa™ met non-inferiority to timolol at IOPs below 25
    - *Brimonidine and CAIs did not*
  - The 12 month interim safety data which showed consistent IOP control from month 3 to month 12
    - *Timolol and brimonidine are known to lose effectiveness through time*

- **There was a great deal of enthusiasm for using Rhopressa™ with a PGA**
  - Synergy with PGAs from Phase 2b and Phase 3 trials
    - *Physicians believe timolol, brimonidine and the CAIs are not very effective as adjuncts to PGAs*
  - QD dose & multiple and new MOAs
  - Safety: No Serious Adverse Events (SAE’s)
    - *Physicians believe the side effects of Rhopressa™ are manageable and are not serious*
Physicians’ Perspectives on Adverse Events

- Glaucoma specialists felt that the Rhopressa™ absence of systemic or serious AE’s was a significant benefit over timolol, brimonidine and CAIs

- After reviewing the data, when asked to select words that best describe Rhopressa™, the 3rd most popular choice (of the 15 selections) was “Safe”
  - #1 was Unique and #2 was Effective

- Additionally:
  - Conjunctival hemorrhages are not an issue when properly characterized as focal and small in size
  - Corneal deposits, although benign, will need to be managed like the ocular side effects of PGAs (pigmentation, orbital fat loss)
  - Hyperemia appears to be the same in incidence and severity as PGAs and can be managed
  - Hyperemia is not as worrisome as brimonidine induced allergic conjunctivitis or timolol induced heart/lung effects

**Data on File**
Physicians’ Perspectives: Rhopressa™ Summary

- Physicians recognized several potential important benefits that Rhopressa™ has over other adjunctive agents:

  - Effectiveness as an additive therapy to PGAs
    - “Rhopressa™ shines as a adjunct to a PGA”

  - QD dosing put Rhopressa™ ahead of all others
    - “The easiest adjunctive regimen”

  - No serious AEs (SAEs)
    - “Takes an unnecessary worry off the table”

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93% of participants put Rhopressa™ in 1st position as an adjunct to PGAs
**Rhopressa™ and Roclatan™ Key Milestones**

- **Q3-2016: Rhopressa™ NDA filing expected**
- **Q4-2016: Rhopressa™ Rocket 4 Topline efficacy (3 mos)**

### 2016

- **Q1-2016: Roclatan™ P3 Mercury 2 to be initiated**
- **Q3-2016: Roclatan™ P3 Mercury 1 Topline efficacy (3 mos)**

### 2017

- **1H-2017: Roclatan™ P3 Mercury 3 (EU) to be initiated**
- **Q2-2017: Roclatan™ P3 Mercury 2 Topline efficacy (3 mos)**
- **2H-2017: Roclatan™ NDA filing expected**
- **Q3-2017: Roclatan™ P3 Mercury 1 Topline safety (12 mos)**