



**aerie**

Pharmaceuticals, Inc.

**Rhopressa™**

**(netarsudil ophthalmic solution) 0.02%**

**Rocket 4 Phase 3 Topline Results**

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# Rhopressa™ Achieves Primary Clinical Endpoint



- Rhopressa™ QD met the criteria for non-inferiority to timolol BID for the primary efficacy analysis (for baseline IOP < 25 mmHg)
  - Also met non-inferiority for baseline IOP < 27 mmHg and <28 mmHg
- Rhopressa™ QD showed stable efficacy from Week 2 to Month 3
- Consistent efficacy results across multiple statistical analysis imputations (PP/ITT/LOCF)
- The main adverse event for Rhopressa™ was conjunctival hyperemia, which was reported in ~40% of patients and was scored as mild for ~85% of the patients
- There were no drug-related serious adverse events and no evidence of treatment-related systemic effects

# Rocket 4 Trial Design

Patients with open angle glaucoma (OAG) or ocular hypertension (OHT)  
with IOP > 20 mmHg and < 30 mmHg at 8am,  
N = 708 subjects randomized at 52 US sites

↓  
Patients randomized  
1:1

Rhopressa™  
(AR-13324) 0.02%  
QD (PM)

Timolol 0.5%  
BID (AM and  
PM)

↓  
Primary endpoints:

- Efficacy: Mean IOP at Weeks 2 and 6 and Month 3 for subjects with baseline IOP > 20 mmHg and <25 mmHg  
(N = 423 subjects per protocol)
- Safety: Ocular and systemic safety during a 6-month treatment period

# Baseline Demographics

	Rhopressa™ QD N = 351	Timolol BID N = 357
<b>Gender, n (%)</b>		
Male	143 (40.7%)	120 (33.6%)
Female	208 (59.3%)	237 (66.4%)
<b>Race, n (%)</b>		
White	259 (73.8%)	274 (76.8%)
Black/African American	84 (23.9%)	75 (21.0%)
Asian	7 (2.0%)	6 (1.7%)
Multiple	0 (0%)	1 (0.3%)
Other	1 (0.3%)	1 (0.3%)
<b>Age (years)</b>		
< 65	165(47.0%)	164 (45.9%)
>65	186 (53.0%)	193 (54.1%)
<b>Iris Color, n (%)</b>		
Brown/Black	241 (68.7%)	227 (63.6%)
Blue/Grey/Green	73 (20.8%)	90 (25.2%)
Hazel	36 (10.3%)	40 (11.2%)
Other	1 (0.3%)	0 (0%)

# Patient Disposition

	Rhopressa™ QD N = 351	Timolol BID N = 357
<b>Completed Month 3</b>	<b>290 (82.6%)</b>	<b>335 (93.8%)</b>
<b>Discontinued Prior to Month 3</b>	<b>61 (17.4%)</b>	<b>22 (6.2%)</b>
<b>Discontinued</b>		
Adverse Event	39 (11.1%)	6 (1.7%)
Withdrawal of Consent	7 (2.0%)	7 (2.0%)
Non-Compliant	1 (0.3%)	1 (0.3%)
Lost to Follow-up	0	0
Lack of Efficacy	5 (1.4%)	0
Disallowed Concurrent Medication	1 (0.3%)	2 (0.6%)
Investigator Decision	0	2 (0.6%)
Protocol Violation	4 (1.1%)	3 (0.8%)
Other	4 (1.1%)	1 (0.3%)

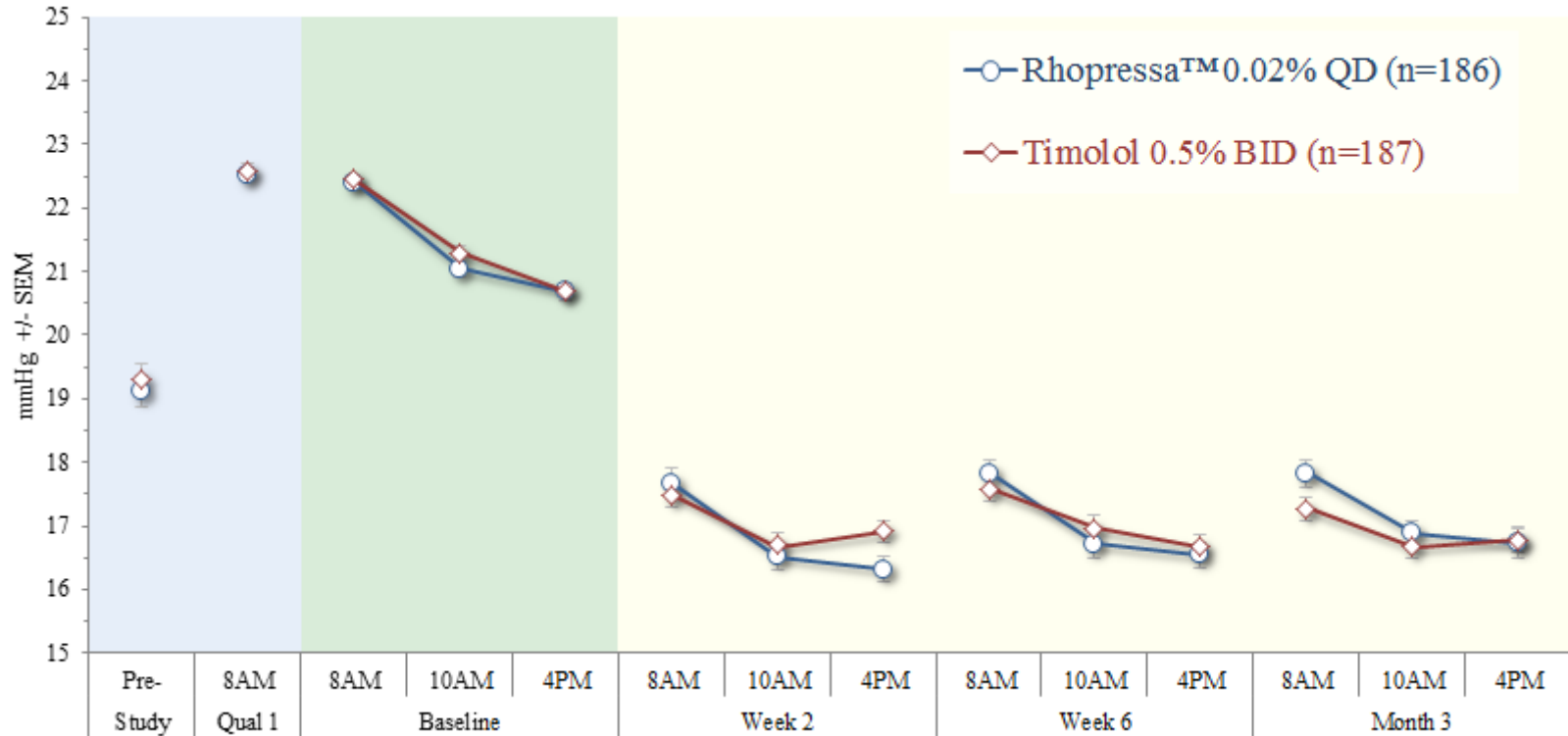
# Patient Disposition (For Baseline IOP < 25 mmHg)

	Rhopressa™ QD N = 214	Timolol BID N = 209
<b>Completed Month 3</b>	<b>189 (88.3%)</b>	<b>199 (95.2%)</b>
<b>Discontinued Prior to Month 3</b>	<b>25 (11.7%)</b>	<b>10 (4.8%)</b>
<b>Discontinued</b>		
Adverse Event	16 (7.5%)	4 (1.9%)
Withdrawal of Consent	3 (1.4%)	2 (1.0%)
Non-Compliant	1 (0.5%)	1 (0.5%)
Lost to Follow-up	0	0
Lack of Efficacy	1 (0.5%)	0
Disallowed Concurrent Medication	1 (0.5%)	1 (0.5%)
Investigator Decision	0	1 (0.5%)
Protocol Violation	2 (0.9%)	1 (0.5%)
Other	1 (0.5%)	0

# Rhopressa™ Achieved Non-Inferiority In the Primary Efficacy Analysis (Baseline IOPs < 25 mmHg)



## Mean IOP at Each Time Point (Per Protocol)



++Data on File  
Based on Rocket 4 Topline Interim 3-month efficacy



# Rhopressa™ Phase 3 Rocket 4, Per Protocol Baseline IOPs < 25 mmHg

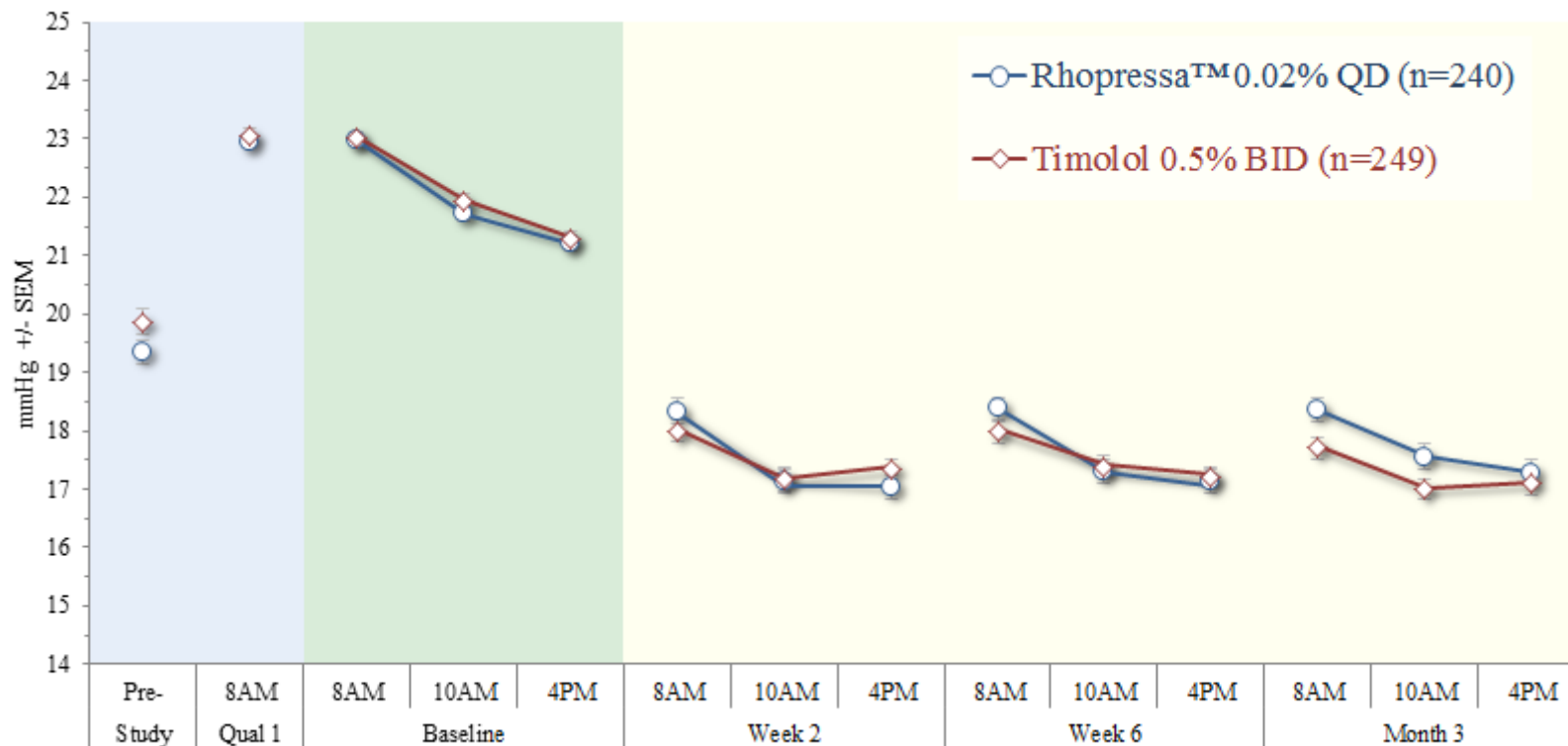
	Mean IOP mmHg		Difference from Rhopressa™ QD (95% CI)
	Rhopressa™ QD N=186	Timolol 0.5% BID N=187	
<b>Baseline</b>			
8:00 AM	22.4	22.4	
10:00 AM	21.1	21.3	
4:00 PM	20.7	20.7	
<b>Mean Diurnal</b>	<b>21.4</b>	<b>21.5</b>	
<b>Day 15</b>			
8:00 AM	17.7	17.5	0.2 (-0.4, 0.8)
10:00 AM	16.6	16.7	-0.2 (-0.7, 0.4)
4:00 PM	16.3	16.9	-0.6 (-1.2, 0.0)
<b>Mean Diurnal</b>	<b>16.8</b>	<b>17.0</b>	<b>-0.2 (-0.7, 0.3)</b>
<b>Day 43</b>			
8:00 AM	17.8	17.6	0.3 (-0.3, 0.9)
10:00 AM	16.8	17.0	-0.2 (-0.8, 0.4)
4:00 PM	16.6	16.7	-0.1 (-0.7, 0.5)
<b>Mean Diurnal</b>	<b>17.0</b>	<b>17.1</b>	<b>0.0 (-0.6, 0.5)</b>
<b>Day 90</b>			
8:00 AM	17.9	17.3	0.6 (0.0, 1.2)
10:00 AM	16.9	16.7	0.2 (-0.4, 0.8)
4:00 PM	16.7	16.8	-0.1 (-0.7, 0.6)
<b>Mean Diurnal</b>	<b>17.2</b>	<b>16.9</b>	<b>0.2 (-0.3, 0.8)</b>

## Summary

- Upper 95% CI ≤ 1.5 mmHg at all time points, ≤ 1.0 mmHg at majority (8/9) time points
  - Rocket 1: ≤ 1.0 mmHg at majority (7/9) time points
  - Rocket 2: ≤ 1.0 mmHg at majority (6/9) time points
- Met the criteria for demonstrating non-inferiority

# Rhopressa™ Achieved Non-Inferiority For Baseline IOP < 27 mmHg

## Mean IOP at Each Time Point (Per Protocol)



# Rhopressa™ Rocket 4 Efficacy Results for Different Baseline IOPs



Baseline IOP (mmHg)	Non-inferiority
<30	Did not meet**
<28	Met
<27	Met
<26	Met
<25*	Met
<24	Met
<22	insufficient power

\*Primary endpoint

\*\* Missed 2 time points by  $\leq 0.03$  mmHg

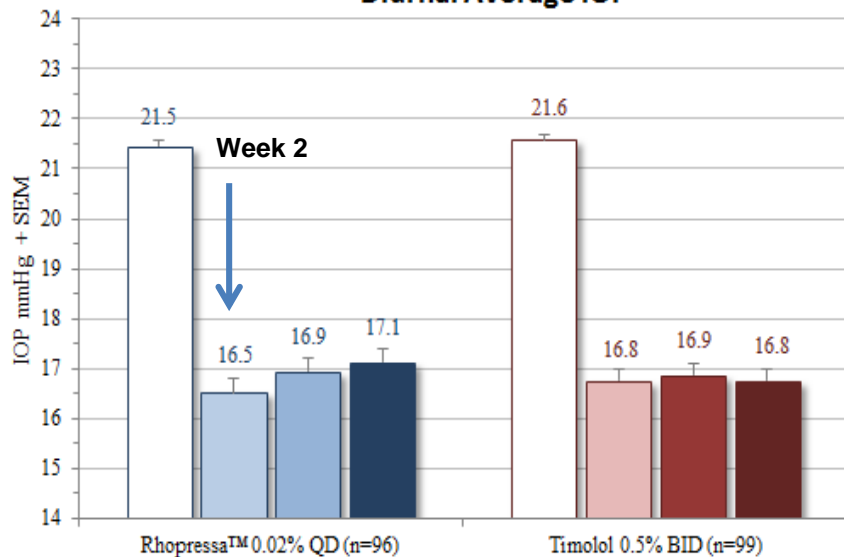
++Data on File

Based on Rocket 4 Topline Interim 3-month efficacy

# Rocket 4

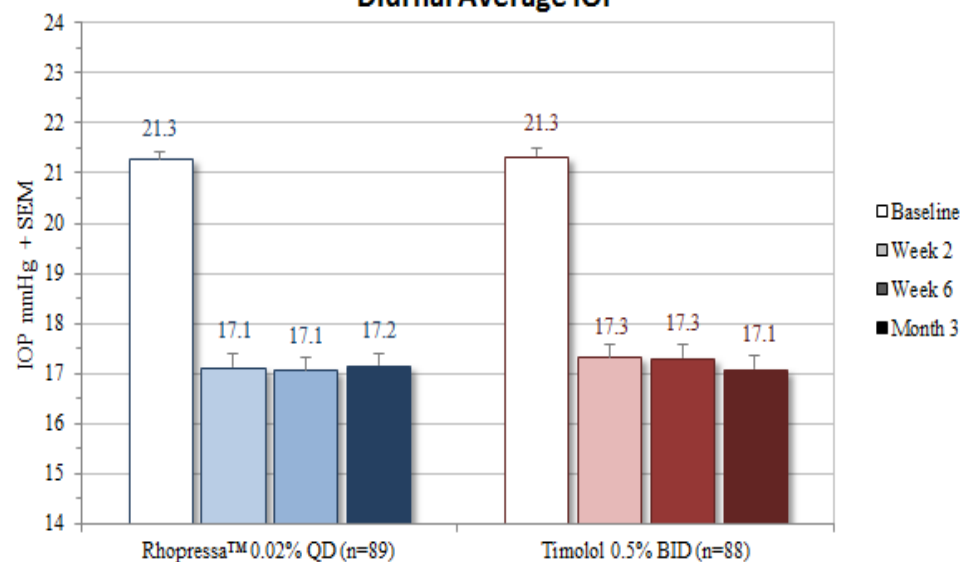
## Rhopressa™ Synergy with PGAs

Diurnal Average IOP



Prior PGA

Diurnal Average IOP



No Prior PGA

- Rhopressa™ synergy with prior PGA use evident at Week 2
- Observed in previous Rhopressa™ trials

# Safety/Tolerability Overview of Rhopressa™



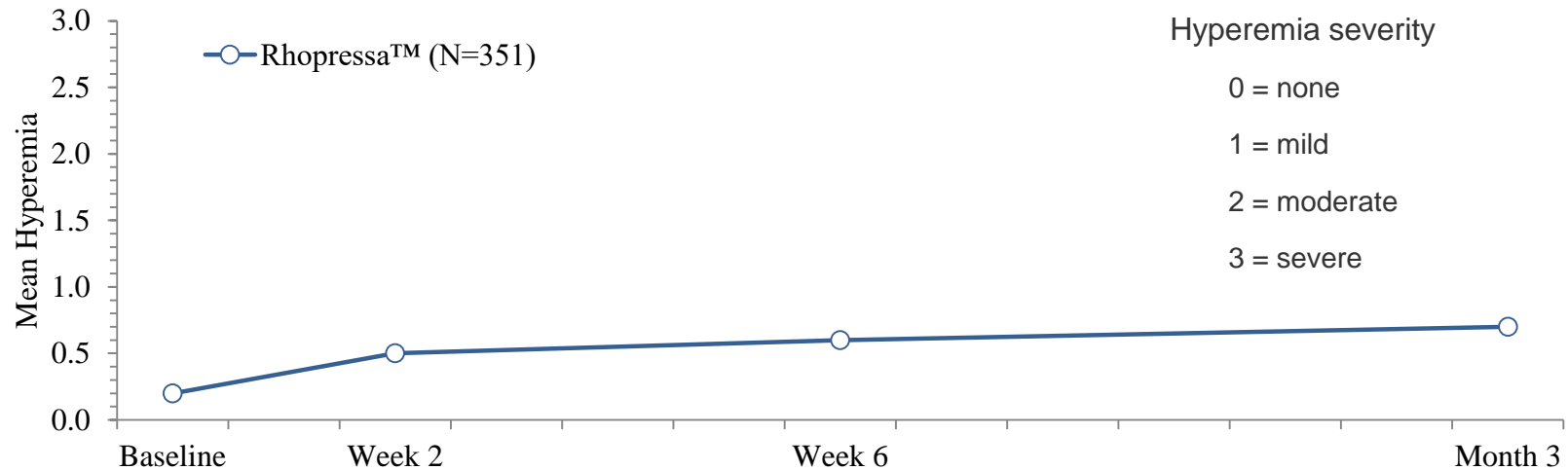
- There were no drug-related serious adverse events (SAEs)
- There was no evidence of treatment-related systemic effects (e.g., clinical laboratory or haematology values, heart rate or blood pressure)
- The most common adverse event was conjunctival hyperemia with ~40% incidence and was scored as mild for ~85% of the patients
- Other ocular AEs
  - AEs occurring in ~5-12% of subjects receiving Rhopressa™ included: conjunctival hemorrhage, cornea verticillata, lacrimation increased and vision blurred

# Rhopressa™ Phase 3 Safety Profile

Adverse Events (≥5% in any group)	Rhopressa™ QD N = 351	Timolol BID N = 357
<b>Eye Disorders</b>		
Conjunctival Hyperemia	148 (42.2%)	24 (6.7%)
Conjunctival Hemorrhage	41 (11.7%)	7 ( 2.0%)
Cornea Verticillata	41 (11.7%)	0 ( 0.0%)
Lacrimation Increased	21 ( 6.0%)	4 ( 1.1%)
Vision Blurred	20 ( 5.7%)	2 (0.6%)
<b>Administration Site Conditions</b>		
Instillation Site Pain	82 (23.4%)	89 (24.9%)
Instillation Site Erythema	36 (10.3%)	3 (0.8%)

Patients with known contraindications or hypersensitivity to timolol were excluded





# No Change in Mean Hyperemia Score Over Time (Interim Month 3)



- Hyperemia severity did not increase with continued dosing
- Hyperemia was sporadic
  - Only ~16% of patients had hyperemia on each study visit day from week 2 to month 3 (similar to the rates seen for Rocket 1, Rocket 2 and Mercury 1)
  - In Rocket 2, only ~10% of patients had hyperemia on each study visit day from week 2 to month 12

# When Present, ~85% of Rhopressa™ Hyperemia Graded as Mild



Grade	Image	Description
0		None/Normal
1		Mild
2		Moderate
3		Severe

**For illustrative purposes only**



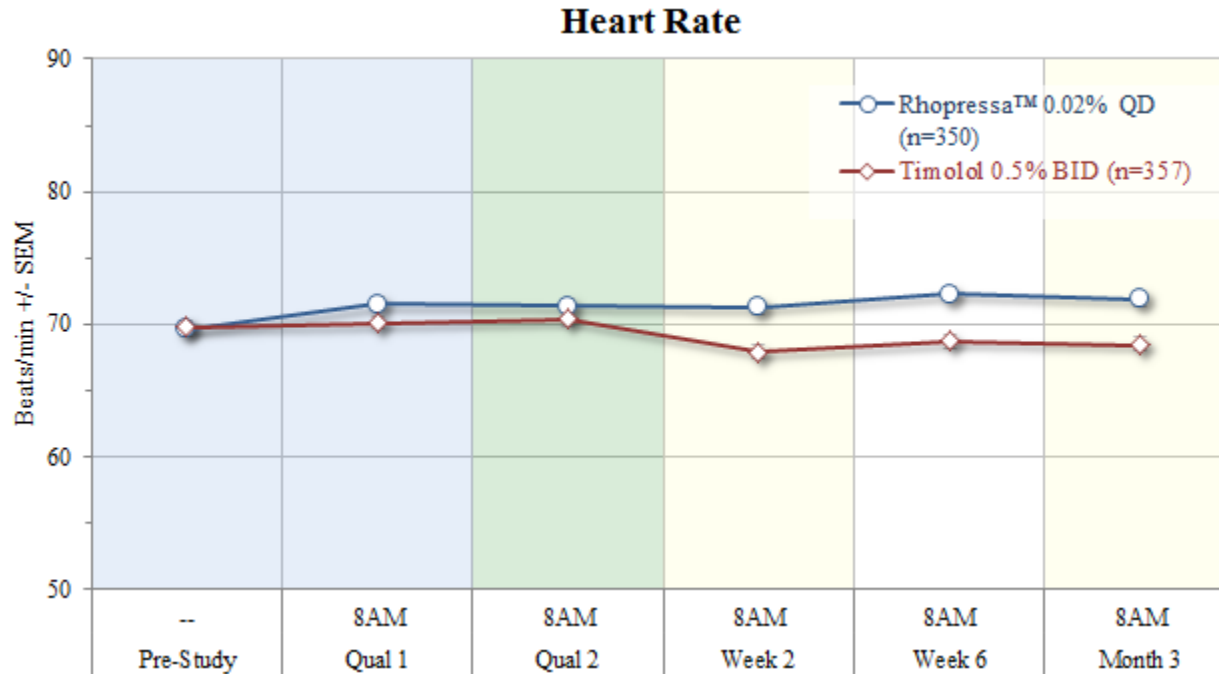
# Rhopressa™ Adverse Events Summary

- Conjunctival Hemorrhage
  - sporadic subconjunctival petechiae
- Cornea Verticillata
  - asymptomatic non-toxic lipid deposits
  - only visible via biomicroscopy evaluation
- Instillation Site Pain
  - same incidence as timolol
  - transient

++Data on File

Based on Rocket 4 Topline Interim 3-month safety

# Timolol Caused Statistically Significant Reduction in Heart Rate (Rocket 4)



- Timolol reduced mean heart rate by 2 - 3 beats per minute (average across all patients;  $p < 0.001$ )
- Despite all measures to exclude patients with possible negative sensitivity to beta-blockers

# Rhopressa™ Performance Summary To Date

Well researched with nearly 2,000 clinical patients

Once-daily efficacy demonstrated in 4 Phase 3 trials  
(Rocket 1, 2, 4 and Mercury 1)

Stable efficacy through 12 months

Synergistic/additive effect with prostaglandin analogues

Well-tolerated with no evidence of treatment-related systemic effects

Promising early results: e.g., trabecular meshwork anti-fibrotic/disease modification and 24-hour IOP control

# Rhopressa™ and Roclatan™ Key Milestones

**Q1-2016: Rhopressa™**  
Rocket 2 Topline safety (12 mos)

**Q4-2016: Rhopressa™**  
Rocket 4 Topline efficacy (3 mos)

**Q1-2017: Rhopressa™**  
NDA re-filing expected

**Q2-2017: Rhopressa™**  
Rocket 4 Topline safety (6 mos)

2016

2017

**Q1-2016: Roclatan™**  
P3 Mercury 2  
initiated

**Q3-2016: Roclatan™**  
P3 Mercury 1  
Topline efficacy (3 mos)

**1H-2017: Roclatan™**  
P3 Mercury 3 (EU)  
to be initiated

**Q2-2017: Roclatan™**  
P3 Mercury 2  
Topline efficacy (3 mos)

**Near YE 2017: Roclatan™**  
NDA filing expected

**Q3-2017: Roclatan™**  
P3 Mercury 1  
Topline safety (12 mos)