



# Company Overview

Investor Presentation

May 2021

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Any discussion of the potential use or expected success of Rhopressa<sup>®</sup> (netarsudil ophthalmic solution) 0.02% or Rocklatan<sup>®</sup> (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, AR-13503, AR-14034 and AR-15512, is subject to regulatory approval. In addition, any discussion of U.S. Food and Drug Administration (“FDA”) approval of Rhopressa<sup>®</sup> or Rocklatan<sup>®</sup> does not guarantee successful commercialization of Rhopressa<sup>®</sup> or Rocklatan<sup>®</sup>. For more information on Rhopressa<sup>®</sup>, including prescribing information, refer to the full Rhopressa<sup>®</sup> product label at [www.rhopressa.com](http://www.rhopressa.com). For more information on Rocklatan<sup>®</sup>, including prescribing information, refer to the full Rocklatan<sup>®</sup> product label at [www.rocklatan.com](http://www.rocklatan.com).

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

- **Rhopressa® and Rocklatan® gaining momentum in the U.S.**
  - Total prescriptions and shipments to pharmacies are achieving record levels
- **Glaucoma Franchise Approved in Europe**
- **Globalization Plan Under Way** – Concluded licensing agreement with Santen for Rhopressa® and Rocklatan®, potential collaborators pursuing European opportunity



## Key Pipeline Opportunities

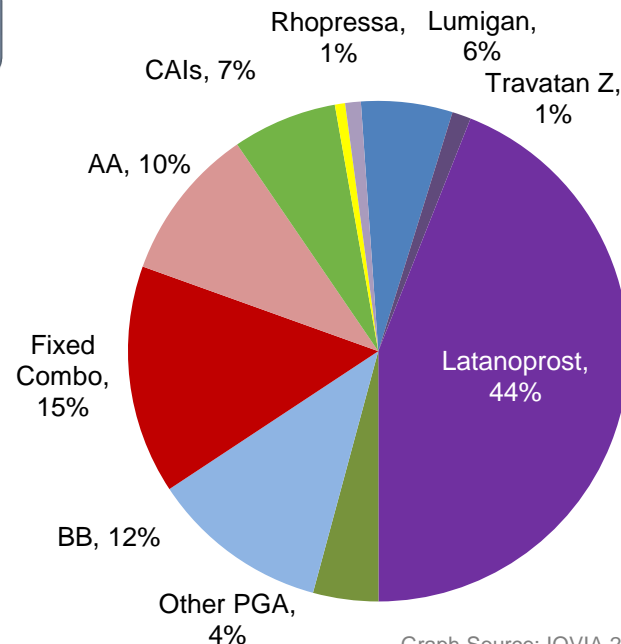
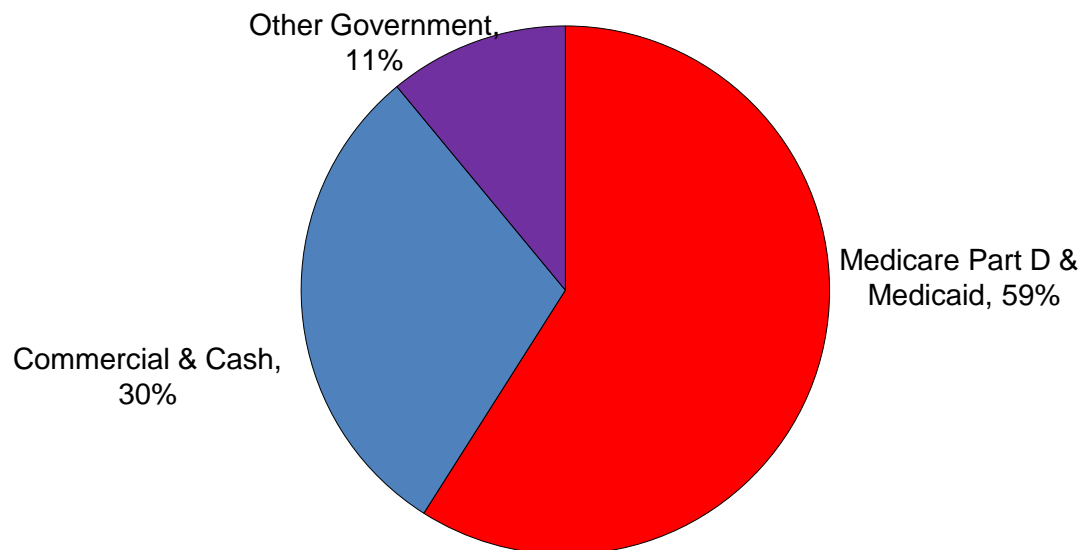
- **Dry Eye**
  - AR-15512 TRPM8 agonist:** Fully enrolled, Phase 2b Topline readout expected Q3 2021
- **Sustained-Release Retinal Implant Platform**
  - AR-1105 (Dex):** Positive Topline P2 results, Phase 3 plans underway for U.S. and Europe
  - AR-13503 SR (ROCK/PKC):** First-in-human clinical study commenced Q3 2019
  - AR-14034 SR (Pan-VEGF inhibitor):** IND-enabling preclinical studies underway; IND filing H2 2022

# Aerie Overview

## 2020 U.S. Glaucoma Market

- ~\$3B Market, 34M TRx, **55M bottles**
- 55% of unit volume first-line (PGAs)
- 45% of unit volume 2-3X/Day Adjuncts

## Estimated Glaucoma Market TRx Mix



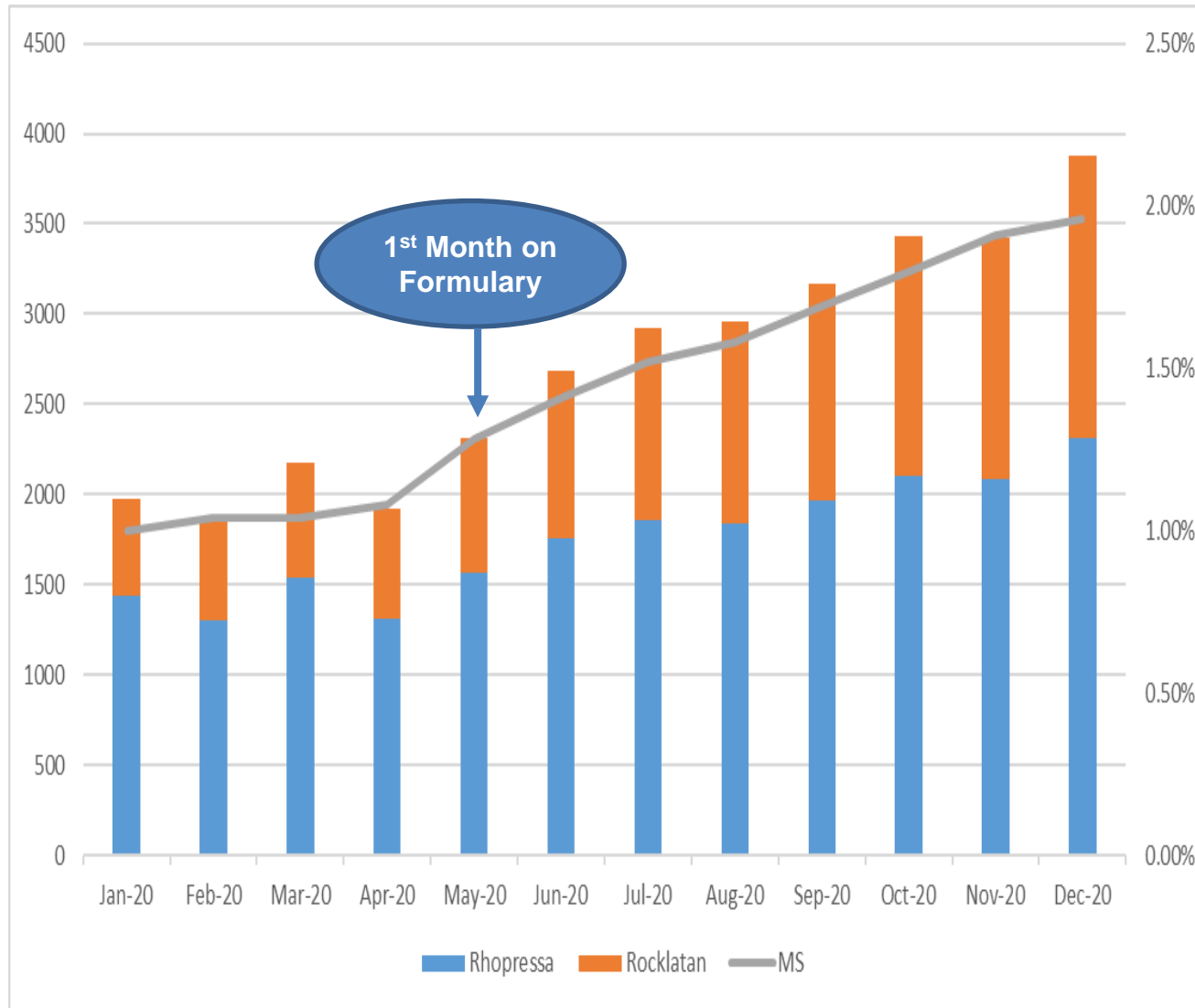
Graph Source: IQVIA 2020  
 CAI: Carbonic Anhydrase Inhibitor  
 AA: Alpha Agonist  
 BB: Beta Blocker

**Aerie's franchise bottles per Rx were 1.44 in Q1 2021, reflecting an increase in 90 days' supply.**

# Glaucoma Commercialization Focus

- Ongoing communication of the MOST Data and coverage via various communication channels
  - **Rhopressa® Coverage: 90% Commercial, 89% Med D**
  - **Rocklatan® Coverage: 89% Commercial, 59% Med D plus 15% Low Income Subsidy**
- Continued execution of the Pulse Strategy, focused on driving **monthly prescribers (now nearly 10,000)** to **weekly prescribers (now nearly 5,000)**
  - Franchise prescribers currently over 18,000
- Increasing share of voice with HCP's to further bolster sales momentum
  - Aerie reps calling on top 10,400 highest prescribers
  - Contract Sales Organization calling on next 1,400 highest prescribers
  - Telesales team calling on next 4,400 highest prescribers

# Focused on “Pull-Through” to Gain Share: Example from 05/01/20 Med D Coverage Win

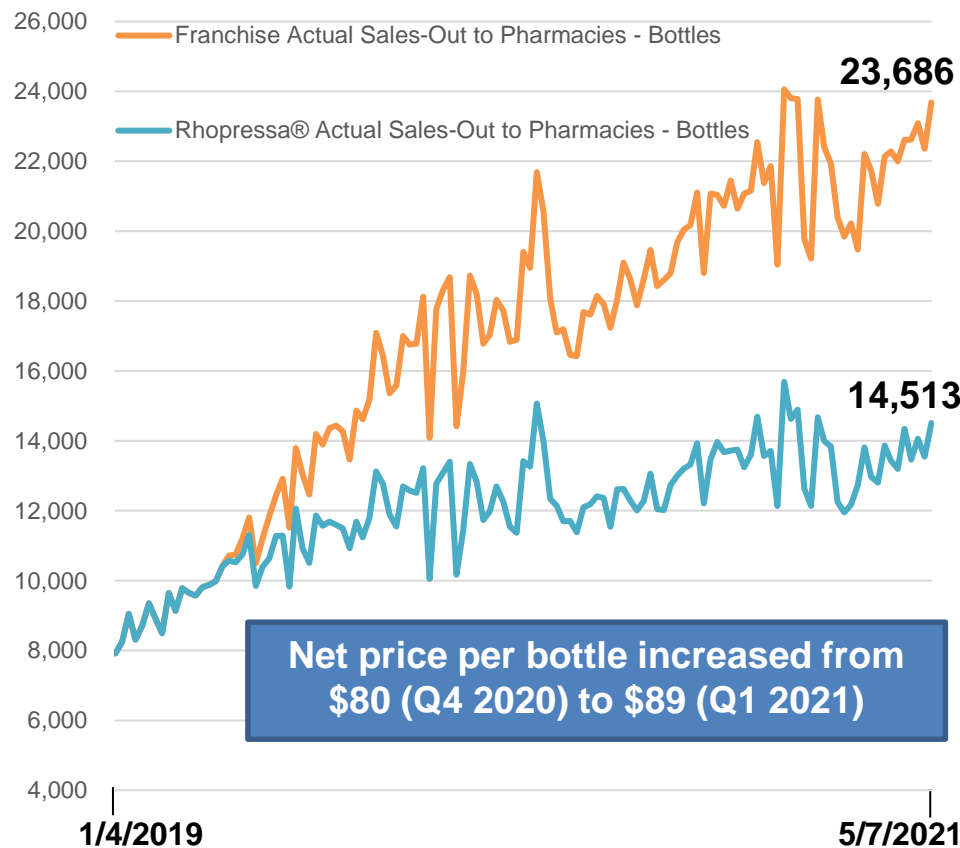


	Apr 2020 <sup>1</sup>	Dec 2020
National Market Share (Part D)	Aerie Franchise	
	1.9%	2.3%
New Payer Part D Market Share	Aerie Franchise	
	1.1%	2.0%
	Difference vs National MS (-0.8%)	Difference vs National MS (-0.3%)

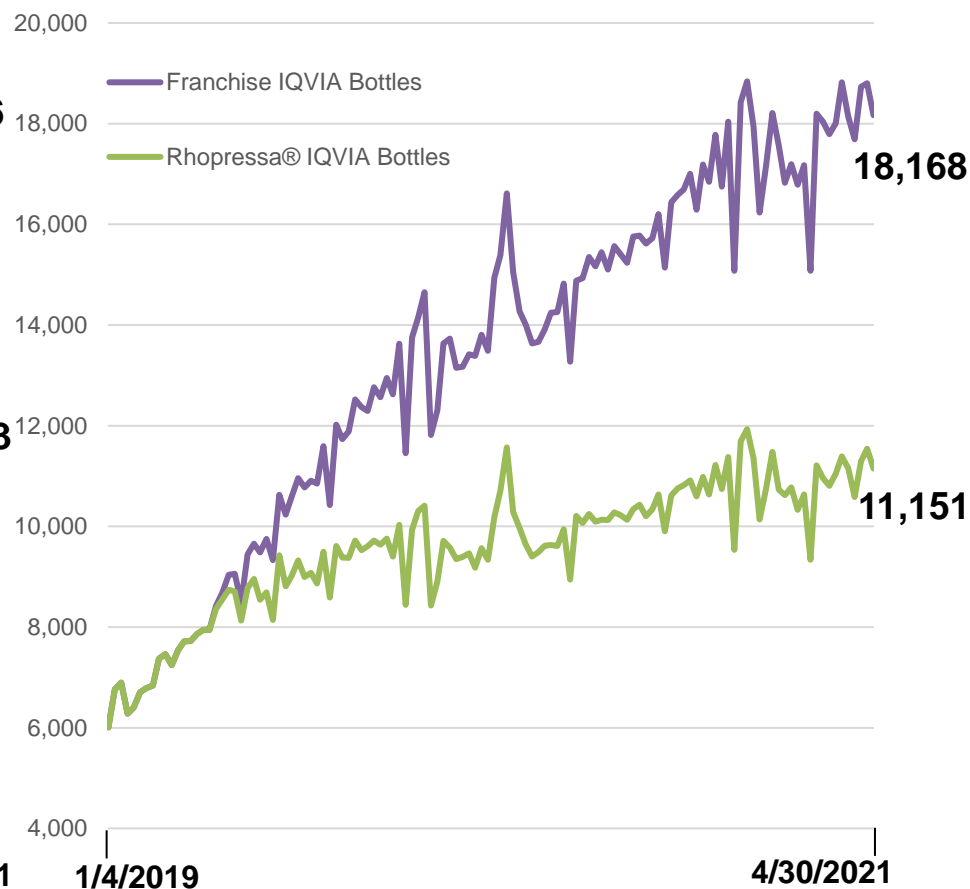


# U.S. Glaucoma Franchise Update

## Actual Weekly Sales-Out to Pharmacies Data as of 5/7/2021



## IQVIA Weekly Data as of 4/30/2021



IQVIA reporting for all reported industry products changed in January 2021 with the prior two years restated, on top of an earlier restatement effective January 2019. Volumes for the weeks of February 1<sup>st</sup>, February 8<sup>th</sup> and February 15<sup>th</sup> (President's Day week) were impacted by the weather. Volumes for the week of April 2<sup>nd</sup> were impacted by the holiday week.

# Aerie Franchise vs Key Brand Competitors



**Aerie franchise continues to far exceed market & competitive product growth**

Product	March '21 TRx	March '21 vs March '20	TRx Gain / (Loss)
<b>Aerie (Rhopressa® &amp; Rocklatan®)</b>	<b>56,700</b>	<b>14%</b>	<b>7,050</b>
Vyzulta®	18,221	12%	1,916
Simbrinza®	32,213	(21%)	(8,691)
Azopt®	25,715	(39%)	(6,122)
Alphagan® P	69,821	(13%)	(10,564)
Combigan®	140,138	(12%)	(18,317)
Lumigan®	180,361	(11%)	(22,887)
Glaucoma Market	2,950,538	(6%)	(190,702)

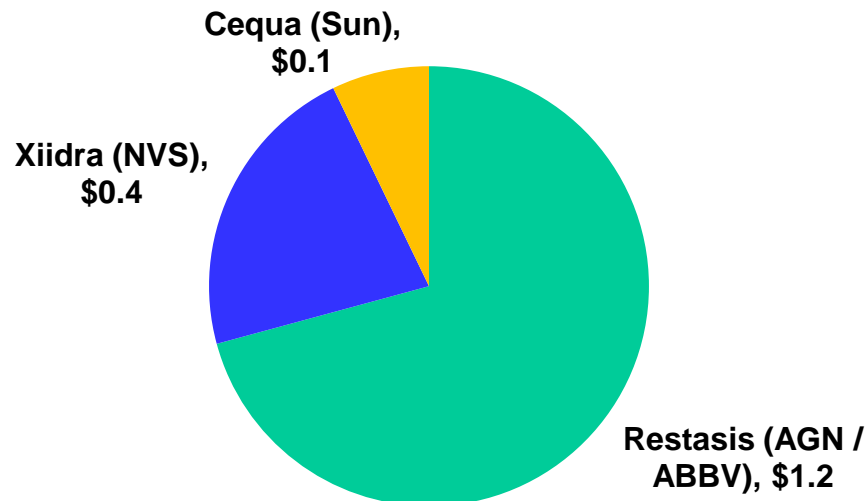


# Advancing the Pipeline

Drug/Target	Indication	Development Stage											
		Preclinical				Phase 1/2a				Phase 2b			
Front of the Eye													
AR-15512 (TRPM8 agonist)	Dry Eye												
Back of the Eye													
AR-1105 Implant (Dexamethasone)	RVO/DME												
AR-13503 SR Implant (ROCK, PKC)	wAMD												
	DME/DR												
	Glaucoma Neuro-enhancement												
AR-14034 SR Implant (VEGF-A/B/C/D)	wAMD/DME												

# U.S. Dry Eye Market: Under-diagnosed and Under-treated

**US 2020 Sales: \$1.7B est.**



- **Estimated 30 million dry eye sufferers in the United States; less than 3 million treated**
- **Dry eye related symptoms are one of the most common reasons for patients to visit an eye care professional**
- **Represents a significant health care burden, contributing to approximately 25% of visits to ophthalmic clinics**
- **Current pharmaceutical therapies are anti-inflammatories, often with poor maintenance on therapy and poor tolerability**
- **DED affects quality of life and interferes with reading, driving ability, computer use, work productivity and is associated with increased anxiety, stress and depression**
- **Unmet need for different MOAs, better tolerability, and treatment of symptoms**

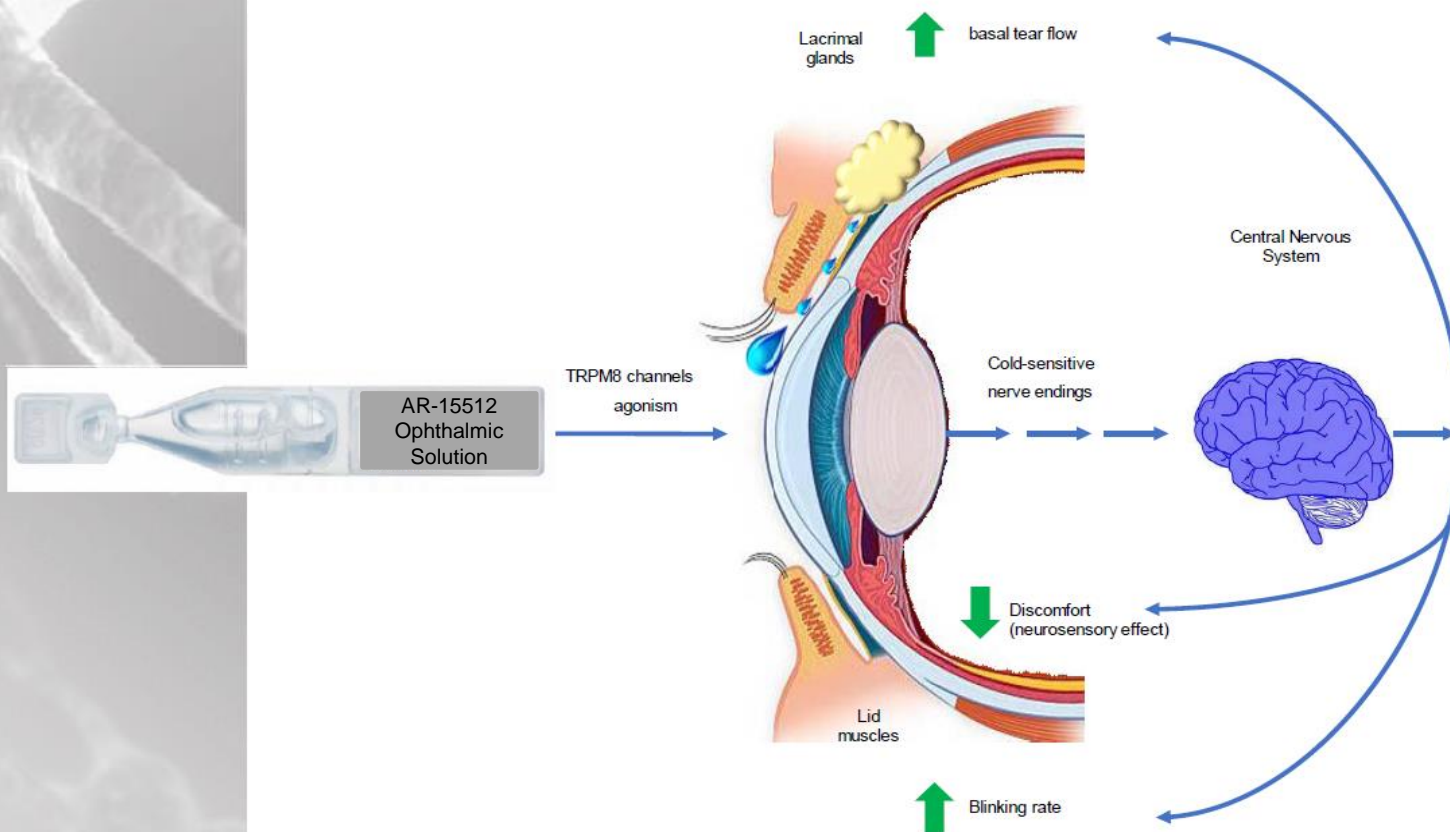
# AR-15512 for Dry Eye

- **Novel Mechanism of Action – Modulation of Corneal TRPM8 receptors**
  - Topical eye drop
  - TRPM8 receptor is a cold thermoreceptor ion channel located on corneal nerve endings
  - Reduced corneal temperature triggered by tear evaporation activates TRPM8 which leads to:
    - **Increased basal tear production (sign for DED)**
    - **A cooling sensation leading to reduction in discomfort / ocular pain (symptom for DED)**
  - This dual mechanism of action is different than those of current prescription dry eye products and supports use as monotherapy as well in conjunction with approved products
- **Basal tearing depending on TRPM8 stimulation is independent of pain-evoked reflex tearing**
- **IP protection for AR-15512 (AVX-012) pharmaceutical composition and method of use through 2031**

# AR-15512 (TRPM8 Agonist) for Dry Eye

How AR-15512 works

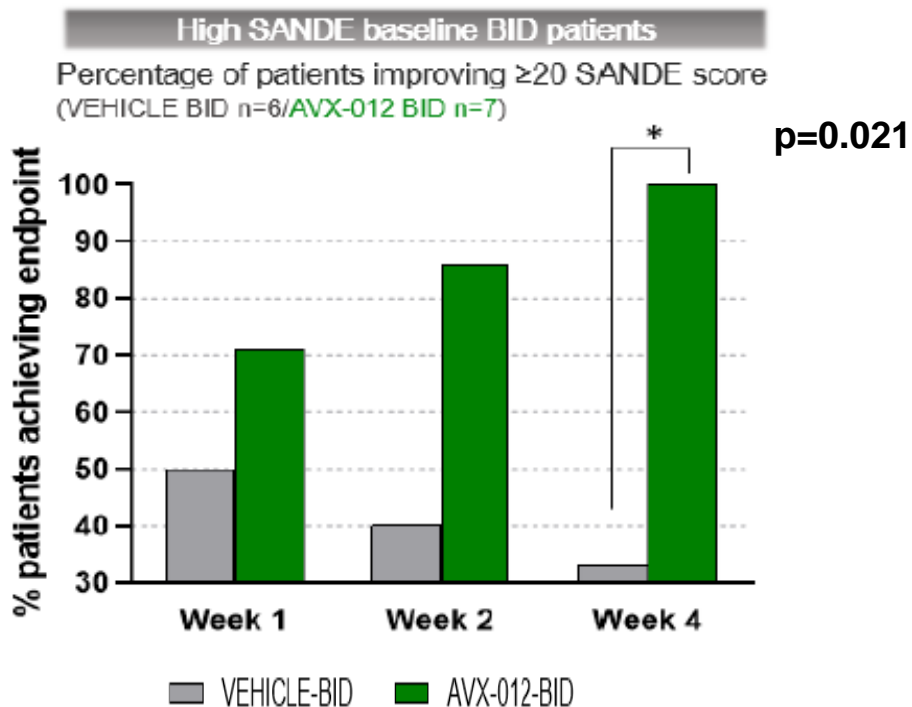
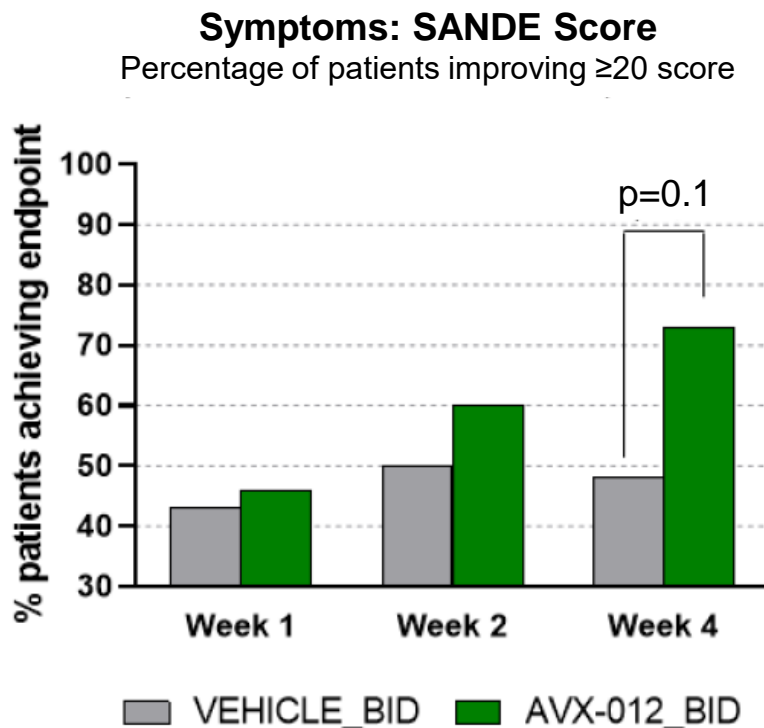
By activating cold thermoreceptors in the cornea increases tear production and blinking rate, restoring tear film stability and reducing discomfort



- **Avizorex completed a Phase 2a study in early 2019 in 109 subjects**
  - One concentration (0.0014%) and two dosing regimens (BID/TID) for 4 weeks were evaluated
  - Primary endpoint: % of patients  $\geq 20$  points change in symptoms questionnaire (SANDE)
  - Secondary endpoints:
    - Schirmer's test (tear production)
    - Tear film break-up-time (TBUT)
    - Corneal staining
- **Key findings:**
  - BID dosing demonstrated greater separation from vehicle, especially in subjects with higher symptoms at baseline
  - Statistical differences from vehicle observed in BID dosing arm in symptoms (severe subjects) and Schirmer's change  $\geq 3$  mm

# AVX-012 (AR-15512) Dry Eye Clinical Trial Highlights

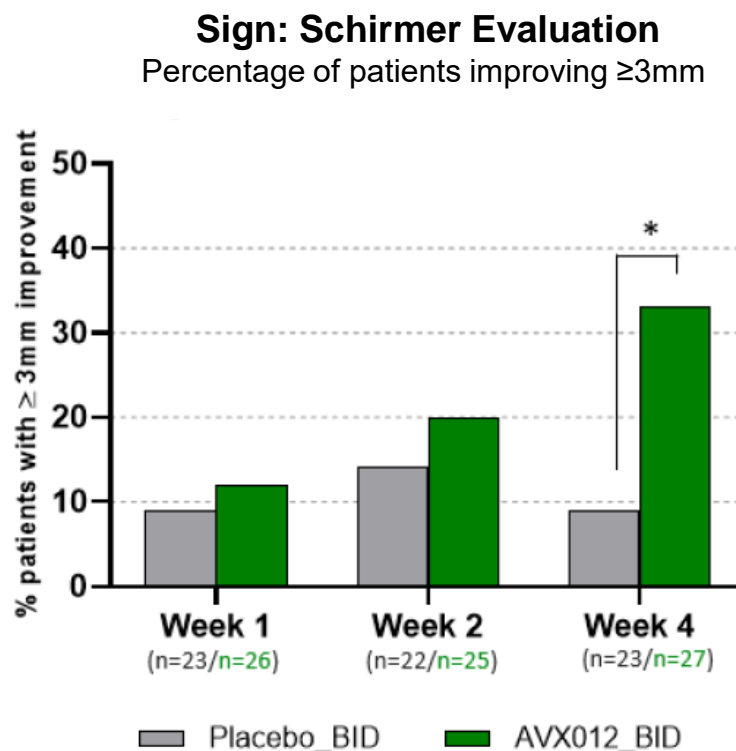
- Significant efficacy achieved for sign and symptoms with BID dosing of 0.0014% (50µM) AVX-012 (AR-15512) over 28 days



- Graph on the right represents primary endpoint with a subset of more severe symptoms
- Demonstrated statistical significance

# AVX-012 (AR-15512) Dry Eye Clinical Trial Highlights

- Significant efficacy achieved for sign and symptoms with BID dosing of 0.0014% (50 $\mu$ M) AVX-012 (AR-15512) over 28 days



- Target symptoms: significant step in addressing the symptoms of dry eye patients and providing a cooling sensation
- Impact basal tear production: production of natural tears and not just an acute reflex tear
- Safe for long-term use
- Other approved products on the market:
  - Xiidra<sup>®</sup>: only approved product for the treatment of signs and symptoms
  - Restasis<sup>®</sup>, Cequa<sup>™</sup> and TrueTear<sup>®</sup>: approved for increase in tear production



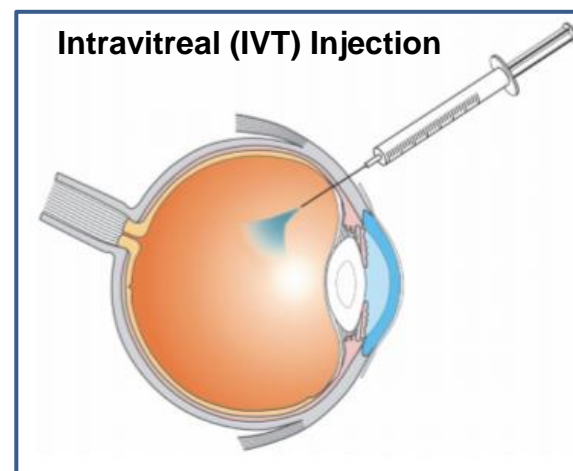
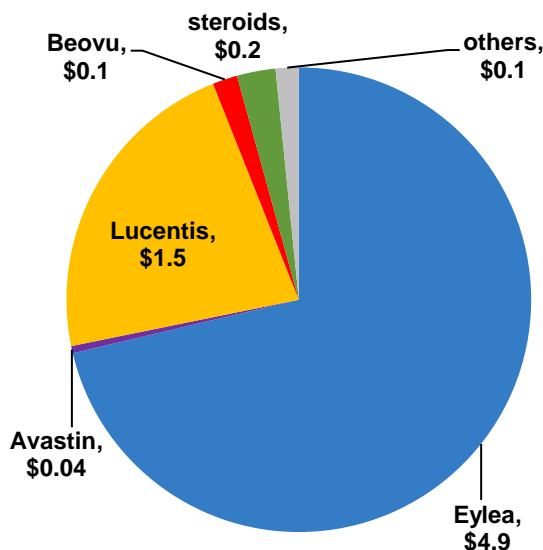
# AR-15512: COMET-1 Phase 2b Underway

- Clinical Trial Series named “COMET” = Cold Thermoreceptor Modulation as an Effective Treatment
- Phase 2b clinical study commenced October 2020; enrollment completed April 2021
- Phase 2b study is evaluating efficacy and safety of 0.0014% and 0.003% BID
  - 360 patients (1:1:1) for 3 months
  - Environmental and Controlled Adverse Environment (CAE) conditions
  - Primary endpoints: ocular discomfort (symptom) and tear production (sign) at day 28
  - Secondary endpoints include: SANDE, staining TBUT, changes post CAE

**COMET-1 Phase 2b topline results expected Q3 2021**

# 2019 U.S. Retinal Disease Market: Need for Reduced Injection Frequency, New MOAs

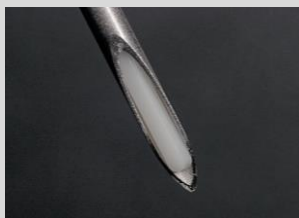
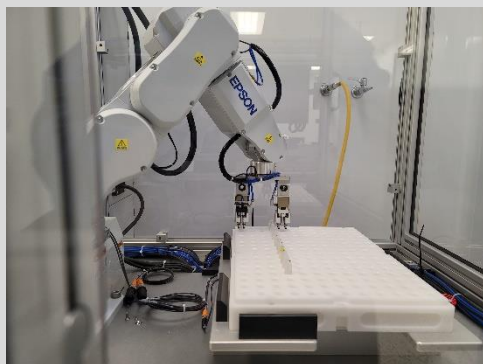
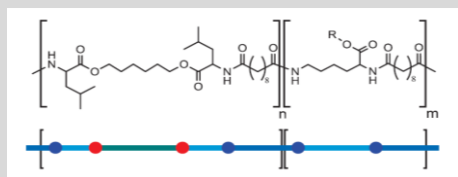
**2020 U.S. Sales: \$6.9B**



- Frequent intravitreal injections required to maintain vision gains
  - Represents a significant burden for patients and physicians
- Only 2 drug classes approved for treatment of wAMD, DME (anti-VEGF, steroids)
  - Not sufficient to fully address complex pathology that drives disease progression
- Opportunity for improved efficacy over current standards of care

# Aerie's Proprietary Drug Delivery Platform for Retinal Disease – Predictable and Flexible

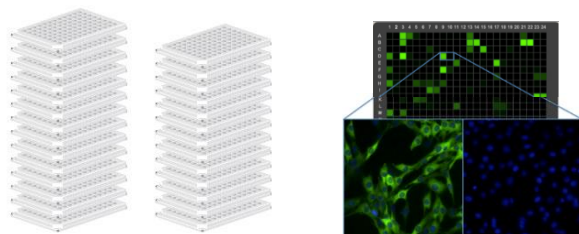
## PRINT<sup>®</sup> Platform



- Customizable drug elution, reproducible manufacturing
    - Proprietary bio-erodible formulations, PRINT<sup>®</sup> manufacturing
  - Longer treatment duration, reduced injection frequency
    - Enables once or twice per year IVT injections
  - Greater diversity of drug targets via small molecule drugs
    - Monoclonal antibodies limited to extracellular targets
- **Potential across a broad range of molecules and a variety of polymers (or custom polymer combinations) uniquely designed to optimize delivery of the active molecule**
  - **Highly predictive when translating from preclinical models to humans**
  - **Efficient low-cost tool to achieve proof of concept**

# Aerie's Proprietary Drug Delivery Technology: A Platform for Future Innovation

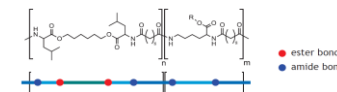
## Small Molecule Drug Candidates



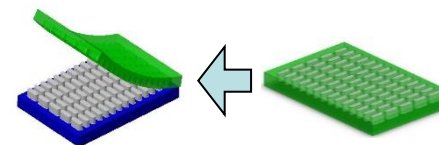
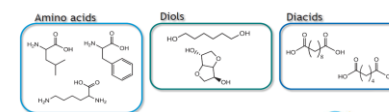
- Aerie Kinase Library
- Non-Aerie drug candidates

## Proprietary Drug Delivery Technology

- DSM PEA Polymer



- PLGA



- PRINT® Mfg



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

wAMD

DME

RVO

Dry AMD/GA

Glaucoma

Others

# AR-1105 (Dexamethasone) Implant

- Positive Topline Phase 2 results in RVO
- Phase 3 plans underway for the U.S. and Europe for DME
- Target product profile vs. Ozurdex®
  - Designed for longer duration of efficacy (6 mo vs 3 mo)
  - Designed for improved administration due to smaller needle
  - Potential for fewer adverse effects due to lower peak drug levels

# AR-1105 (Dexamethasone) Implant: Phase 2 Topline Summary



- The Phase 2 clinical trial (AR-1105-CS201) was conducted at 19 centers in the United States.
- The objective was to evaluate two clinical formulations of AR-1105, CF-1 and CF-2 (each containing 340 µg dexamethasone), with different release profiles, in patients with chronic macular edema secondary to retinal vein occlusion (RVO).
- A total of 49 patients completed the study. Both formulations demonstrated sustained treatment effects in best corrected visual acuity and reductions in macular edema. Peak efficacy was observed earlier with CF-1, while CF-2 demonstrated a longer overall duration of effect of up to six months.
- Both formulations were well tolerated with no unexpected safety findings. Adverse events were consistent with other corticosteroid treatments and intravitreal injection procedures.

**The results match expectations from preclinical models and demonstrate the flexibility and predictability of the PRINT® technology platform in developing longer duration therapies**

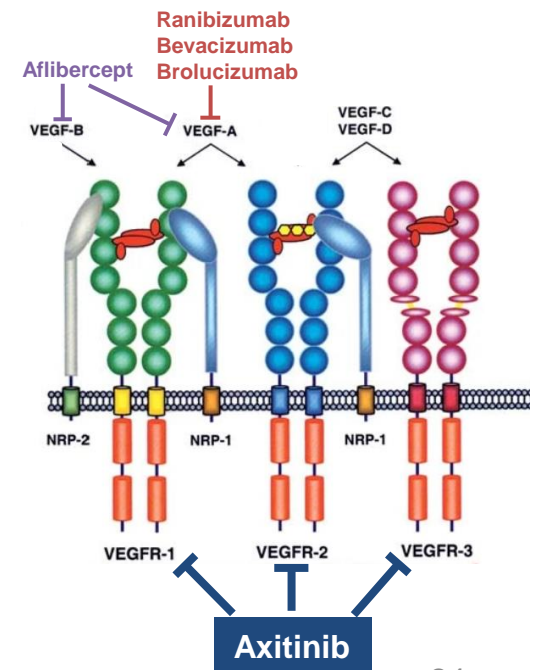
# AR-1105 Opportunity

- The DME market is growing in the United States and abroad
- The 6-month sustained efficacy of AR-1105 in the P2 study may render this product, if approved, highly competitive in both the U.S. and European markets
- AR-1105 may be viewed as a more favorable treatment alternative for anti-VEGF non-responders
- Aerie's exclusive PRINT® platform may allow for low-cost production and significant pricing flexibility
- Six-month dosing may also benefit physician productivity and overall health economics
- Opportunity for market expansion – market currently over \$100M in the U.S. and nearly \$300M in Europe

**Positive AR-1105 P2 topline sustained efficacy data supports advancement as a potentially significant pipeline asset for Aerie, of particular value in Europe**

# AR-14034 SR (Axitinib) Implant Opportunity

- 2019 IVT anti-VEGF worldwide market \$13B; est. \$22B by 2025<sup>1</sup>
- Current anti-VEGF pipeline dominated by longer duration products targeting injection every 4 - 6 months
  - Significant value to healthcare system of longer duration therapies
- AR-14034 SR (axitinib) Implant offers multiple potential advantages vs. current and future products
  - Duration: targeting once-per-year injection to treat a patient for up to 12 months
  - Efficacy: potential for greater efficacy through broad inhibition of all VEGF receptor signaling (pan-VEGF inhibitor; blocks VEGF-A/B/C/D)
  - Safety: proprietary polymer blend provides controlled drug release, avoids microparticles that can migrate to front of the eye



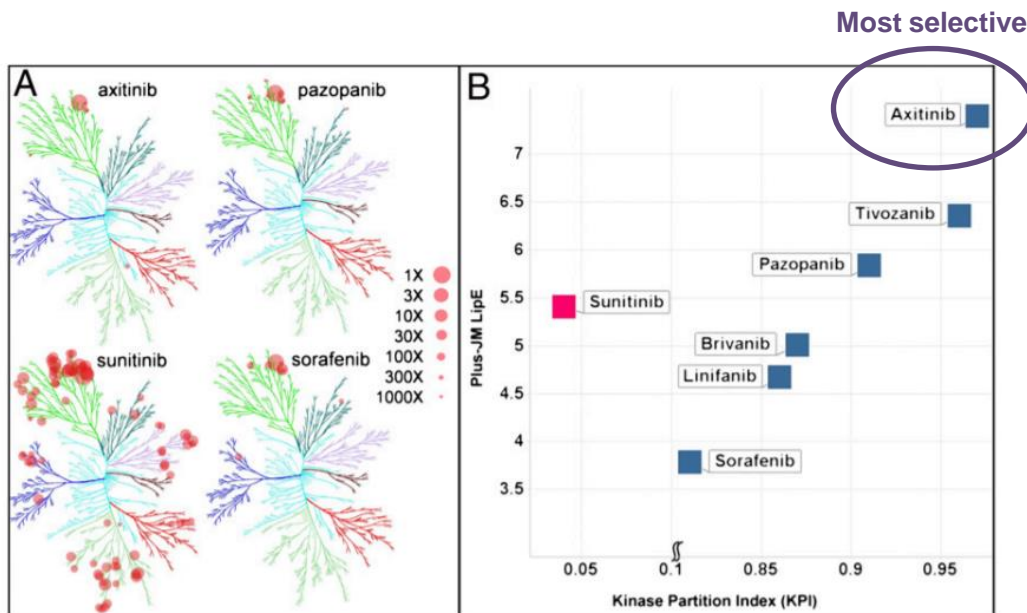
AR-14034 is a development stage product candidate and is not approved by any regulatory agency.



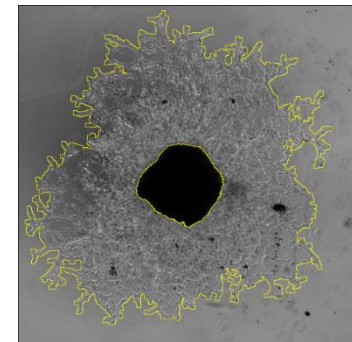
# Axitinib Is Preferred Small Molecule for VEGF Inhibition

- Pan-VEGF receptor inhibitor (inhibits all isoforms of VEGF-R)
- Approved for systemic use in 2012 for the treatment of renal cell carcinoma
- Higher potency and less off-target activity than other small molecule inhibitors

## Kinase Selectivity Assay



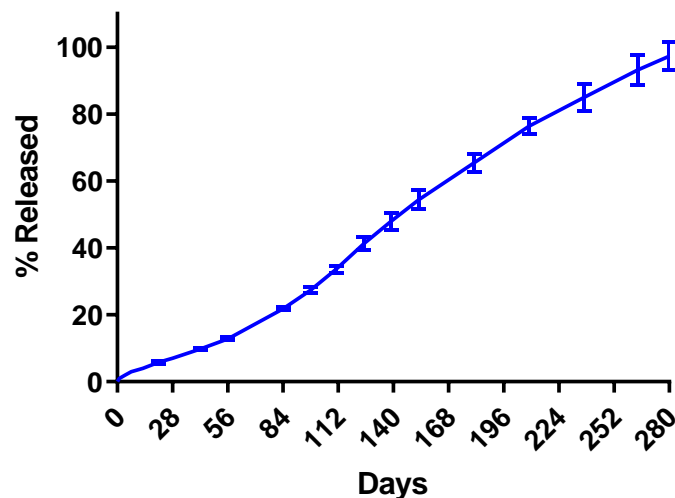
## Choroid Sprouting Assay



Compound	IC50 (nM)	IC90 (nM)
Axitinib	65 ±43	124 ±62
Sunitinib	676 ±500	1901 ±1103

# Axitinib Implant: Results Support Up to 12 Months Duration in Clinic

## Cumulative Drug Release In Vitro



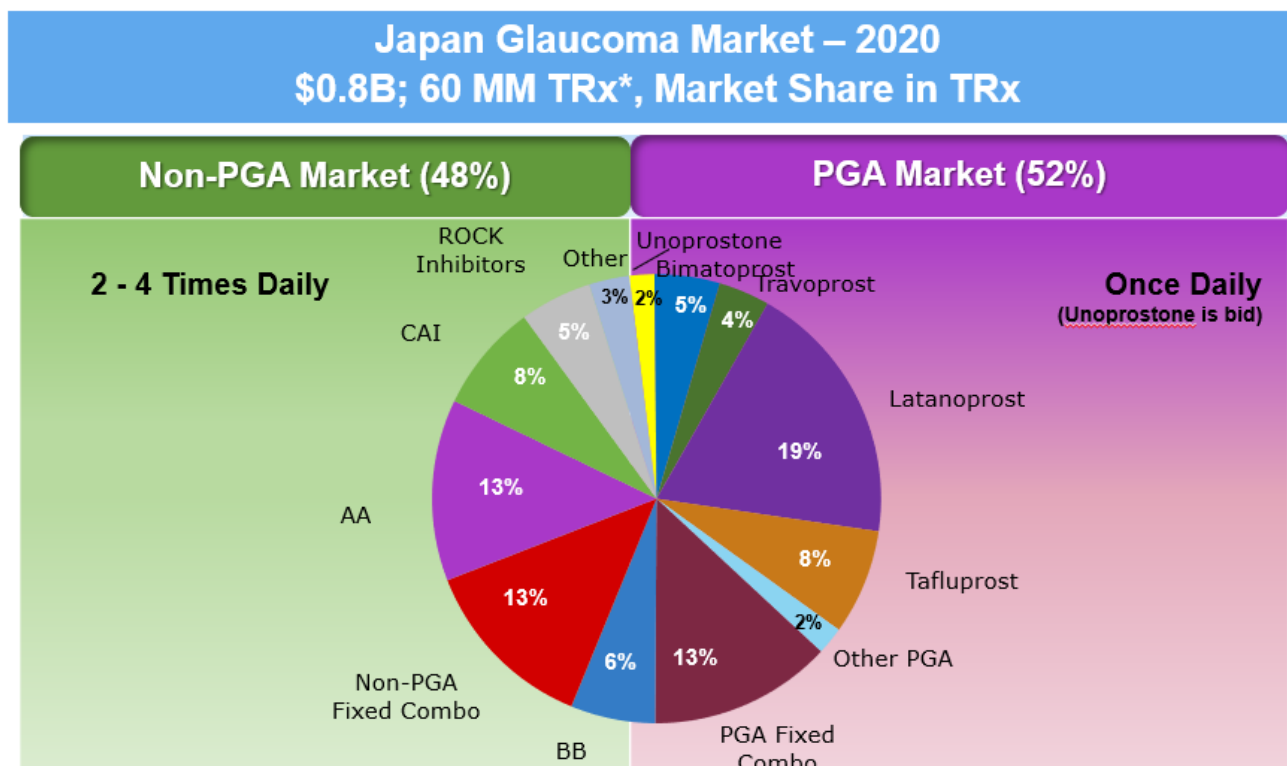
## In vitro: In vivo Comparison

Time	Percent drug released	
	In vitro	In rabbits
Day 14/16	10%	6-9%
Day 29/31	17%	14%
Month 5	60%	50-60%

- Proprietary polymer blend produces optimal drug elution profile
  - Maintains high elution rate over time
- Drug release rate in rabbits predicts up to 12-months duration (once a year injection) in clinic
  - Aerie rabbit data accurately predicted AR-1105 6-month duration in clinic

**IND-enabling preclinical studies underway;  
IND filing planned for 2H 2022**

# Expanding Aerie Franchise: Japan



- Phase 2 study successful topline results released in November 2019
- First Phase 3 trial commenced in Japan in December 2020

**Recently announced licensing agreement with Santen for Japan along with rights for several other Asian countries**

# AR-13324-CS208 Japan Phase 2 Study

## Topline Results

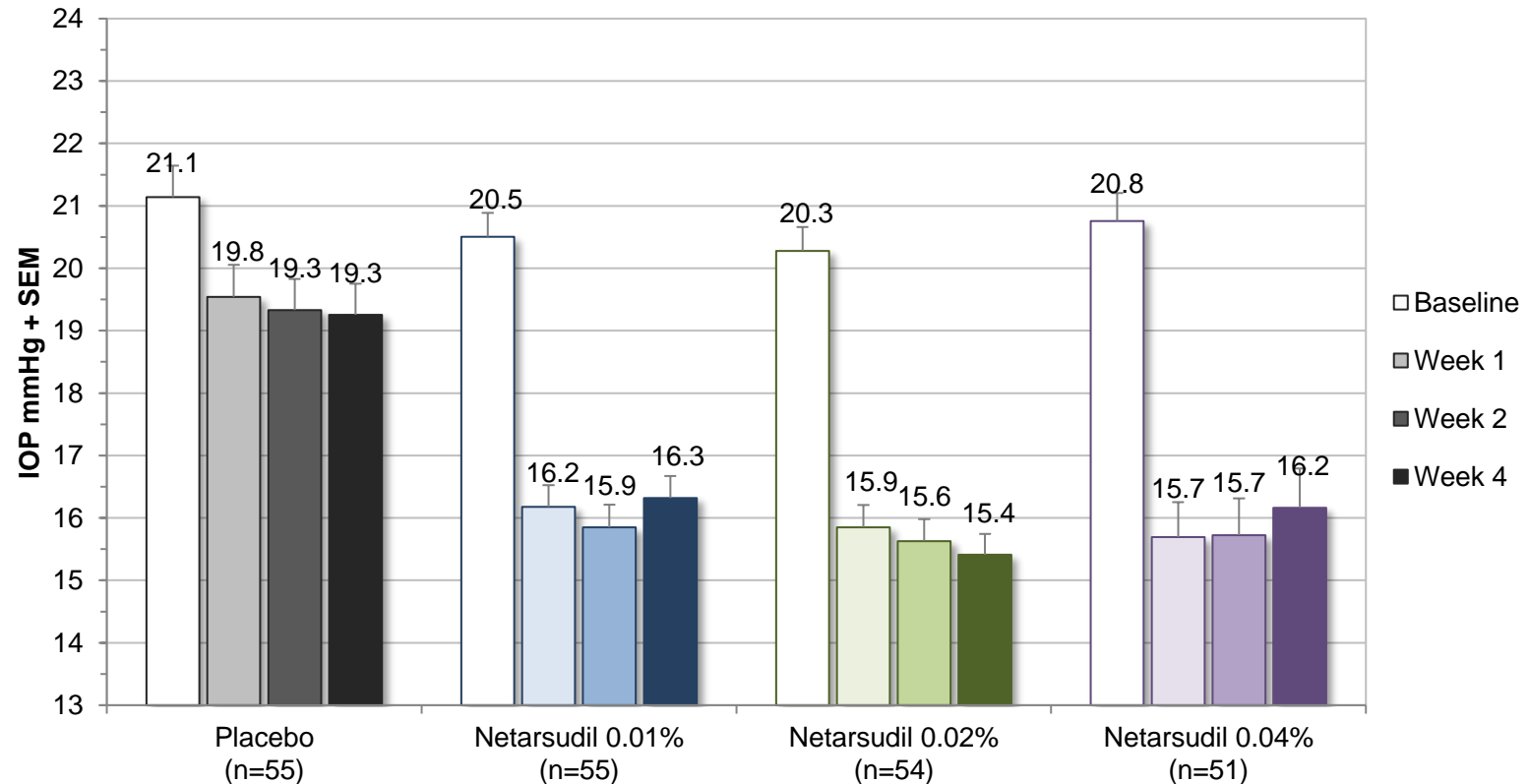


- **28-day prospective, double-masked, placebo-controlled, dose-ranging study of netarsudil efficacy and safety in Japanese subjects with open-angle glaucoma (OAG) or ocular hypertension (OHT)**
- **Netarsudil 0.01%, 0.02% and 0.04% were efficacious, met primary endpoint of superiority to placebo in mean diurnal IOP at Week 4<sup>1</sup>, were safe and generally well tolerated**
  - Baseline mean diurnal IOPs 20-21 mmHg across study arms<sup>2</sup> (Japanese IOPs ~3 – 4 mmHg lower than in the U.S.)
  - Week 4 mean diurnal IOP was 16.3 (-4.1), 15.4 (-4.8), 16.2 (-4.8) and 19.3 (-1.7) mmHg in the netarsudil 0.01%, 0.02%, 0.04%, and placebo groups, respectively<sup>2</sup>
  - No serious adverse events
- **Netarsudil 0.02% (concentration of Rhopressa<sup>®</sup> in the U.S) provided best balance of efficacy and safety**
  - Most common AE was Conjunctival Hyperemia (37.0%), discontinuation rate was 1.9%, all lower than in US trials<sup>3-5</sup>

**Netarsudil generated up to 4.8 mmHg reduction in IOP from baseline**

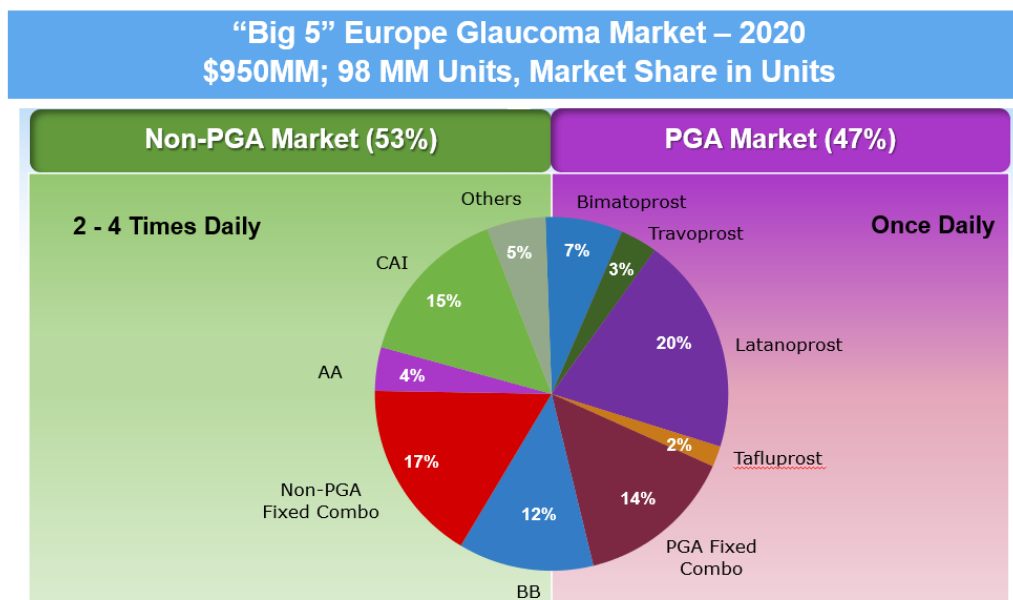
# AR-13324-CS208 Japan Phase 2 Study Topline Results

Mean Diurnal IOP (ITT, Observed Data)



- $P < 0.0001$  vs. placebo at Week 4 for all dose levels<sup>1</sup>
- 0.02% achieved lowest mean diurnal IOP at Week 4

# Expanding Aerie Franchise: Europe



- Marketing authorisation granted for Rhokiinsa<sup>®</sup> (Rhopressa<sup>®</sup>) in November 2019 and for Roclanda<sup>®</sup> (Rocklatan<sup>®</sup>) in January 2021
- Mercury 3: Reported successful 90-day topline data in September 2020; Rocklatan<sup>®</sup> (known as Roclanda<sup>®</sup> in Europe) achieved non-inferiority to a fixed-dose combo in Europe (Ganfort<sup>®</sup>)
- Ireland Plant approved for U.S. production of Rhopressa<sup>®</sup> and Rocklatan<sup>®</sup>

**Preparing for pricing discussions in Germany;  
Potential collaborators actively pursuing European opportunity**

- **Key Priorities**

- Driving continued Rhopressa<sup>®</sup> and Rocklatan<sup>®</sup> volume growth in the U.S.

- **Globalization Strategy**

- Japan: Santen collaboration commencing and first Phase 3 trial underway
- Europe: Significant interest from potential collaborators
- Ireland Manufacturing Facility approved for U.S. production of Rhopressa<sup>®</sup> and Rocklatan<sup>®</sup>

- **Research Initiatives**

- TRPM8 agonist for dry eye P2b underway
- Retina Programs, including AR-1105 prospects with positive P2 topline; and
- AR-14034 SR (Axitinib Pan-VEGF inhibitor) sustained-release implant

- **Well-Financed**

- \$208.2M cash/investments at 3/31/21
- Santen upfront payment of \$50M received in fourth-quarter 2020