Roclatan™
Mercury 2 Phase 3 Topline Results

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

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Roclatan™ Achieves Primary Efficacy Endpoint in Mercury 2

- Roclatan™ met the criteria for demonstrating superiority ($p<0.0001$) over both latanoprost and Rhopressa™ for the primary efficacy analysis
- IOP-lowering effect of Roclatan™ was greater (1-3 mmHg) than monotherapy with either latanoprost or Rhopressa™ throughout the duration of the study (i.e., Week 2, Week 6, Month 3)
- Roclatan™ reduced mean diurnal IOPs to 16 mmHg or lower in 56% of patients, a significantly higher percentage than observed in the comparator arms (25% Rhopressa™, 36% latanoprost)
- The most common adverse event for Roclatan™ was conjunctival hyperemia, which was reported in nearly 55% of patients and was scored as mild for ~70% of these patients
- There were no drug-related serious or systemic adverse events

Mercury 2 Results Consistent with Mercury 1 90-day Efficacy Results

[++]Data on File
Based on Mercury 1 Topline Interim 3-Month and Mercury 2 Topline

Roclatan™ U.S. Registration Trial Design

"Mercury 1"
One Year Safety (3 Mo. Interim Efficacy) Registration Trial U.S.

- Roclatan™ 0.02%/0.005% QD 238 patients
- Rhopressa™ 0.02% QD 244 patients
- latanoprost QD 236 patients

"Mercury 2"
90-Day Efficacy Registration Trial U.S. and Canada

- Roclatan™ 0.02%/0.005% QD 245 patients
- Rhopressa™ 0.02% QD 255 patients
- latanoprost QD 250 patients

ClinicalTrials.gov Identifier: NCT02558400, NCT02674854

Mercury 2 Trial Design

Patients with open angle glaucoma (OAG) or ocular hypertension (OHT)

with IOP >20 mmHg and < 36 mmHg at 8am

N=750 subjects randomized at 59 sites in US and Canada

Patients randomized 1:1:1

Roclatan™
PG324
(netarsudil/latanoprost)
0.02%/0.005%
QD (PM)

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

Latanoprost
0.005%
QD (PM)

Primary endpoints:

- Efficacy: Mean IOP at nine time points (08:00, 10:00, and 16:00 at Week 2, Week 6, and Month 3)
- Safety: Ocular and systemic safety during a 3-month treatment period

ClinicalTrials.gov Identifier: NCT02674854

Mercury 2 Patient Disposition

	Roclatan™ N = 245	Rhopressa™ N = 255	Latanoprost N = 250
Completed Month 3	**221 (90.2%)**	**228 (89.4%)**	**236 (94.4%)**
Discontinued Prior to Month 3	**24 (9.8%)**	**27 (10.6%)**	**14 (5.6%)**
Reasons for Discontinuation			
Adverse Event	17 (6.9%)	15 (5.9%)	5 (2.0%)
Withdrawal of Consent	1 (0.4%)	5 (2.0%)	4 (1.6%)
Non-Compliant	1 (0.4%)	0	1 (0.4%)
Lost to Follow-up	1 (0.4%)	0	2 (0.8%)
Lack of Efficacy	0	3 (1.2%)	0
Disallowed Concurrent Medication	2 (0.8%)	2 (0.8%)	0
Protocol Violation	1 (0.4%)	1 (0.4%)	2 (0.8%)
Other	1 (0.4%)	1 (0.4%)	0

++Data on File
Based on Mercury 2 Topline

Study Design and Analysis

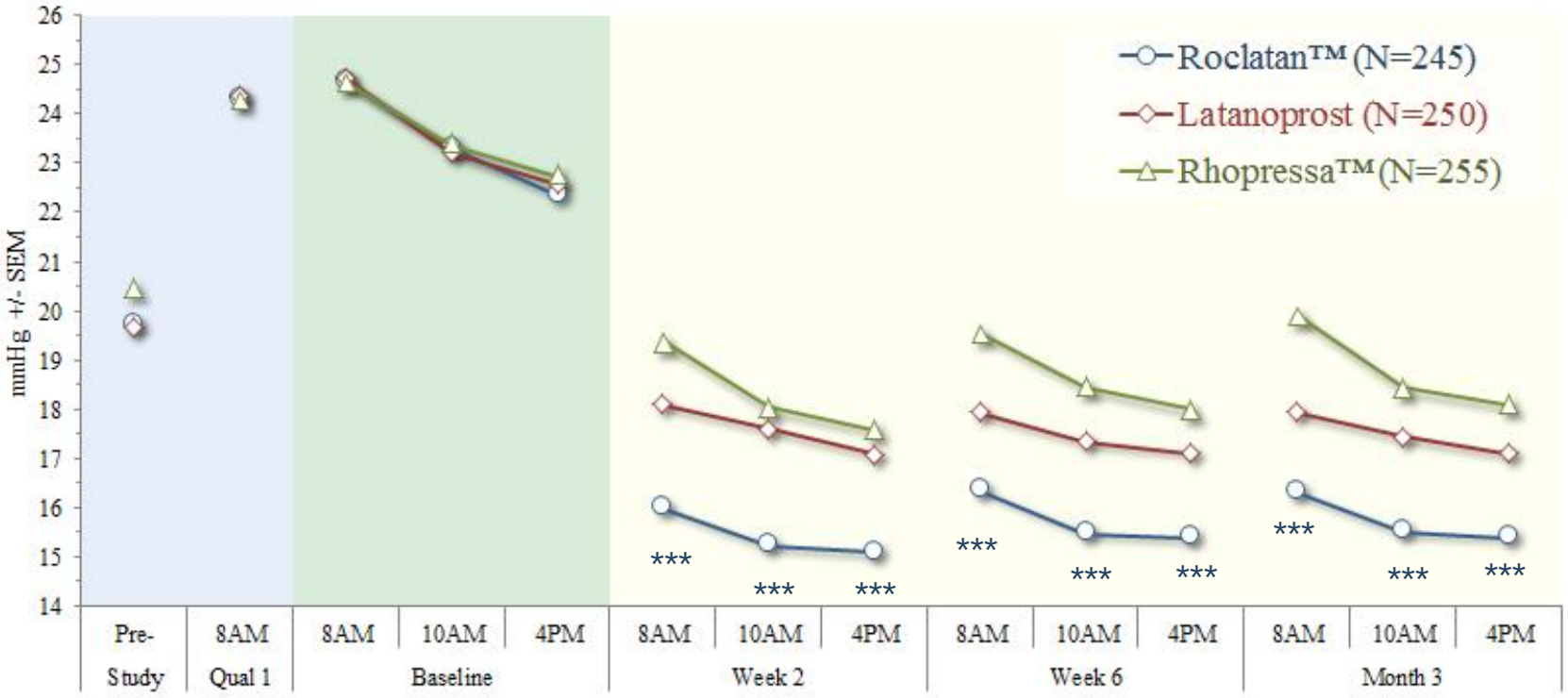
- Trial design followed FDA requirement for fixed dose combinations
  - Superiority of combination over each individual component
  - Statistically significant difference at each measured time point
  - Higher combo efficacy vs. components at ~1-3 mmHg, as previously accepted by FDA for product approval (i.e., Simbrinza®*)
- The primary statistical modeling of the primary efficacy analysis was agreed with the FDA using the intent to treat (ITT) population with imputation for any missing data (ANCOVA-MCMC), consistent with Mercury 1

Based on PG324 End Of Phase 2 meeting

*Simbrinza® accessed on 29th Sept 2016 http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/204251Orig1s000MedR.pdf

Roclatan™ Achieved Statistical Superiority Over Individual Components at All 9 Time Points

Mean IOP at Each Time Point (ITT)



***p<0.0001 vs Latanoprost and Rhopressa™

Same p values obtained in Per Protocol, LOCF analyses

++Data on File
Based on Mercury 2 Topline

Mercury 2 Roclatan™ Phase 3, ITT

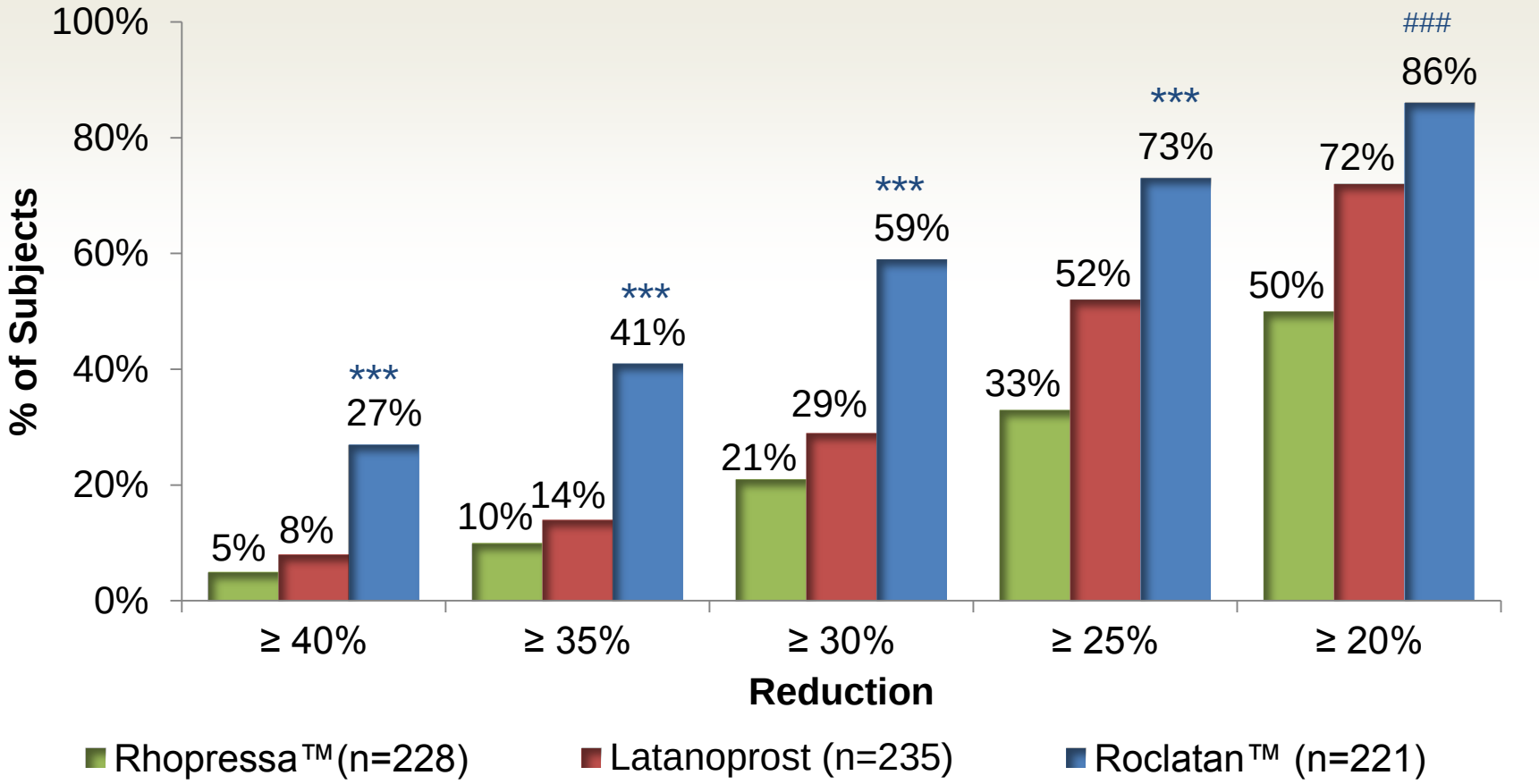
	Mean IOP mmHg			Difference from Roclatan™ (95% CI)	
	Roclatan™ N=245	Rhopressa™ N=255	Latanoprost N=250	Rhopressa™	Latanoprost
Baseline					
8:00 AM	24.7	24.7	24.8		
10:00 AM	23.3	23.4	23.2		
4:00 PM	22.4	22.8	22.6		
Mean Diurnal	**23.5**	**23.6**	**23.5**		
Day 15					
8:00 AM	16.1	19.4	18.1	-3.3 (-3.9, -2.8)	-2.0 (-2.6, -1.5)
10:00 AM	15.3	17.9	17.7	-2.6 (-3.2, -2.1)	-2.4 (-2.9, -1.8)
4:00 PM	15.3	17.4	17.1	-2.2 (-2.7, -1.7)	-1.8 (-2.3, -1.3)
Mean Diurnal	**15.6**	**18.2**	**17.6**	**-2.7 (-3.1, -2.2)**	**-2.1 (-2.5, -1.6)**
Day 43					
8:00 AM	16.4	19.5	17.9	-3.1 (-3.7, -2.5)	-1.5 (-2.1, -0.9)
10:00 AM	15.5	18.4	17.4	-2.8 (-3.4, -2.3)	-1.9 (-2.4, -1.3)
4:00 PM	15.6	17.9	17.1	-2.3 (-2.8, -1.7)	-1.5 (-2.1, -1.0)
Mean Diurnal	**15.9**	**18.6**	**17.5**	**-2.7 (-3.2, -2.2)**	**-1.6 (-2.1, -1.1)**
Day 90					
8:00 AM	16.5	19.8	18.0	-3.3 (-3.9, -2.7)	-1.5 (-2.1, -0.9)
10:00 AM	15.6	18.3	17.5	-2.7 (-3.3, -2.1)	-2.0 (-2.5, -1.4)
4:00 PM	15.6	17.9	17.1	-2.2 (-2.8, -1.7)	-1.5 (-2.1, -0.9)
Mean Diurnal	**15.9**	**18.6**	**17.5**	**-2.7 (-3.2, -2.2)**	**-1.7 (-2.1, -1.2)**

- Roclatan™ superior to latanoprost by 1.5 - 2.4 mmHg ($p<0.0001$)
- Roclatan™ superior to Rhopressa™ by 2.2 - 3.3 mmHg ($p<0.0001$)

++Data on File
Based on Mercury 2 Topline

Mercury 2 Roclatan™ Responder Analysis

Day 90: % of Patients with IOP Reductions of ≥ 20%



***p<0.0001 vs Latanoprost and Rhopressa™

###p<0.0001 vs Rhopressa™, p<0.001 vs Latanoprost

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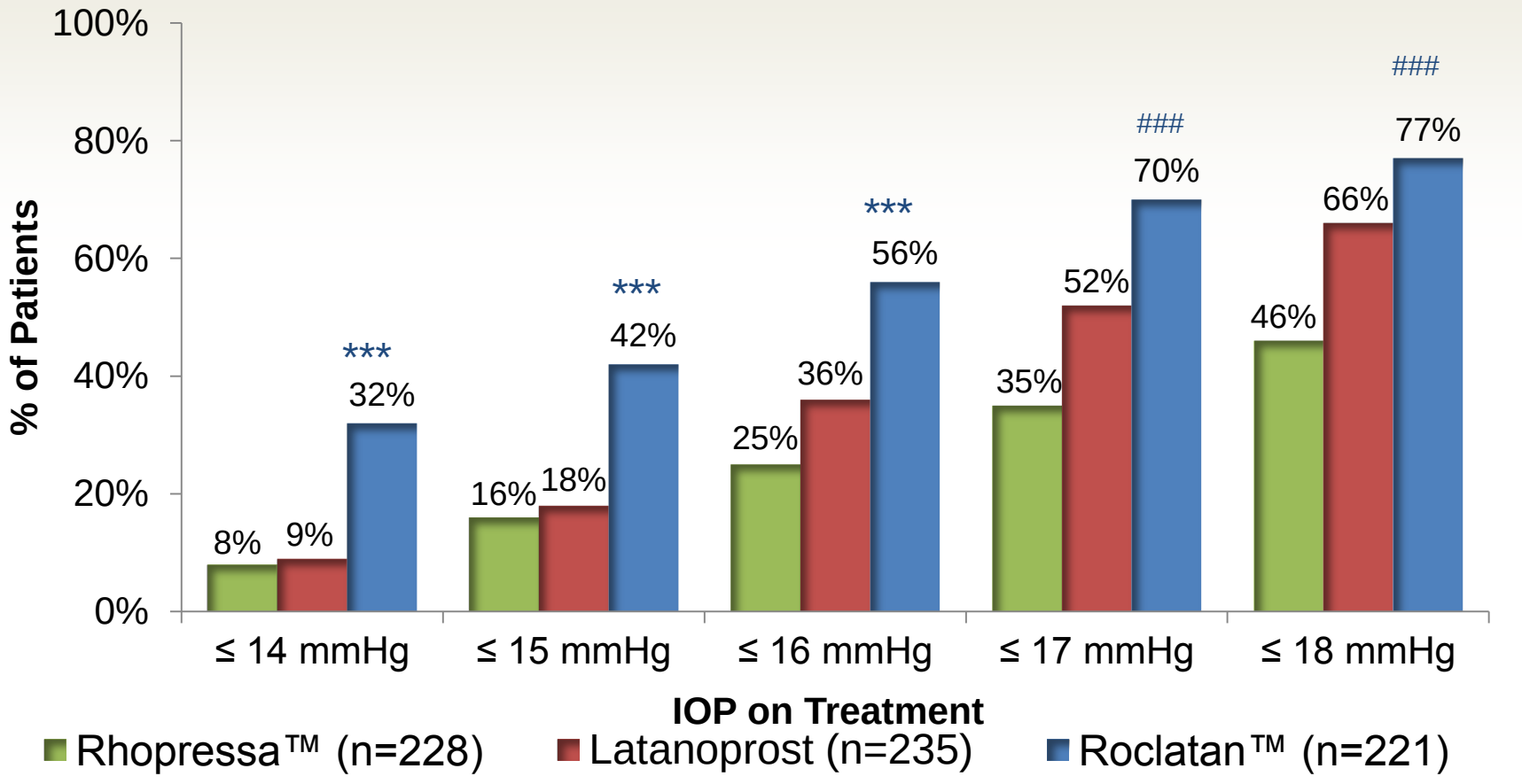
Based on Mercury 2 Topline

N's are Day 90 subject numbers

Mercury 2 Roclatan™ Responder Analysis

Day 90: % of Patients with IOP Reduced to 18 mmHg or Lower



***p<0.0001 vs Latanoprost and Rhopressa™

###p<0.0001 vs Rhopressa™, p<0.05 vs Latanoprost

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Based on Mercury 2 Topline

N's are Day 90 subject numbers

Mercury 2 Roclatan™ Safety Profile

- 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 in nearly 55% incidence, ~70% graded as mild on biomicroscopy
- Other ocular AEs
  - AEs occurring in ~5-13% of subjects receiving Roclatan™ included: cornea verticillata, conjunctival hemorrhage (petechiae) and corneal disorder (asymptomatic change in appearance of corneal endothelial cells)

++Data on File
Based on Mercury 2 Topline

Mercury 2 Roclatan™ Safety Profile

Adverse Events (≥5.0% in any group)	Roclatan™ n=244	Rhopressa™ n=255	Latanoprost n=251
Eye Disorders			
Conjunctival Hyperemia	133 (54.5%)	109 (42.7%)	56 (22.3%)
Cornea Verticillata	32 (13.1%)	25 (9.8%)	0 (0.0%)
Conjunctival Hemorrhage	21 (8.6%)	28 (11.0%)	2 (0.8%)
Corneal Disorder	14 (5.7%)	12 (4.7%)	0 (0.0%)
Administration Site Conditions			
Instillation Site Pain	42 (17.2%)	23 (9.0%)	15 (6.0%)
Instillation Site Discomfort	15 (6.1%)	16 (6.3%)	2 (0.8%)

Patients with known contraindications or hypersensitivity to latanoprost were excluded

++Data on File
Based on Mercury 2 Topline

Corneal Endothelial Cell Evaluation

- FDA requires specular microscopy in at least 100 subjects to ensure no loss of corneal endothelial cell density over 3 months
  - Conducted in Mercury 2 for Roclatan™ (Rocket 2 for Rhopressa™)
  - Centralized reading center confirmed no cell loss for Roclatan™ and Rhopressa™
  - Slight increase in cell density observed for Roclatan™ or Rhopressa™ (also in Rocket 2 for Rhopressa™), slight decrease for latanoprost
- No significant changes in corneal endothelial cell hexagonality (shape)
- Corneal disorder AE noted upon specular microscopy by 2 of 35 sites
  - Asymptomatic change in appearance of corneal endothelial cells noted by two investigators
  - No change in endothelial cell count or corneal thickness, and no corneal edema
  - Similar finding reported for ROCK inhibitor, ripasudil (marketed in Japan), which was identified as transient*

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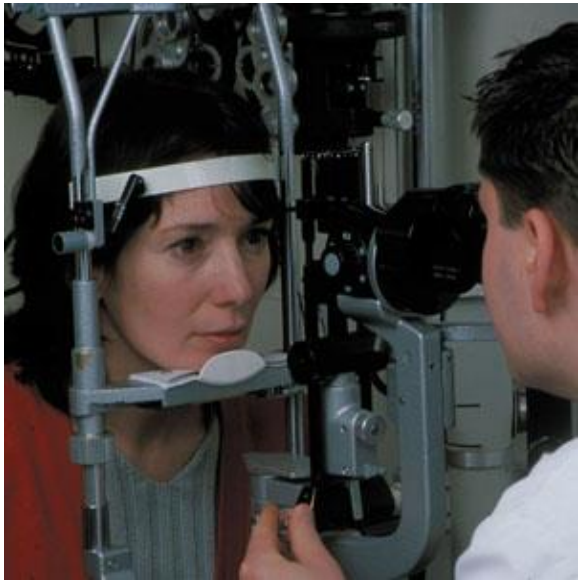
Based on Rocket 2 12-month safety and Mercury 2 Topline

*Okumura et al. Rho-Associated Kinase Inhibitor Eye Drop (Ripasudil) Transiently Alters the Morphology of Corneal Endothelial Cells. IOVS, November 2015. Vol. 56. No. 12; 7560-7567.

When Present, ~70% of Roclatan™ and Rhopressa™ Hyperemia Graded as Mild



Grade	Image	Description
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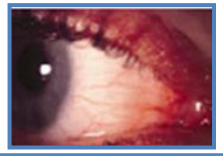
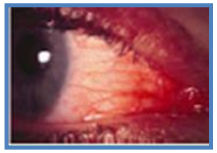
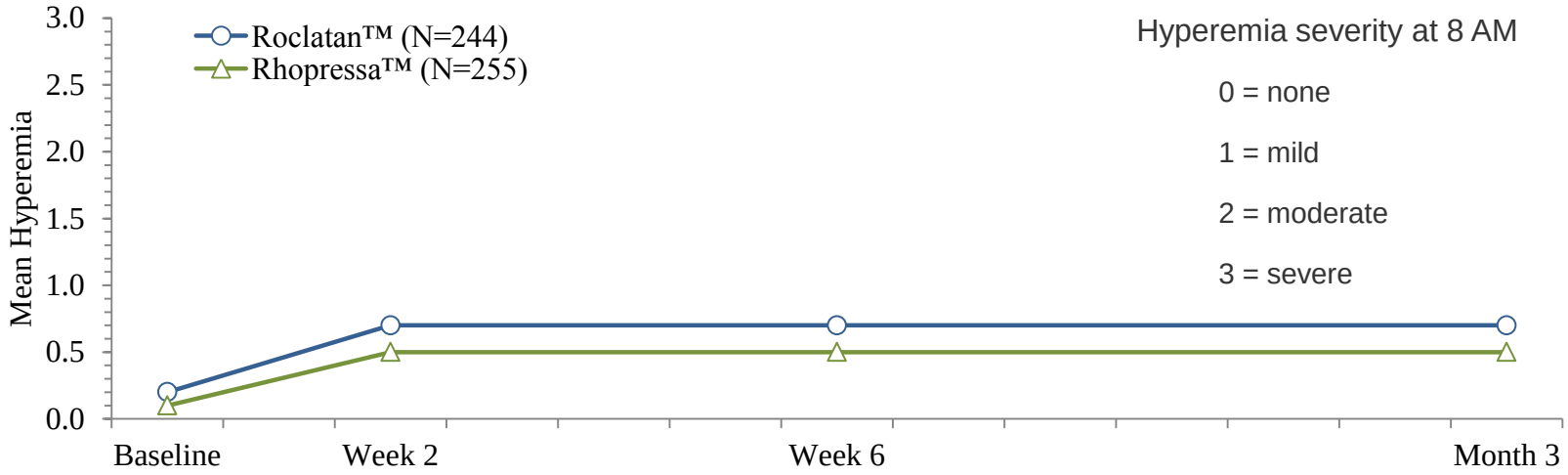
1		Mild
2		Moderate
3		Severe

For illustrative purposes only

++Data on File
Based on Mercury 2 Topline

No Change in Mean Hyperemia Score Over Time



- Hyperemia severity did not increase with continued dosing
- Hyperemia was sporadic
  - Only 23% of Rhopressa™ patients and 25% of Roclatan™ patients had hyperemia on each study visit day from week 2 to month 3 (similar to the rate seen for Mercury 1)
- ~ 15% of all patients had hyperemia at baseline (similar to the rates seen in Mercury 1)
- *Only 2.0% of all Rhopressa™ patients and 2.5% of all Roclatan™ patients discontinued due to hyperemia*

++Data on File
Based on Mercury 2 Topline

Mercury 2 Rhopressa™ Performance

- Two populations were pre-specified for comparison of Rhopressa™ to latanoprost: subjects with baseline IOP <25 mmHg and baseline IOP <23 mmHg
- Rhopressa™ demonstrated non-inferiority to latanoprost in patients with baseline IOP < 23 mmHg
- Rhopressa™ did not achieve non-inferiority to latanoprost in patients with baseline IOP < 25 mmHg
  - Missed at 2 of 9 time points by 0.2 and 0.7 mmHg
  - Rhopressa™ achieved non-inferiority to latanoprost in Mercury 1 at baseline IOP <25 mmHg
- Rhopressa™ maintained consistent level of IOP lowering across all baseline IOPs including ≥ 25 mmHg
- Stable efficacy across the duration of the trial
- Adverse event profile consistent with previous studies

++Data on File
Based on Mercury 1 Topline Interim 3-Month and Mercury 2 Topline

Mercury 2 Roclatan™ Summary

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Mercury 2 Results Consistent with Mercury 1 90-day Efficacy Results

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Based on Mercury 1 Topline Interim 3-Month and Mercury 2 Topline

Roclatan™ Next Steps

- Mercury 1 Topline 12-month safety results expected Q3 2017
- Roclatan™ NDA filing expected H1 2018
- Aerie Ireland plant and 2 contract manufacturers are expected to support Roclatan™ US commercial activities
- Mercury 3 to commence in Europe mid-2017; regulatory submission expected in H2 2019