



# Retinal Disease Program

OIS®ASRS Presentation  
July 2019

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Any discussion of the potential use or expected success of Rhopressa® (netarsudil ophthalmic solution) 0.02% or Rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%, with respect to foreign approval or additional indications, and our current or any future product candidates, including AR-1105 and AR-13503, is subject to regulatory approval. In addition, any discussion of U.S. Food and Drug Administration (“FDA”) approval of Rhopressa® or Rocklatan® does not guarantee successful commercialization of Rhopressa® or Rocklatan®. For more information on Rhopressa®, including prescribing information, refer to the full Rhopressa® product label at [www.rhopressa.com](http://www.rhopressa.com). For more information on Rocklatan®, including prescribing information, refer to the full Rocklatan® product label at [www.rocklatan.com](http://www.rocklatan.com).

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## Aerie IOP-Reducing Products (IP 2030+)

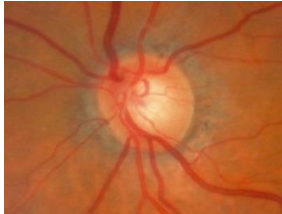
- **Rhopressa<sup>®</sup>** (netarsudil ophthalmic solution) 0.02%
  - *Successful U.S. Launch in 2018*
- **Rocklatan<sup>®</sup>** (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%
  - *Launched May 1, 2019*
- **Aerie Ireland manufacturing plant expected to be online early 2020**
- **Globalization Plan Under Way – Europe and Japan**



## Pipeline Activities

- **Rhopressa<sup>®</sup>** – normal tension glaucoma, pseudo ex glaucoma, corneal healing...
- **Retina Program** – AR-13503 (IND accepted by FDA Q2 2019) and AR-1105 (Phase 2 clinical study commenced Q1 2019) implants
- **Sustained-Release Implant Manufacturing Platform**
- **Beyond Ophthalmology** – potential for Aerie-owned molecules

# Advancing the Pipeline



## Glaucoma

IOP-lowering  
Neuro-  
enhancement



## Retina

Inflammation  
Fibrosis  
Edema  
Angiogenesis



## Dry Eye

Tear quality  
Inflammation  
Discomfort



## Refractive

Increase  
visual acuity  
Prevent vision  
loss



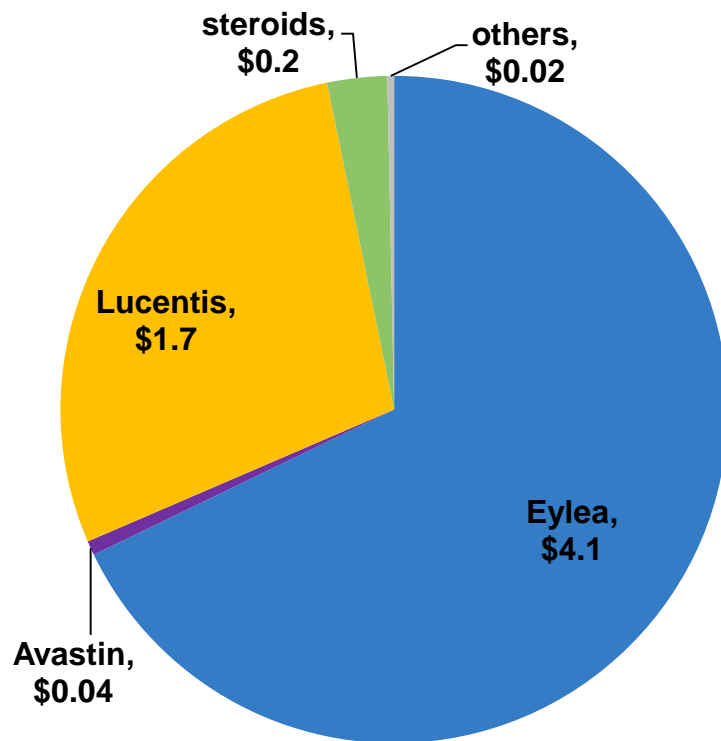
## Psoriasis

Inflammation  
Pain  
Macules

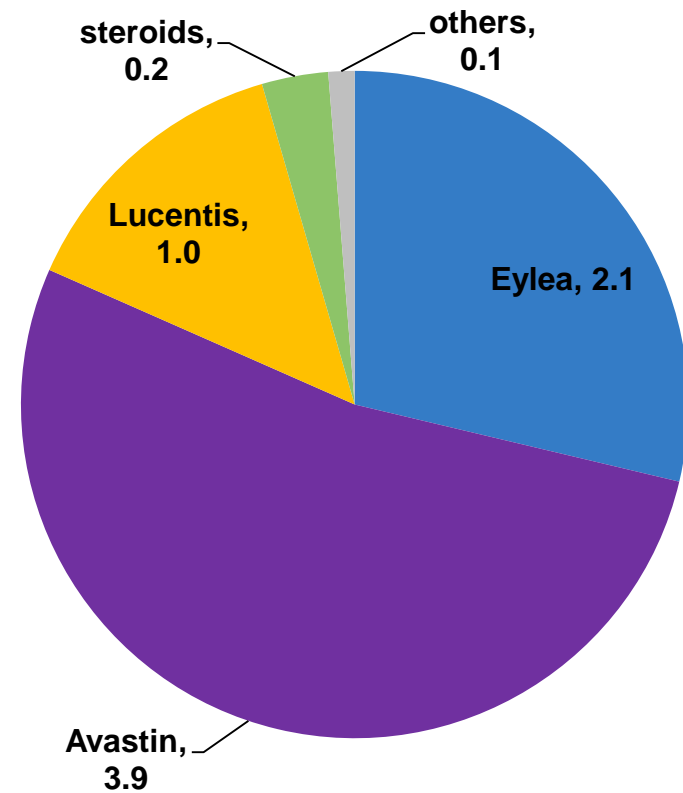
**Evaluating Aerie's 4,000+ Owned Molecules**

# 2018 U.S. Retinal Disease Market

## 2018 Sales: \$6.0B

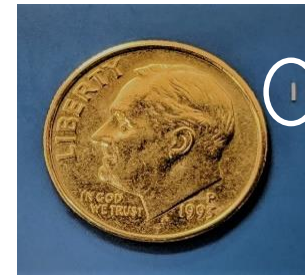


## 2018 Unit Sales: 7.3MM



## Bringing Small Molecule Therapy to Back of the Eye

- Most retinal drugs in use and in pipeline are protein therapeutics
  - Longer half-life allows monthly to bimonthly IVT injections
- Protein therapeutics address limited number of extracellular targets
- Small molecules address a wider array of therapeutic targets, but are rapidly cleared from back of the eye

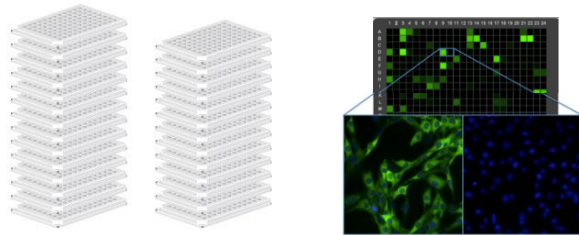


### The Solution:

**Pair small molecules with a safe and effective sustained delivery technology to enable IVT injections every 4 - 6 months**

# Aerie's Innovation in Retinal Disease

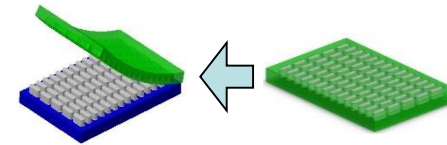
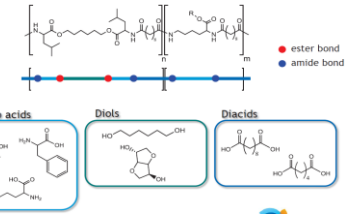
## Small Molecule Drug Candidates



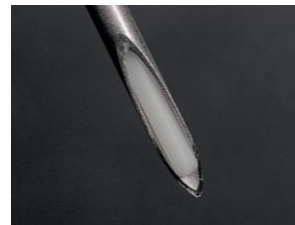
- Aerie Kinase Library
- Non-Aerie drug candidates

## Proprietary Drug Delivery Technology

- DSM PEA Polymer
- PLGA



- PRINT<sup>®</sup> Mfg



- Bio-erodible, sustained-release implant for intravitreal injection

AMD    DME    RVO    Dry AMD/GA    Glaucoma    Others

- Need new treatments to address disease mechanisms beyond VEGF
  - Complex pathology cannot be addressed by a single drug class
  - Anti-VEGFs are used to treat the eye with wet AMD, while the second eye typically has dry AMD and a high risk of converting to wet AMD over time. There are no current treatment approaches to prevent this conversion.
- Many patients do not achieve and/or maintain sufficient efficacy
  - AMD: Anti-VEGF efficacy often lost after 5–7 years of treatment<sup>1</sup>
  - DME: Anti-VEGF is ineffective for ~1/3 of DME patients<sup>2</sup>

**Need treatments that are effective with less frequent intravitreal injections**



## AR-1105 (Dexamethasone) Implant

- Indications: retinal vein occlusion (RVO) and DME
- Target product profile vs. Ozurdex®
  - Longer duration of efficacy (6 mo vs 3 mo)
  - Improved administration due to smaller needle
  - Potential for fewer adverse effects due to lower peak drug levels

## AR-13503 (ROCK/PKC) Implant

- Initial indications: neovascular AMD and DME
- Novel MOA: anti-angiogenesis PLUS anti-fibrosis, anti-inflammation
- Effective as monotherapy or adjunctive therapy to anti-VEGF
- Targeting injection once every 6 months

# Preclinical Studies Support ROCK as a Therapeutic Target for Vitreoretinal Diseases

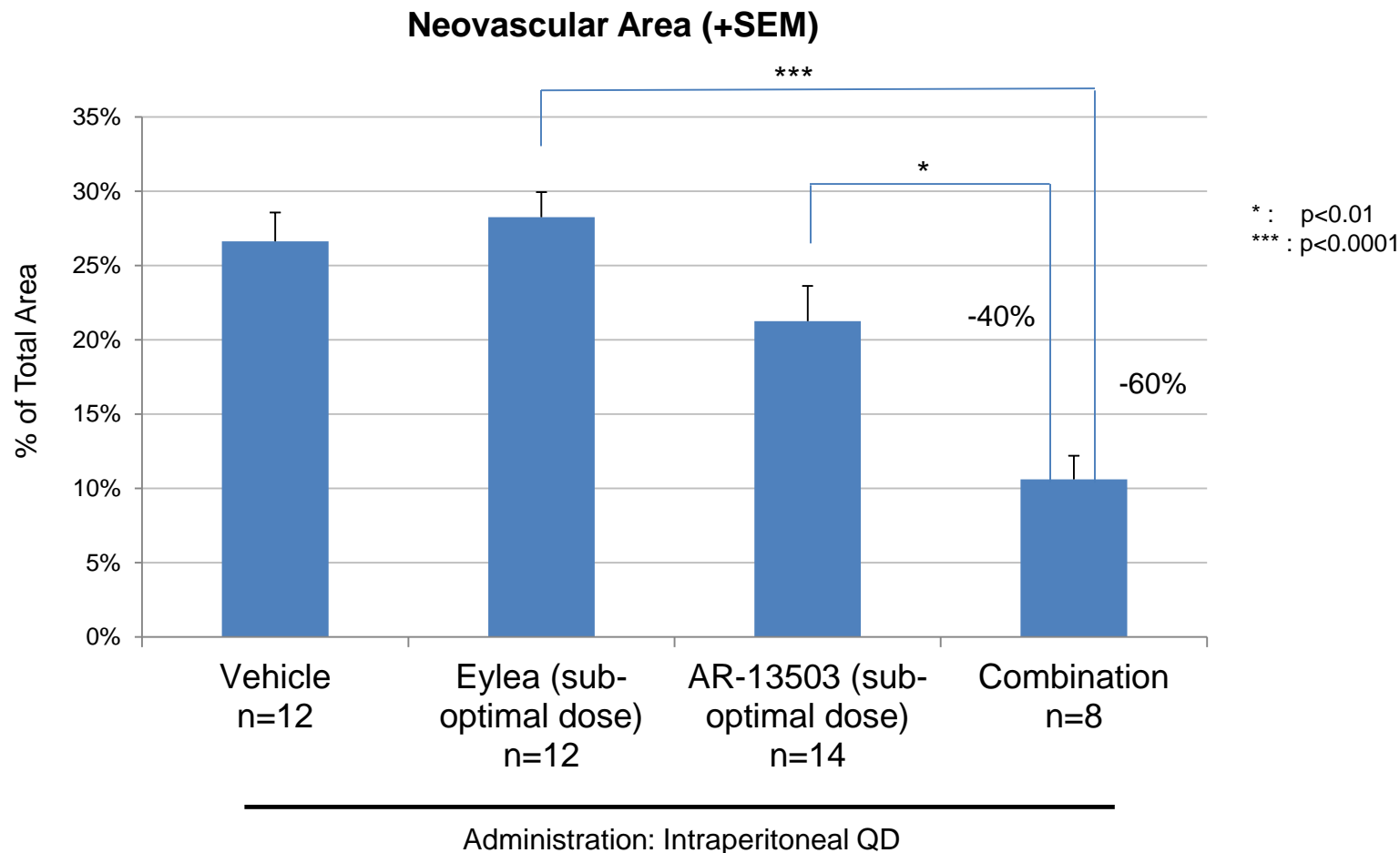
TABLE 2: ROCK inhibitors in animal models of vitreoretinal diseases.<sup>1</sup>

Animal model	OIR model (oxygen-induced retinopathy)	STZ model (streptozotocin-induced diabetes model)	CNV model (choroidal neovascularization model)	PVR (proliferative vitreoretinopathy model)
Fasudil	Antiangiogenesis [45]	Antileukostasis [38]	Antipermeability [63]; anti-M2 macrophage [63]; antiangiogenesis [63]	Inhibition of membrane contraction [50]
Ripasudil (K115)	Vascular normalization via pericyte coverage [45]; antiangiogenesis [45]	No report	No report	No report
Y27632	Antiangiogenesis [43]	No report	No report	Inhibition of membrane contraction [73]
AMA0428	Antiangiogenesis [89]; inhibition neuronal cell death [89]	Antileukostasis [89]; antipermeability [89]; neuroprotection of RGC [89]	Antiangiogenesis [66]; antifibrosis [66]; antiinflammation [66]	No report

- ROCK inhibitors target multiple drivers of disease<sup>2,3</sup>
  - Angiogenesis, blood-retinal barrier breakdown, vascular leakage, inflammation, fibrosis

# AR-13503 Synergistic to Eylea® in Mouse Model of Proliferative Diabetic Retinopathy

## Oxygen-induced retinopathy (OIR) mouse model - PDR



Data on File

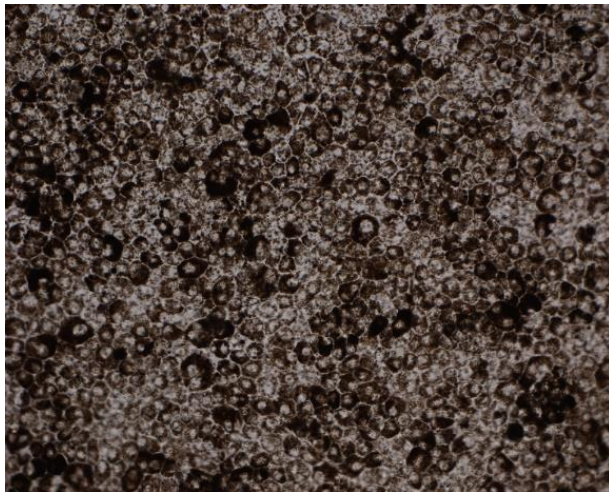
Sub-optimal dose levels selected in the study to provide less than maximal efficacy

For more information on Eylea® please see the product webpage <https://www.eylea.us/>

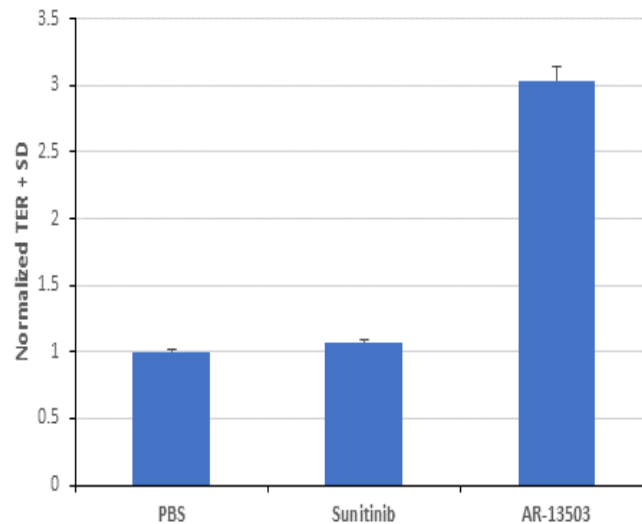
AR-13503 is a development stage product candidate and is not approved by any regulatory agency

# AR-13503 Improves RPE Barrier Function In Vitro

## Transepithelial Resistance Measured in Primary Porcine RPE Cells



RPE monolayer on trans-well filter



- Dysfunction of RPE/blood-retinal barrier leads to retinal edema in AMD, DR
- AR-13503 improves in vitro RPE barrier function by approximately 200%
- VEGFR inhibitor sunitinib had no effect on RPE barrier function

# Aerie Pipeline Summary

Drug/Target	Indication	Development Stage											
		Discovery				Preclinical				Phase 1/2a			
AR-1105 Implant (Dexamethasone)	RVO												
AR-13503 Implant (ROCK, PKC)	wAMD										IND✓		
	DME/DR										IND✓		
	Glaucoma Neuro-enhancement												
AR-xxxxx Implant (ROCK/JAK/IKK)	Dry AMD/GA												
AR-xxxxx (JAK, IKKb)	Dry Eye/MGD												
AR-xxxxx (ROCK, JAK, IKKb)	Psoriasis												

**Evaluating Aerie's 4,000+ Owned Molecules**