



eyenovia

Making it Possible | December 2021

Except for historical information, all the statements, expectations and assumptions contained in this presentation are forward-looking statements. Forward-looking statements include, but are not limited to, statements that express our intentions, beliefs, expectations, strategies, predictions or any other statements relating to our future activities or other future events or conditions, including estimated market opportunities for our product candidates and platform technology. These statements are based on current expectations, estimates and projections about our business based, in part, on assumptions made by management. These statements are not guarantees of future performance and involve risks, uncertainties and assumptions that are difficult to predict. Therefore, actual outcomes and results may, and in some cases are likely to, differ materially from what is expressed or forecasted in the forward-looking statements due to numerous factors discussed from time to time in documents which we file with the U.S. Securities and Exchange Commission.

In addition, such statements could be affected by risks and uncertainties related to, among other things: risks of our clinical trials, including, but not limited to, the costs, design, initiation and enrollment (which could still be adversely impacted by COVID-19 and resulting social distancing), timing, progress and results of such trials; the

timing of, and our ability to submit applications for, obtaining and maintaining regulatory approvals for our product candidates; the potential impacts of COVID-19 and related economic disruptions on our supply chain, including the availability of sufficient components and materials used in our product candidates; the potential advantages of our product candidates and platform technology; the rate and degree of market acceptance and clinical utility of our product candidates; our estimates regarding the potential market opportunity for our product candidates; reliance on third parties to develop and commercialize our product candidates; the ability of us and our partners to timely develop, implement and maintain manufacturing, commercialization and marketing capabilities and strategies for our product candidates; intellectual property risks; changes in legal, regulatory and legislative environments in the markets in which we operate and the impact of these changes on our ability to obtain regulatory approval for our products; and our competitive position.

Any forward-looking statements speak only as of the date on which they are made, and except as may be required under applicable securities laws, Eyenovia does not undertake any obligation to update any forward-looking statements.



**We have designed our microdose array print (MAP™) technology to improve the lives of patients with ophthalmic diseases and disorders**

- Advanced options for diseases and disorders with no or few existing therapies
- Therapies that reduce patient burden due to tolerability, safety or administration issues
- Therapies that improve compliance and adherence





Transforming ophthalmology through the development and commercialization of high-value therapeutics based upon our proprietary Optejet® Microdose Array Print (MAP™) technology



## CLINICALLY TESTED

in multiple Phase 2 and Phase 3 studies

## DEVELOPMENT AND COMMERCIALIZATION PARTNERSHIPS

with leading eyecare companies validate technology and provide significant non-dilutive capital.

**Arctic Vision** – MicroPine, MicroLine and MydCombi for Greater China and South Korea

**Bausch Health** – MicroPine in the US and Canada

## LATE-STAGE THERAPEUTICS PIPELINE

### **Mydcombi™ for mydriasis / pupil dilation:**

- Under FDA review

### **MicroPine for pediatric progressive myopia:**

- Phase 3 CHAPERONE study full enrollment expected 2022

### **MicroLine for presbyopia / improved near vision:**

- Phase 3 VISION-1 study successfully completed 2Q 2021
- Second Phase 3 VISION-2 study completion targeted 1H 2022

## PLATFORM TECHNOLOGY

for potential pipeline expansion into further high-value ophthalmic indications



**Sean Ianchulev, MD, MPH**  
CEO, CMO and Co-Founder



**John Gandolfo**  
CFO



**Michael Rowe**  
COO



**Jennifer Clasby**  
CVP Regulatory, Clinical and Quality



**Malini Batheja**  
VP, Pharmaceutical R&D



**Beth Scott**  
VP, Medical Affairs



**Norbert Lowe**  
VP Sales & Marketing





Product Candidate	Therapeutic Area	Phase 3	NDA
<b>MydCombi™</b> <sup>1</sup> <i>(trop+phen)</i>	Pharmacologic Mydriasis	\$250M+ US market opportunity* MIST-1 MIST-2	
<b>MicroLine<sup>1</sup></b> <i>(pilocarpine)</i>	Presbyopia	~\$7.7B US market opportunity <sup>2</sup> VISION-1	VISION-2
<b>MicroPine<sup>3</sup></b> <i>(atropine)</i>	Progressive Myopia	\$5B+ US market opportunity* CHAPERONE <sup>4</sup>	

Potential pipeline expansion activities leveraging Optejet® technology are ongoing

- ↓ Potential overexposure to drug and preservatives
  - Conventional droppers can overdose the eye by as much as 300%+<sup>1</sup>
  - Known to cause ocular and systemic side effects<sup>1</sup>



- ↓ Protruding tip may create cross-contamination risk
  - More than 50% of administrations touch ocular surface<sup>2</sup>
- ↓ More difficult to use with poor compliance
  - Requires head tilting and aiming which may be compromised in pediatric and elderly populations
  - No dosage reminders or tracking which may lead to missed doses

<sup>1</sup>Abelson, M., 2020. The Hows And Whys Of Pharmacokinetics. ReviewofOphthalmology.com; accessed 11/3/20

<sup>2</sup>Brown MM, Brown GC, Spaeth GL. Improper topical self-administration of ocular medication among patients with glaucoma. Can J Ophthalmol. 1984 Feb;19(1):2-5. PMID: 6608974.

## ➤ Precise, Physiological Dosing

Directly coats the cornea with ~80% less exposure to drug and preservative toxicity (based on 8µL dose).<sup>1</sup>  
Designed to eliminate drug overflow for a more comfortable patient experience.

## ➤ Efficacy

Demonstrated statistical and clinical benefit in IOP reduction, pharmacological mydriasis and presbyopia (improvement in near vision)<sup>1,2,5</sup>

## ➤ Safety

Low systemic drug absorption and good ocular tolerability.<sup>3,4</sup>  
Non-protruding nozzle for no-touch spray application, potentially minimizing risk of cross contamination seen with traditional eyedroppers.



## ➤ Ease of Use

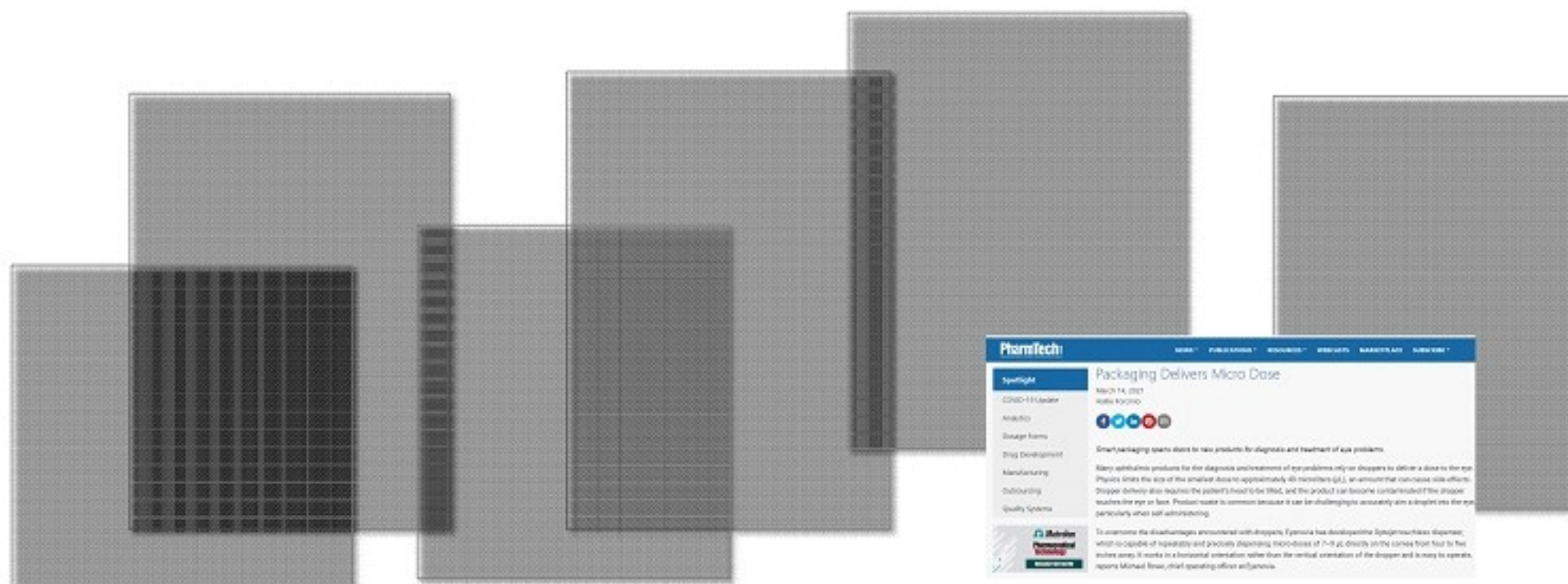
Horizontal drug delivery means no need to tilt the head back. Demonstrated first-time success with both medical professionals and patients.<sup>2</sup>

## ➤ Compliance and Adherence

Can be paired with smart devices to enable dosage reminders and tracking.

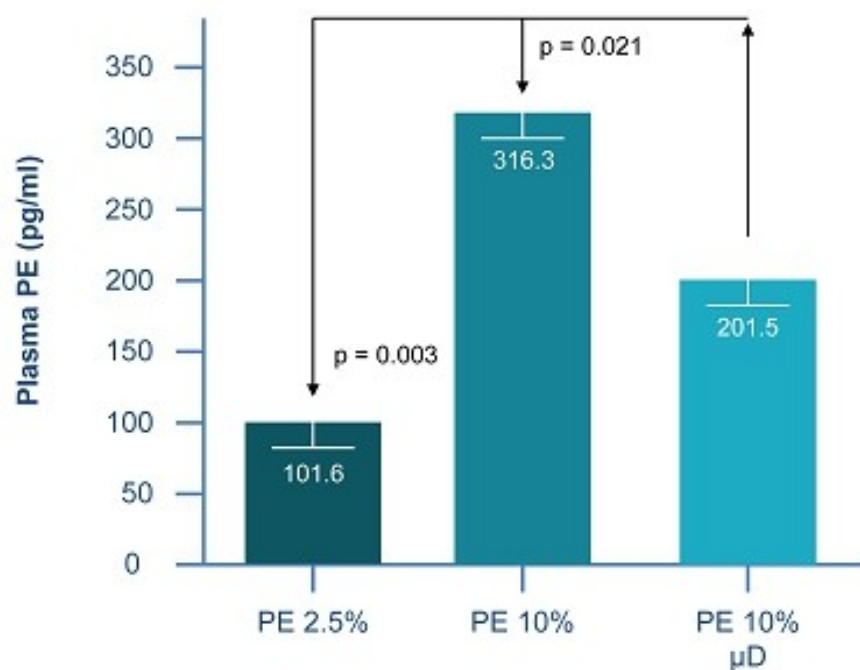






Seven Phase 2 or Phase 3 clinical trials to date featured in dozens of publications and major meetings including ASCRS, AAO, AAOpt, OIS and EYEcelerator.

## REDUCED SYSTEMIC LEVELS



Drugs in traditional eyedroppers can **enter systemic blood circulation** and may cause **significant side effects**.<sup>1</sup>

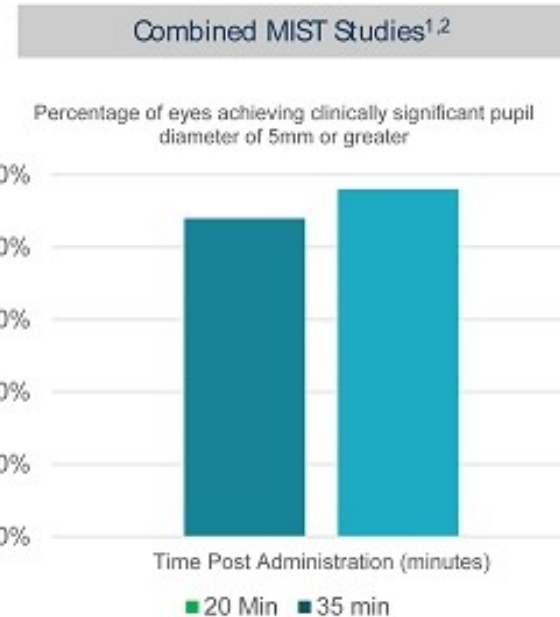
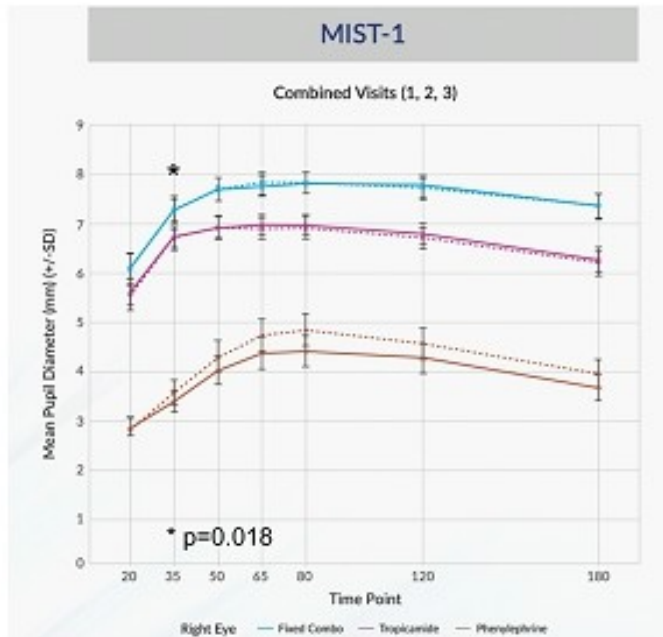
**Microdose delivery** of phenylephrine 10% (PE- $\mu$ D) **was associated with significantly less systemic exposure** than traditional eye drops (PE 10%).<sup>2</sup>

<sup>1</sup> Muller, M., van der Velpe, N., Jaap, W., van der Cammen, T.; Syncope and falls due to timolol eye drops. BMJ, 2006 April; 332:960-961

<sup>2</sup> Ianchulev, I. High-precision piezo-ejection ocular microdosing: Phase II study on local and systemic effects of topical phenylephrine. Ther Deliv, 2018 Jan;9(1):17-27

**Microdosing** a fixed combination of tropicamide-phenylephrine had a superior mydriatic effect compared to either component formulation<sup>1</sup>

MICRODOSE EFFICACY



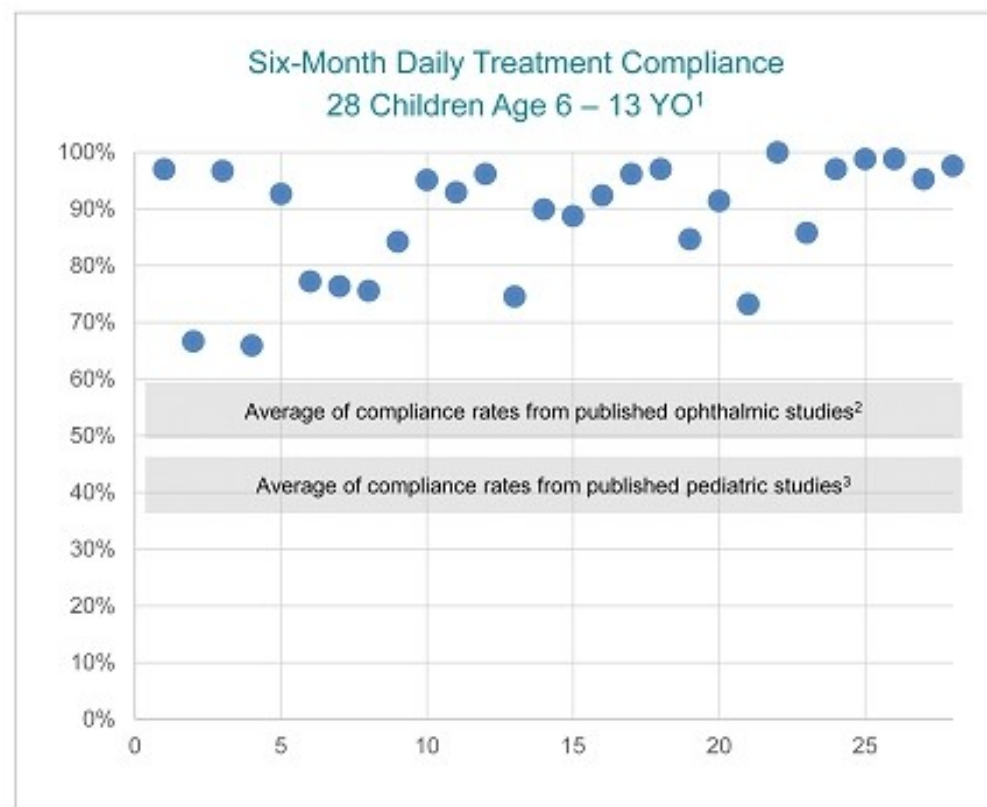
1. Wirta DL, Walters TR, Flynn WJ, Rathi S, Ianchulev T. Mydriasis with micro-array print touch-free tropicamide+phenylephrine fixed combination MIST: pooled randomized phase III trials. Ther Deliv; 2021  
 2. Data on File, Eyenovia 2021



### Real Improvement in Real World Use

In an ongoing late-stage trial, among the initial group of children using the Optejet once-daily, average compliance was nearly 90% during 6 consecutive months of Optejet use

This compares favorably to the approximately 50% compliance rate for pediatric medications as a whole, or the 59 – 69% range published for adult topical ophthalmic drug users<sup>2,3</sup>



**Estimated Gross Margins  
Based on \$100/Month Price<sup>1</sup>**

**82% - 94%**

### **Next-Generation Ophthalmic Therapeutics**

- Eyenovia's microdose therapeutics are regulated as drug-device combination products, with primary mode of action being the drug. Primary oversight is by CDER, with additional input from FDA device reviewers

### **Eyenovia Products Aim to Provide Competitive Pharmaceutical Margins:**

- All pipeline products are Eyenovia's own proprietary micro-formulations
- Eyenovia currently owns the pharma-economics of the entire prescription value chain
- MicroLine has strong potential as a cash-pay cosmeceutical

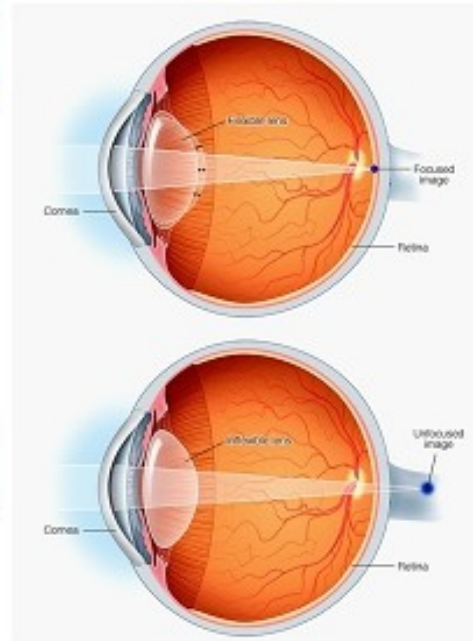
## Etiology

- The progressive loss of ability to focus on nearby objects
- Non-preventable, age-related hardening of the lens

## Symptoms

- Tendency to hold reading material farther away to make the letters clearer
- Blurred vision at normal reading distance
- Eye strain, headaches after reading or doing close-up work

## Normal Vision



## Presbyopic Vision

## Risk Factors

- Age
- Medical conditions and co-morbidities such as cardiovascular conditions, multiple sclerosis, and type 2 diabetes
- Drugs associated with premature symptoms include antidepressants, anti-histamines and diuretics

## Diagnosis

- Basic eye exam, with refraction assessment



- Majority of presbyopia patients have never had to wear glasses prior to having difficulty with near vision
- Having to wear glasses can be an inconvenience and an outward signal of aging
- An alternative to glasses may be valuable and more convenient to patients
- Eyenovia's **MicroLine** is intended to be a companion product to spectacles, not a replacement
- **MicroLine** provides freedom to use the product as needed



**18 million** people 40-55 years of age who never previously needed glasses suffer from presbyopia in the US alone

A 7.7 billion dollar<sup>1</sup> addressable market

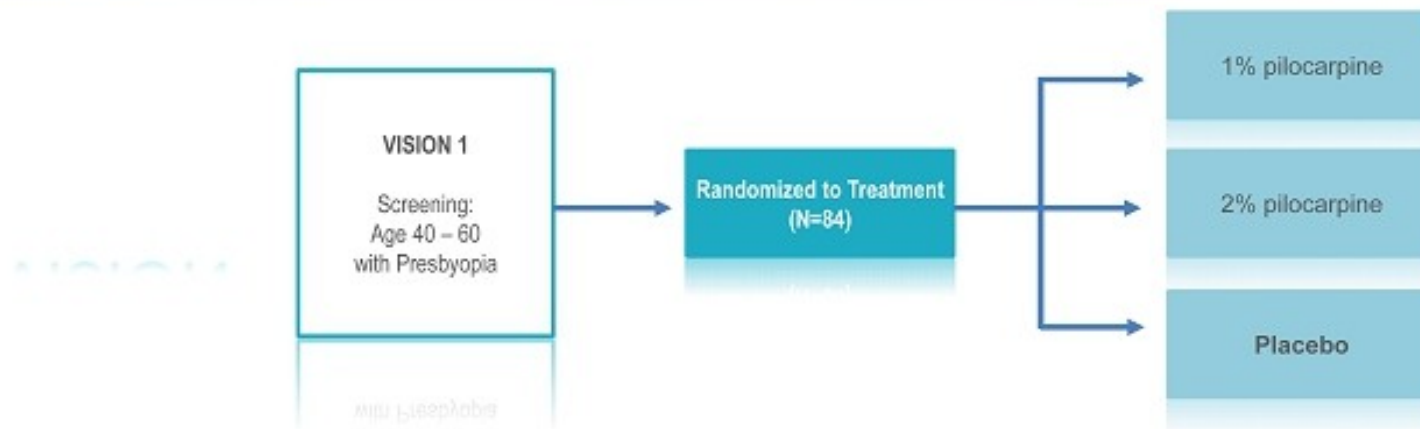
- ✚ A well-known and established drug
- ✚ **Pilocarpine has been demonstrated to constrict the pupil of the eye and create a “pinhole” effect that increases the depth of field.**
- ✚ Onset 10-30 minutes, with duration of action 4-8 hours
  - *The most frequently reported adverse reactions occurring in  $\geq 5\%$  of patients in the pilocarpine 2% populations were: **headache/brow ache\***, accommodative change, blurred vision, eye irritation, visual impairment (dim, dark, or “jumping” vision), and eye pain.*

\*Microdosing is hypothesized to reduce/eliminate headache

- Effective at restoring functional vision, such as the ability to read a menu or cell phone
- Ability to use “as needed” without chronic dosing
- Rapid onset of action
- Easy to administer
- Comfortable instillation with low incidence of brow or headache to drive patient satisfaction and re-use



- Phase 3, double-masked, placebo-controlled, cross-over superiority trial
  - Microdosed pilocarpine 1%, 2% and placebo ophthalmic sprays
- Primary endpoint: mesopic high-contrast binocular DCNVA gain at 120 minutes post-treatment
  - Analyzed separately for 2 cohorts: baseline DCNVA < 0.6 logMAR and  $\geq$  0.6 logMAR
- Study time period: December 2020 – March 2021



1° Outcome  
≥3-line gain

**OR7.7<sup>2</sup>**  
p-value < 0.05

Patients Report  
seeing improvement

**71%**

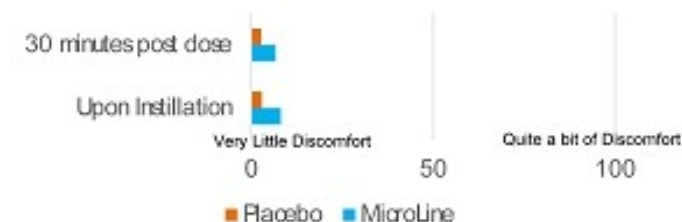
Exit survey: Percent reporting  
significant improvement in near  
vision

## Key Safety Outcomes

All AEs were Transient in Nature

	MicroLine	Placebo
Moderate Hyperemia <sup>1</sup>	2%	0%
Instillation Discomfort	2%	0%
Brow ache	2%	0%

## Patient Comfort Assessment

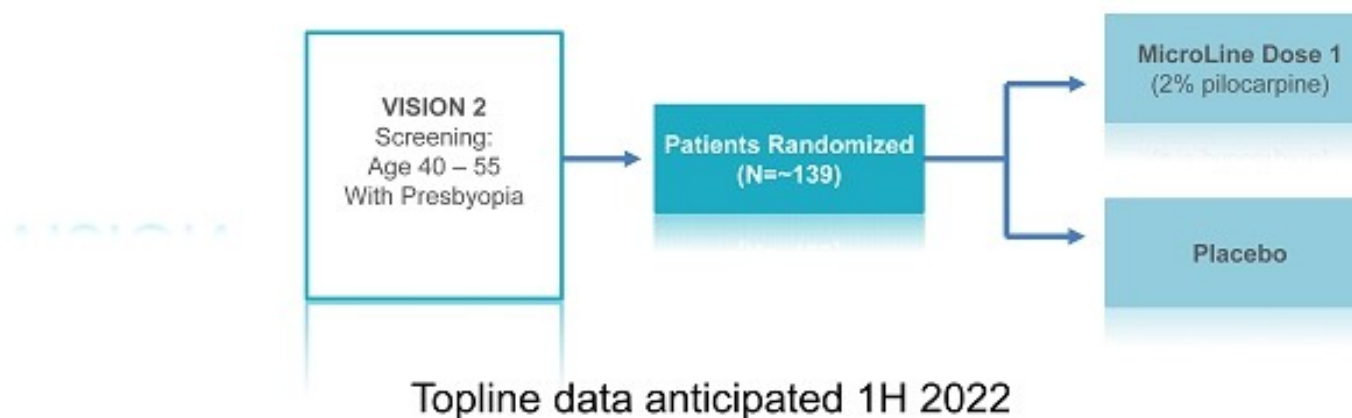


In a separate study among 100 presbyopic patients and 100 optometrists . . .

- ✓ Most likely users were between 40 and 55 years old in the top half of household incomes
- ✓ A price of approximately \$30 - \$35 a month is not an issue for the vast majority of potential users
- ✓ Four hour duration of action is appropriate
- ✓ Lack of side effects, especially headache, was deemed "very important"



- Phase 3 double-masked, placebo-controlled, cross-over superiority trial
  - microdosed pilocarpine 2% and placebo ophthalmic sprays
- Primary endpoint: improvement in mesopic distance corrected near visual acuity 2 hours post-treatment
- First patient enrolled November 4, 2021





Progressive of Myopic Maculopathy

Affects ~25M children in the US alone, with ~5M considered to be at high risk<sup>4</sup>

- Back-of-the-eye disease
- Mostly begins in early childhood, with a genetic link to myopic parents<sup>1</sup>
- Pathologic elongation of sclera/retina which can lead to significant morbidity and visual sequelae<sup>2</sup>
  - Retinal detachment
  - Myopic retinopathy
  - Vision loss
  - Quality of life
- Currently, no FDA-approved drug therapies to slow myopia progression
- Atropine may slow myopia progression by 60% or more<sup>3</sup>

### Current treatment options for myopia include:

- Eyeglasses
- Contact Lenses
- Orthokeratology
- Atropine

Atropine 0.01% must be compounded by a specialty pharmacy and is not approved by the FDA for myopia control. It is not covered by insurance and can cost \$100 per bottle for a 3-month supply.

Significant variability in the efficacy and side effect profile of the same concentration of atropine across different studies.

*Patient medical insurance does not typically cover myopia clinic visits or treatment.*



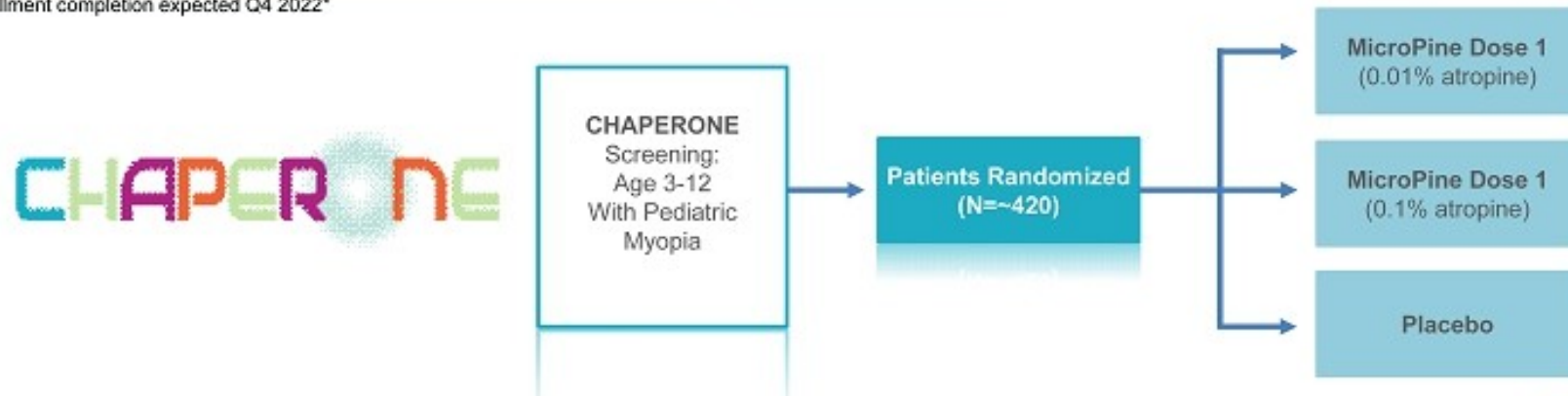


**Chaperone Study - Single Phase III Trial initiated in June 2019.**

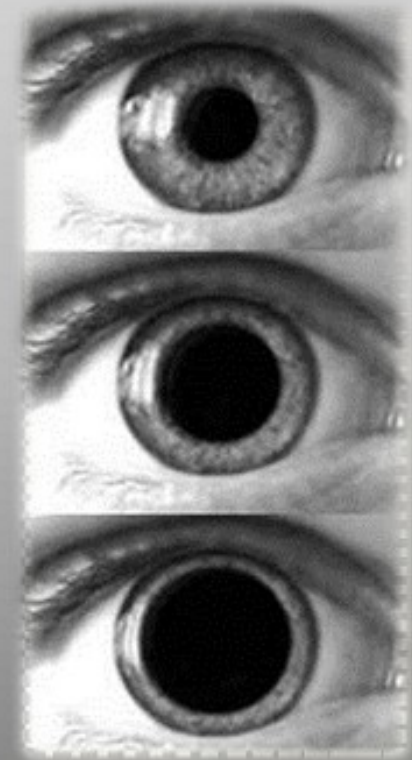
Primary Endpoint: Proportion of subjects with  $<0.5$  diopter change in refractive error (myopia progression) from baseline through 36 months.

Patients are then re-randomized to the same or an alternative treatment arm and followed for an additional 12 months.

Enrollment completion expected Q4 2022\*



- Pharmacologic mydriasis (pupil dilation) is part of the comprehensive eye exam
  - Estimated 100 million office-based comprehensive and diabetic eye exams and 4 million ophthalmic surgical dilations performed annually in the United States
  - Essential for diabetic retinopathy, glaucoma and retina disease screening
  - An estimated \$250 million US market opportunity<sup>1</sup>
- Places technology at the initial point-of-care with prescribers (ophthalmologists and optometrists)
- No direct contact increases patient safety by reducing potential cross contamination associated with the use of shared dilating drops in OD/OPH offices
- No anticipated reimbursement hurdles; expect to sell directly to ophthalmology and optometry practices
- Able to commercialize efficiently with a small, targeted sales force
- **Now being reviewed as as drug-device combination product**



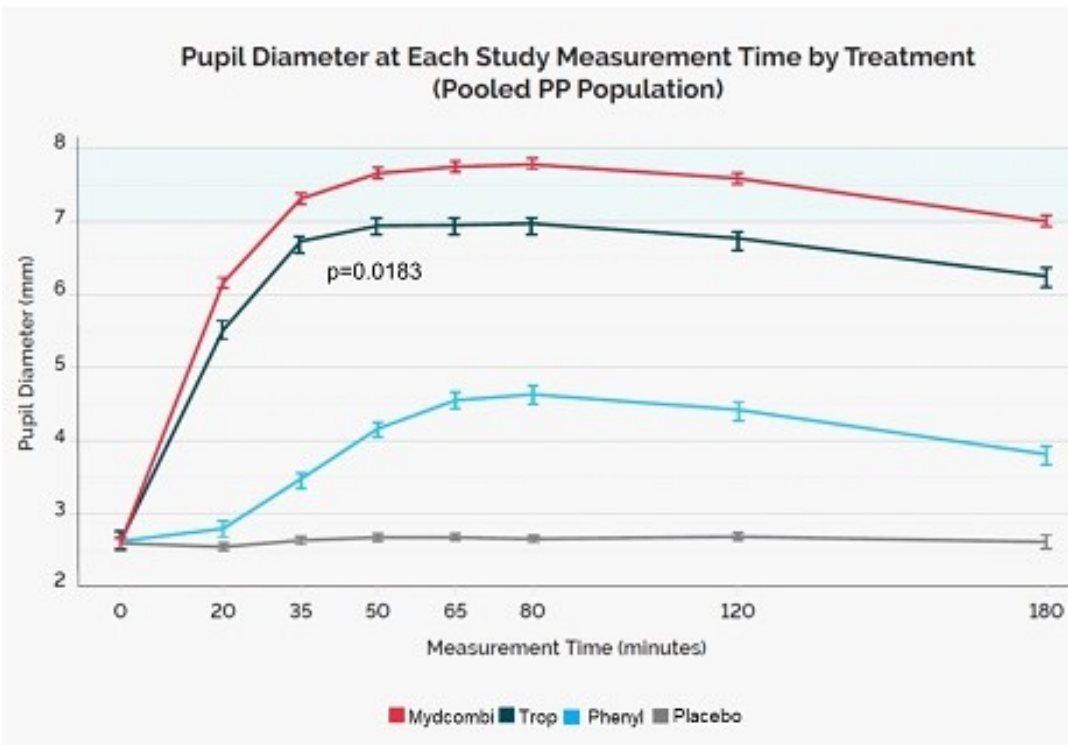


# MydCombi™

(tropicamide and phenylephrine HCl  
ophthalmic spray) 1%/2.5%

- If approved, the only fixed combination of the two leading mydriatic medications in the US
- Administered with the push of a button, saving up to ten minutes of technician time<sup>1</sup>
- Touch-free, comfortable application with fewer than 1% of patients experiencing stinging discomfort<sup>2</sup>
- Lower drug and preservative exposure, including systemic absorption of phenylephrine, which can be problematic in hypertensive patients<sup>2,3</sup>
- Reliable in numerous patient practices. More than 9 out of 10 patients achieved clinically significant mydriasis at 35 minutes post-dosage<sup>2</sup>





### Prompt Mydriasis

Mydriasis >5mm achieved in 88% of patients at 20 minutes, without the delay of instilling multiple drops

### Superior Efficacy

MydCombi achieved superior efficacy over single-agent components

### Office & Surgical Use

Mydriasis >6 mm achieved in >93% of patients at 35 minutes post-dosage which is clinically meaningful for both office retinal exam and surgical dilation

In the MIST-1 and MIST-2 studies, adverse events were infrequent and generally mild with none over 5% in incidence.



## Big Eye Pharma

<p>11 FTE for \$2.2 million</p> <p>Calling on large group practices in largest population centers for 50% reach at launch</p>	<p>Sales Team</p> 	<p>100 FTE for \$20.0 million</p> <p>Calling on 18,000 doctors across the US for 80% reach at launch</p>
<p>Not needed.</p> <p>Product is a diagnostic bought by the practice.</p>	<p>Managed Care Group</p> 	<p>8 FTE for \$1.6 million</p> <p>Often delay of up to 1 year to obtain formulary access.</p>
<p>\$2.0 million</p> <p>Glossy pieces and interactive programs are not needed. Key Account People will train and leave a sample for evaluation.</p>	<p>Promotion</p> 	<p>\$10.0 million</p> <p>Dinner meetings, large convention booths, investigational grants, advertising, lunch and learns.</p>
<p><b>Total: ~\$4.2 million</b></p>		<p><b>Total: ~\$31.6 million</b></p>



Validating partnership for the development and commercialization of **MydCombi™, MicroPine** and **MicroLine**

+

Upfront payment: \$4M

+

Potential milestone payments and reimbursed development costs: \$41.75M

Commercial supply terms or royalties: mid-single digits

Territory: **Greater China (mainland China, Hong Kong, Macau and Taiwan) and South Korea**

*Impacted population estimated at approx. more than 8x the US<sup>1</sup>*



**BAUSCH** Health

Strategic partnership for the development and commercialization of **MicroPine**

+

Upfront payment: \$10M

+

Potential milestone payments and reimbursed development costs: \$50M

*Reimbursed development costs associated with Phase 3 CHAPERONE trial to begin immediately*

US impacted population with high myopia estimated at approx. 3M<sup>2,3</sup>

Royalties on gross profit: mid-single digit to mid-teen percentages

Territory: **US and Canada**



Technology that has Multiple Layers of IP,  
Clinical and Regulatory Protection

**13** U.S. Patents Issued

**84.** O.U.S. Patents Issued

Volume delivered, method of delivery, speed of delivery, data capture

Various patent coverage in effect until late 2031

Provisional patents filed to bring protection through 2040





**Nasdaq: EYEN**

<b>Common Shares Outstanding</b>	26.0M
----------------------------------	-------

<b>Equity Grants Outstanding Under Stock Plans</b>	4.3M
--	------

<b>Warrants</b>	1.2M
-----------------	------

<b>Fully Diluted Shares</b>	31.5M
-----------------------------	-------

<b>Cash</b>	\$21.4M
-------------	---------

<b>Debt</b>	\$7.3M
-------------	--------



**Dr. Fred Eshelman**  
Chairman

Founder and former CEO of PPDI, founding chairman of Furiex Pharmaceuticals, and founder of Eshelman Ventures



**Dr. Ernest Mario**  
Board Member

Former Chairman and CEO of Reliant Pharmaceuticals, ALZA, and Glaxo Holdings



**Dr. Curt LaBelle**  
Board Member

Managing Director of GHIF venture fund and Co-Founder of Eyenovia



**Kenneth Lee Jr.**  
Board Member

General partner of Hatteras Venture Partners



**Charles Mather IV**  
Board Member

Managing Director, Equity Capital Markets at Suntrust Robinson Humphrey



**Dr. Anthony Sun**  
Board Member

CEO, Zentalis Pharmaceuticals, Inc.



**Dr. Sean Ianchulev**  
Board Member

CEO, CMO and Co-Founder of Eyenovia



**Dr. Julia Haller**  
Board Member

Ophthalmologist-in-Chief  
Wills Eye Hospital