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- This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning the regulatory timelines, commercial timelines, product labels, cash runway, scalability, and future clinical trials in reversal of mydriasis (RM), presbyopia, dim light/night vision disturbance (NVD) and diabetic retinopathy (DR)/diabetic macular edema (DME), including the potential for Nyxol to be a “best in class” presbyopia drop and the potential market opportunity in RM. These forward-looking statements are based upon the Company’s current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) the success, costs, and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; (ii) regulatory requirements or developments; (iii) changes to clinical trial designs and regulatory pathways; (iv) changes in capital resource requirements; (v) risks related to the inability of Ocuphire to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vi) legislative, regulatory, political and economic developments, (vii) changes in market opportunities, (viii) the effects of COVID-19 on clinical programs and business operations, (ix) the success and timing of commercialization of any of Ocuphire’s product candidates, including the scalability of Ocuphire’s product candidates and (x) the maintenance of Ocuphire’s intellectual property rights. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by the Company from time to time with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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Differentiated, Late-Stage Pipeline for Front and Back of the Eye

- Nyxol with > 575 patients treated across 11 trials (505(b)(2) regulatory pathway)
- APX3330 with > 340 patients treated across 11 trials (NCE development pathway)
- Nyxol and APX3330 achieved promising clinical data and favorable safety profile across multiple Phase 1, 2, and 3 trials

Near-term Commercialization Opportunities in Multiple Large Unmet Markets

- Addressing 4 large markets with unmet needs: RM, Presbyopia, NVD, and DR/DME
- Successful trial execution with 3 recent positive Phase 3 & Phase 2 data read-outs for Nyxol in RM and Nyxol + LDP in Presbyopia, respectively
- Stable, small-molecule drugs with commercial scalability
- Robust and growing IP portfolio: US and global patents issued thru 2034 for both assets as well as new 2039 Nyxol patent issued for presbyopia

Multiple data readouts in 2022 with Track Record of Execution

- $24.5 million cash reported at 12-31-21 sufficient for operations into 2Q 2023
- Highly experienced management, Board and KOLs with broad ophthalmic and biotech drug development and commercialization success
- Low-cost, fast-enrolling, short-duration clinical trials
- Favorable precedent regulatory environment for ophthalmic drug approval
- Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and HCW

Multiple Catalysts in 2022:

- Nyxol alone VEGA-1 P2 trial for P JAN 2022
- Nyxol MIRA-3 P3 trial for RM MAR 2022
- Nyxol Pediatric trial for RM APR 2022
  - Nyxol LYNX-1 P3 trial for NVD 2Q22
  - APX3330 ZETA-1 P2b trial for DR/DME 2H22
  - NDA Filing for Nyxol for RM LATE 2022

P= Presbyopia
RM = Reversal of Mydriasis
NVD = Night Vision Disturbances
DR/DME = Diabetic Retinopathy/Diabetic Macular Edema
Ophthalmology – An Attractive Biotech Sector
Demographics, M&A, Regulatory Approvals and Efficient Trials Favor Ophthalmic Drugs

**Deal Activity**

- **April 2021**
  - Novartis / Alcon (Regeneron)
  - $355M

- **October 2021**
  - Théa / Curature
  - ~$2B

- **December 2021**
  - Novartis / Gyroscope
  - ~$1.5B
  - Genentech
  - $670M

**New Product Approvals**

7 of 60 FDA Drug Approvals in 2021 Were Ophthalmic Drugs¹ and 1 in 2022

**Favorable Regulatory Environment**

**Lower Cost, Quick Enrolling, Short Duration Clinical Trials**

**Active Partnering in 2021**

**Aging Population**

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**Source:**
1. Endpoint Dec 29, 2021- Hitting a new record on drug approvals, the FDA offers a thumbs-up to another atopic dermatitis contender;
2. OIS Year in Review 2021;
3. Company press releases

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### Nyxol® & APX3330: Development History and Patents

#### Significant Preclinical & Clinical Data Supporting Safety, MOA, Efficacy, and PK Profile

<table>
<thead>
<tr>
<th>Refractive</th>
<th>Nyxol®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>11</strong> Completed Phase 1, Phase 2, and Phase 3 Trials</td>
<td>Novel α1/α2 Blocker 505(b)(2)</td>
</tr>
<tr>
<td><strong>&gt;575</strong> Subjects Dosed</td>
<td>Exposure in Humans <strong>28</strong> Days</td>
</tr>
<tr>
<td><strong>Patent Coverage 2034+</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Retina</th>
<th>APX3330</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>11</strong> Completed Phase 1 and Phase 2 Trials</td>
<td>Oral REF-1 Inhibitor New Chemical Entity</td>
</tr>
<tr>
<td><strong>&gt;340</strong> Subjects Dosed</td>
<td>Exposure in Humans <strong>365</strong> Days</td>
</tr>
<tr>
<td><strong>Patents to 2034+</strong></td>
<td></td>
</tr>
</tbody>
</table>

#### Prevalence (US) & US Market Opportunity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Market Opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reversal of Mydriasis</td>
<td>~100 M</td>
<td>$500+M</td>
</tr>
<tr>
<td>Presbyopia</td>
<td>~128 M</td>
<td>$10+B</td>
</tr>
<tr>
<td>Night Vision Disturbances</td>
<td>~36 M</td>
<td>$2+B</td>
</tr>
<tr>
<td>Retina</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td>~8 M</td>
<td>$10+B Oral Rx Revenues*</td>
</tr>
<tr>
<td>Diabetic Macular Edema</td>
<td>~2 M</td>
<td>$10+B</td>
</tr>
</tbody>
</table>

Source: Eisai and Apexian Data; GlobalData Market Research Report, 2020; Company Estimates for US Market Size; *Ocuphire internal estimates
Looking Ahead: Ocphhire Pipeline & Clinical Milestones

*Multiple Phase 3 & Phase 2 Clinical Data Readouts Anticipated this Year*

<table>
<thead>
<tr>
<th>Indication</th>
<th>Product Candidate</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Regulatory Approval</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversal of Mydriasis (RM)</td>
<td>Nyxol® Eye Drop</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>Reported positive MIRA-3 Phase 3 data in Q1 2022 (n=368)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔️</td>
<td>Reported positive MIRA-4 Pediatric data in 2Q 2022 (n=23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>❑</td>
<td>File Nyxol NDA for RM in late 2022</td>
</tr>
<tr>
<td>Presbyopia (P)</td>
<td>Nyxol® Eye Drop</td>
<td>✔️</td>
<td>✔️</td>
<td>❑</td>
<td>✔️</td>
<td>✔️</td>
<td>Reported positive VEGA-1 Nyxol alone data in Q1 2022 (and in combination with LDP mid-2021)</td>
</tr>
<tr>
<td></td>
<td>Nyxol® + 0.4% Low Dose Pilocarpine (LDP) Eye Drops</td>
<td>✔️</td>
<td>✔️</td>
<td>❑</td>
<td>✔️</td>
<td></td>
<td>VEGA Phase 3 program planned to initiate in mid-2022 for single agent and combination with LDP</td>
</tr>
<tr>
<td>Dim Light or Night Vision Disturbances (NVD)</td>
<td>Nyxol® Eye Drop</td>
<td>✔️</td>
<td>✔️</td>
<td>❑</td>
<td>✔️</td>
<td>❑</td>
<td>LYNX-1 Phase 3 data expected in 2Q 2022 (n=145)</td>
</tr>
<tr>
<td>Diabetic Retinopathy (DR)/Macular Edema (DME)</td>
<td>APX3330 Oral Pill</td>
<td>✔️</td>
<td>❑</td>
<td>❑</td>
<td>✔️</td>
<td>❑</td>
<td>ZETA-1 Phase 2b data expected in 2H22 (n=103)</td>
</tr>
<tr>
<td>DME or Wet Age-Related Macular Degeneration (wAMD)</td>
<td>APX2009 (Intravitreal or Local Delivery)</td>
<td>✔️</td>
<td>❑</td>
<td>❑</td>
<td>✔️</td>
<td>❑</td>
<td>Seeking partner funding for IND enabling studies and further development</td>
</tr>
</tbody>
</table>

Note: 0.75% Nyxol (Phentolamine Ophthalmic Solution) is the same as 1% Nyxol (Phentolamine Mesylate Ophthalmic Solution)
NYXOL® EYE DROPS

- **RM** Reversal of Mydriasis
- **P** Presbyopia
  1. Nyxol as a Single Drop for Presbyopia
  2. Nyxol with LDP Adjunctive Therapy
- **NVD** Night Vision Disturbance
Nyxol’s Differentiated MOA as an Alpha-1 Blocker

*Phentolamine Mesylate Reformulated as a Proprietary Topical Eye Drop ➔ Nyxol®*

---

**Phentolamine Mesylate is the Active Ingredient in Nyxol: a Non-selective α1 & α2 Antagonist**

<table>
<thead>
<tr>
<th>Blocking α1</th>
<th>Blocking α1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduces Pupil Size</td>
<td>Dilates Blood Vessels</td>
</tr>
</tbody>
</table>

- **Iris Dilator Muscle**
- **Iris Sphincter Muscle**

Nyxol blocks α1 receptors only found on the Iris Dilator Muscle ↓

Decrees Pupil Size (Moderate Miosis) without Affecting the Ciliary Muscle

---

Phentolamine mesylate is approved for 2 indications:

- **Regitine®** (Pheochromocytoma) – intravenous injection approved in 1952
- **OraVerse®** (Reversal of oral anesthesia) – intramuscular injection approved in 2008

---

505(b)(2) Regulatory Approval Pathway
Nyxol Product Candidate Profile

*Novel, Differentiated Alpha 1/2 Blocker Eye Drop for Refractive Indications*

<table>
<thead>
<tr>
<th>Nyxol: 0.75% Phentolamine Ophthalmic Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preservative Free, EDTA Free, and Stable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Efficacy Data</th>
<th>Favorable Safety Profile</th>
<th>Durable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nyxol Improves Vision by Decreasing Pupil (~1-1.5mm)</strong></td>
<td><strong>No Systemic Effects</strong></td>
<td><strong>Effects Last $\geq$ 24 Hours</strong></td>
</tr>
<tr>
<td>↑ Near Vision</td>
<td>No Changes in Blood Pressure</td>
<td>Chronic daily dosing of Nyxol at bedtime reduces pupil size for up to 24 to 36 hours</td>
</tr>
<tr>
<td>↑ Distance Vision</td>
<td>No Changes in Heart Rate</td>
<td></td>
</tr>
<tr>
<td>↑ Contrast Sensitivity (night)</td>
<td><strong>Well-Tolerated Topical Effects</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild, Transient, Reversible Eye Redness</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>IOP Unchanged or Decreased</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Minimal to No Headaches</td>
<td></td>
</tr>
</tbody>
</table>
I have to visit my retina MD for my monthly injections, where I am dilated. Being dilated every month is a huge burden on my day.

I had a premium cataract procedure by my MD, and I was unable to see clearly for two days. My doctor said it was due to my dilation. I did not expect my dilation to last that long.

I have to stay indoors. They say it only lasts a few hours but it lasts all day, and it is very annoying.

I have to visit my retina MD for my monthly injections, where I am dilated. Being dilated every month is a huge burden on my day.
Problem: Dilated Eyes for Exams and Procedures

Patients Report Significant Side Effects after Dilated Eye Exam

The Problem

Pharmacologically-induced pupil dilation is part of standard care for annual and specialty eye exams…

…but there is 6 to 24 hours of impaired vision including:

- Inability to Focus
- Photophobia (sensitivity to light)
- Cycloplegia (loss of accommodation)
- Difficulty Reading and Driving
- Halos and Glare

1. GlobalData Market Research Survey; Oraverse and Regitine Label

The Problem: Tropicamide and Cyclopentolate have same MOA

Physician’s Use of Mydriatic Agents

<table>
<thead>
<tr>
<th>Mydriatic Agent</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tropicamide Alone</td>
<td>52%</td>
</tr>
<tr>
<td>Tropicamide and Phenylephrine</td>
<td>18%</td>
</tr>
<tr>
<td>Phenylephrine Alone</td>
<td>16%</td>
</tr>
<tr>
<td>Paremyd</td>
<td>9%</td>
</tr>
<tr>
<td>Cyclopentolate</td>
<td>5%</td>
</tr>
<tr>
<td>Tropicamide and Phenylephrine</td>
<td>18%</td>
</tr>
</tbody>
</table>

Note - Tropicamide and Cyclopentolate have same MOA

NO REVERSAL DROPS COMMERCIALLY AVAILABLE
Nyxol® is the only eye drop in clinical development for multiple indications with a MOA that does not affect the ciliary muscle

Nyxol Has Potential To Be The Only Option For RM
Physicians AVOID Use of Cholinergic Agonists (Pilocarpine) Due to Safety Risk on Ciliary Muscle

2 Classes of Mydriatic Agents

**Phenylephrine**
(α1 agonist)

*Parasympathetic* innervation stimulates the iris sphincter and ciliary muscle

**Tropicamide**
(anti-cholinergic)

*Sympathetic* (primarily α1) innervation stimulates the iris dilator muscles

Reversal via the Ciliary Muscle by Cholinergic Agonists* is Not a ‘Safe’ Option

- Retinal tear has been reported in some patients, especially high myopes
- Induces accommodation spasm and reduction in distance vision
- Induced anterior shift of the lens can increase the risk of acute angle-closure glaucoma
- High incidence of brow ache and headache following installation

*Cholinergic Agonists include pilocarpine, carbachol, and aceclidine. Note, pilocarpine is rarely used off-label for RM given these safety concerns.

1 Pilocarpine FDA Label (2017)
2. Optician (2012): Mydriatic Drugs: Practical Considerations
Reversal of Mydriasis Unmet Need & Landscape

With No Commercially Available Treatment, Nyxol is Uniquely Positioned as a New Reversal Drop

The Problem

- At many annual eye exams and specialty visits, pupils are pharmacologically dilated, impairing vision for **6-24 hours**
- Dilated eyes experience:
  - Heightened sensitivity to light
  - Inability to focus, headaches
  - Difficulty reading, working & driving
  - Halos and glare
  - Cycloplegia (loss of accommodation)

No Currently Available Treatments

Current Landscape:

- Rare off-label use of cholinergic agonists (e.g., pilocarpine) given ciliary muscle safety issues
- Optomap® is offered by optometrists to avoid dilations for ~$50 cash-pay, however images may provide limited view of retina and disease pathology

Nyxol’s MOA Uniquely Suited As A Reversal Drop For Dilations
MIRA-3 Phase 3 Registration Trial Design

Randomized, Double-Blind, Placebo-Controlled, Parallel, Multi-Center, One-Day Trial

0.75% Nyxol

16 US sites
368 subjects

Mydriasis -1 Hour

Mydriatic Agent A, B, or C

Nyxol drop(s)
(2 drops study eye, 1 drop fellow eye)

Follow Up Visit

Primary Endpoint

Mydriatic Agent A, B, or C

Placebo drop(s)
(2 drops study eye, 1 drop fellow eye)

Mydriatic Agent A, B, or C

Placebo

Screening
Randomization

1:1

Endpoints

Primary: % of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min

Key Secondary:
- % of subjects returning to baseline at 0min, 30min, 1h, 90 min 2h, 3h, 4h, 6h, 24h (overall, by mydriatic agent, by iris color)
- Mean time to return to baseline PD
- Mean change in pupil diameter at all timepoints
- Distance-Corrected Near Vision
- Accommodation (Tropicamide/Paremyd)
- Safety and tolerability

Key Eligibility Criteria

Inclusion: Healthy ≥ 12 years of age

Exclusion: Clinically significant ocular trauma, surgery, or non-refractive laser treatment within the 6 months prior to screening; and recent or current evidence of ocular disease, infection or inflammation in either eye

MIRA-3 Started in Nov 2021 ➔ Enrolled 368 in Feb 2022
Phase 3 Results Reported March 2022

Mydriatic Agents 3:1:1 – A: 2.5% phenylephrine (alpha-1 agonist), B: 1% tropicamide (cholinergic blocker), C: Paremyd® (combination)
Primary Endpoint Achieved in Two FDA Registration Phase 3 Trials

Rapid, Consistent and Sustained Reversal of Pupil Dilation with Nyxol

### MIRA-3 Phase 3 Trial

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Percent of Subjects Returning to ≤ 0.2 mm of Baseline PD Study Eye (mITT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>Placebo (n=124): 4%</td>
</tr>
<tr>
<td>1</td>
<td>Placebo (n=124): 2%</td>
</tr>
<tr>
<td>1.5</td>
<td>Placebo (n=124): 6%</td>
</tr>
<tr>
<td>2</td>
<td>Placebo (n=124): 7%</td>
</tr>
<tr>
<td>3</td>
<td>Placebo (n=124): 14%</td>
</tr>
<tr>
<td>4</td>
<td>Placebo (n=124): 17%</td>
</tr>
<tr>
<td>6</td>
<td>Placebo (n=124): 36%</td>
</tr>
<tr>
<td>24</td>
<td>Placebo (n=124): 72%</td>
</tr>
</tbody>
</table>

### MIRA-2 Phase 3 Trial

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Percent of Subjects Returning to ≤ 0.2 mm of Baseline PD Study Eye (mITT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>Placebo n=91: 3%</td>
</tr>
<tr>
<td>1</td>
<td>Placebo n=91: 1%</td>
</tr>
<tr>
<td>1.5</td>
<td>Placebo n=91: 2%</td>
</tr>
<tr>
<td>2</td>
<td>Placebo n=91: 7%</td>
</tr>
<tr>
<td>3</td>
<td>Placebo n=91: 11%</td>
</tr>
<tr>
<td>4</td>
<td>Placebo n=91: 18%</td>
</tr>
<tr>
<td>6</td>
<td>Placebo n=91: 30%</td>
</tr>
<tr>
<td>24</td>
<td>Placebo n=91: 66%</td>
</tr>
</tbody>
</table>

Source: (Left panel) MIRA-3 Table 14.2.1.1 (mITT); (Right panel) MIRA-2 Table 14.2.1.1 (mITT). Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd).
MIRA-3: Mean Pupil Diameter Over Time

Nyxol Treatment Significantly Reduced PD Starting at 1 Hour Post-Dose Through 6 Hours

Source: MIRA-3 Table 14.2.2.1 (mITT). The p-values are change from max pupil dilation treatment compared to placebo. Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd). Standard Error bars are shown.
### MIRA-3: Mean Time to Return to Baseline PD

**Saving of ~4 Hours in Return to Normal PD Overall and Across Mydriatic Agents**

<table>
<thead>
<tr>
<th>Mydriatic Agent (study eye)</th>
<th>Overall</th>
<th>Fellow Eye</th>
<th>Placebo</th>
<th>Nyxol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Irides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>n=108</td>
<td>n=26</td>
<td>2.0</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Nyxol</td>
<td>n=56</td>
<td>n=47</td>
<td>2.1</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Dark Irides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>n=122</td>
<td>n=23</td>
<td>2.3</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Nyxol</td>
<td>n=59</td>
<td>n=46</td>
<td>2.5</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>n=66</td>
<td>n=26</td>
<td>1.3</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Nyxol</td>
<td>n=137</td>
<td>n=46</td>
<td>1.3</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Tropicamide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>n=230</td>
<td>n=137</td>
<td>2.7</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Nyxol</td>
<td>n=115</td>
<td>n=66</td>
<td>2.1</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Paremyd</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>n=230</td>
<td>n=115</td>
<td>2.7</td>
<td>p=&lt;0.001</td>
</tr>
<tr>
<td>Nyxol</td>
<td>n=66</td>
<td>n=26</td>
<td>2.1</td>
<td>p=&lt;0.001</td>
</tr>
</tbody>
</table>

**Time to Return to Baseline PD (Hours)**

- **Overall**: Placebo 6.4 Hours, Nyxol 6.3 Hours
- **Fellow Eye**: Placebo 6.4 Hours, Nyxol 6.3 Hours
- **Phenylephrine**: Placebo 5.6 Hours, Nyxol 5.6 Hours
- **Tropicamide**: Placebo 4.4 Hours, Nyxol 4.4 Hours
- **Paremyd**: Placebo 7.1 Hours, Nyxol 7.1 Hours
- **Light Irides**: Placebo 5.0 Hours, Nyxol 5.0 Hours
- **Dark Irides**: Placebo 5.7 Hours, Nyxol 5.7 Hours

Source: MIRA-3 Table 14.2.3.2 (PP Population).
# Summary of MIRA Registration Trial Designs

*Randomized, Double-Masked, Placebo-Controlled, Parallel, Multi-Center, One-Day Trials*

<table>
<thead>
<tr>
<th></th>
<th>MIRA-2 Phase 3</th>
<th>MIRA-3 2nd Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of US Sites</strong></td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td><strong>Subjects Enrolled</strong></td>
<td>185</td>
<td>368</td>
</tr>
<tr>
<td><strong>Eligibility</strong></td>
<td>Healthy ≥ 12 years of age</td>
<td>Healthy ≥ 12 years of age</td>
</tr>
<tr>
<td><strong>Randomization</strong></td>
<td>1:1</td>
<td>2:1</td>
</tr>
<tr>
<td><strong>Positive Data Readout</strong></td>
<td>1Q 2021</td>
<td>1Q 2022</td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>% of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min</td>
<td>% of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min</td>
</tr>
</tbody>
</table>

- **Total Subjects Enrolled**: >550
- **Total Exposure To POS**: >330

Over 300 subjects have been treated with POS and evaluated at 24-hours in the MIRA trials → satisfying regulatory requirements for drug safety exposure for the acute RM indication.

In addition, 32 subjects were enrolled in positive MIRA-1 Phase 2 trial, a randomized, double-masked, placebo-controlled, crossover, multi-center trial.
Summary of Positive MIRA-3 Phase 3 Results for Nyxol Eye Drops

*Confirms Prior Phase 3 Study Showing Substantial Benefit in Accelerating Reversal of Mydriasis*

**Efficacy**
- Met primary endpoint at 90 minutes with 58% of subjects returning to pre-dilation PD vs. 6% on placebo (p < 0.001)
  - MIRA-2 Phase 3 (49% vs 7%; p<0.0001)
- Saving of ~4 hours in time to return to normal pupil diameter
- Met all key secondary endpoints with high statistical significance
  - Efficacy seen at all timepoints from 60 minutes to 24 hours
  - One drop efficacy similar to two drops
  - Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Accelerated return to normal distance-corrected near visual acuity

**Safety**
- No deaths, serious AEs, or withdrawals due to AEs
- All treatment related AEs were mild in severity
- The only AE occurring in ≥ 5% of subjects treated with Nyxol was mild and transient conjunctival hyperemia (11% Nyxol vs. 0% placebo)
- Less than 1% of subjects reported instillation site discomfort, pain, or irritation
- Visual acuity (distance and near) was not adversely affected by Nyxol
- Over 300 subjects have been treated with Nyxol and evaluated at 24-hours in the MIRA trials → satisfying regulatory requirements for drug safety exposure for the acute RM indication
MIRA-4 Pediatric Trial Design

Well-Controlled, Randomized, Double-Masked Placebo-Controlled Study of Pediatrics Patients

**Key Eligibility Criteria**

**Inclusion:** Healthy subjects 3 to 11 years of age, inclusive.

**Primary Safety**

- Adverse events
- Vital signs
- Best-Corrected Distance Visual Acuity (BCDVA)
- Conjunctival hyperemia

**Efficacy Endpoints**

- % of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 minutes
- Change (in mm) in photopic pupil diameter from baseline at 90 minutes, 3 hours and 24 hours
- Time to return to baseline photopic pupil diameter

**MIRA-4 Started in Dec 2021 ➔ Results Reported April 2022**

Mydriatic Agents 3:1:1 – A: 2.5% phenylephrine (alpha-1 agonist), B: 1% tropicamide (cholinergic blocker), C: Paremyd® (combination)
MIRA-4: Efficacy Endpoints of Return to Baseline PD and Mean PD

Nyxol Rapidly Reversed Dilation Starting at 90 Minutes, 3 Hours and 24 Hours in Pediatric Subjects

Source: MIRA-4 Table 14.2.2.1 (mITT). Study and Fellow Eye Pupil Diameter. Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd). When presented, statistics represent LS (least-squares) Mean Difference between Nyxol vs. Placebo Change from Maximum Dilation.
MIRA-4: Safety and Efficacy Summary

Confirms Phase 3 Trials of Favorable Safety and Tolerability Profile and Rapid Mydriasis Reversal

- **Efficacy**
  - At 90 minutes post-dose, 64% of Nyxol returned to baseline PD compared to 25% on placebo
  - Efficacy seen at 3 timepoints measured from 90 minutes to 24 hours
  - Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Time savings of ~3 hour with one drop of Nyxol

- **Safety**
  - No Adverse Events
  - No reported instillation site discomfort or pain, burning, stinging, or irritation
  - No distance visual acuity loss
  - No change in vital signs
  - Completion of MIRA-4 study satisfies Pediatric Research Equity Act (PREA) requirement

Source: mITT Population, MIRA-2 and MIRA-3 Trial
NDA Submission Targeted in Late 2022
Potential Regulatory Approval in 2023

Target Label Indication
The treatment of pharmacologically induced mydriasis produced by adrenergic (e.g., phenylephrine) or parasympatholytic (e.g., tropicamide) agents, or a combination thereof.

Preservative-Free Single Unit Vial (5-pack)

Nyxol®

P3 Clinical Trial
Completed 2nd Phase 3 trial in RM (enrolled 368 subjects), which also meets 24-hour safety population exposure requirement

Pediatric Safety
Completed trial with 23 subjects ages 3 to 11 per agreed FDA initial pediatric study plan

Pediatric Safety
Completed trial with 23 subjects ages 3 to 11 per agreed FDA initial pediatric study plan

Ongoing

Manufacturing
Completed 3 registration batches; 1-year CMC stability will be available for NDA

Regulatory Approval
Submit NDA by late 2022, with expected approval review of 10 months

Preservative-Free Single Unit Vial (5-pack)
Reversal of Mydriasis (RM) Market Opportunity

With No Commercially Available Treatment, Nyxol May Achieve Significant Revenue Potential

GlobalData Market Research Findings

- 100M Annual Eye Dilations
- MIRA Trials Represent 95% of Dilation Drops Used in Practice
- 65% Report Moderate to Severe Impact to Daily Function
- 80% of Patients Likely to Request Drop
- Patient Willingness to Pay $10 - $20+

$500+M

Estimated US RM Market Opportunity

Source: GlobalData Market Research Survey
Calculation: 100M Annual Eye Dilations X 65% X 80% X $10 per patient = $500+M Opportunity

- 58% physicians would start prescribing Nyxol within 1st year
- 0 Current Commercially Available Treatments
- 81% patients would be more likely to schedule yearly eye exams with a reversal drop
- 68% physicians would be willing to use Nyxol even if patients had to still wear sunglasses within 1st hour
More Efficient Launch Opportunity for Nyxol in RM

*Launch is Poised to be Disruptive, Cost-Effective and Not Payor-Driven*

<table>
<thead>
<tr>
<th>Traditional Ophthalmic Launch</th>
<th>Ocuphire’s Nyxol RM Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>✗ Highly competitive markets (e.g., dry eye, glaucoma, allergy); little differentiation</td>
<td>✓ No competition or approved reversal drop → potential for Nyxol to be the only safe option</td>
</tr>
<tr>
<td>✗ Launch success takes time given payor (reimbursement) dependence</td>
<td>✓ Cash pay (no reimbursement barriers) allowing for quicker adoption</td>
</tr>
<tr>
<td>✗ Significant prior authorization &amp; step-edits hurdles with burden to the practices</td>
<td>✓ Offering a significant value proposition to patients and practices</td>
</tr>
<tr>
<td>✗ Lengthy sales cycles and touchpoints due to chronic use and market access upkeep</td>
<td>✓ Shortened sales-cycle with acute use product</td>
</tr>
<tr>
<td>✗ Significant product education requirement</td>
<td>✓ No training given dilations routine in practices</td>
</tr>
<tr>
<td>✗ Complex distribution channel including specialty and retail pharmacies</td>
<td>✓ No specialty/retail pharmacy → direct to physician</td>
</tr>
<tr>
<td>✗ “One product, one indication” commercial model is inefficient with fixed cost infrastructure</td>
<td>✓ “One product, several indications” offers efficiencies in commercial operations</td>
</tr>
</tbody>
</table>
Pre-Commercial 2022 & Go-To-Market Strategy 2023

Activities Underway to Support Capital-Efficient Nyxol RM Commercial Launch

Pre-Commercial Activity

Market Development (KOLs)
Physician Targeting
Patient Journey
Brand Awareness

Go-To-Market Strategy

Potential Options for Commercialization

Work with strategic or channel partner with existing commercial ophthalmic products

Hire contract commercial organization

Build own salesforce

Landscape
No approved drug/competition; data-mining for high volume practices

Easy Adoption
Dilations are a routine part of practice; adoption requires no staff or patient training

Components of an Efficient Launch

Direct to Physicians
No need for pharmacy; no reimbursement, private pay

Sources: ASRS; AMA; AAO; Women in Optometry (WO); AOA Excel and Jobson Medical Information; Physician Interviews Conducted by Ocuphire; GlobalData market research
“By age 45, 80% of Americans will struggle with Presbyopia, and by age 50, nearly everyone will.”

NY Times

“Effectively everyone over 40 will have the problems with reading.”

Physician KOL
2021: The Time for Presbyopia Drops

"The correction of presbyopia remains ophthalmology's 'Holy Grail'…"

-OIS
Nyxol® and Nyxol + Low Dose Pilocarpine Presbyopia Eye Drops

Differentiated MOA with Two Product Candidates for Functional Near Vision Improvement

0.75% Nyxol

- Phentolamine (alpha1/2 antagonist)
- Novel MOA (iris dilator)
- 24+ hour PD durability
- Moderate pupil reduction
- Well-tolerated with no systemic effects
- Stable, preservative-free, single-use vial

Evening drop

Iris Dilator Muscle Inhibition

Iris Sphincter Muscle Activation

Potential One Drop Solution
Nyxol with Durable Functional Near Vision

Optimal Pupil Target is 2-3 mm

0.4% LDP

- Pilocarpine (cholinergic agonist)
- Known MOA on sphincter (and ciliary) muscle
- Potent miotic at approved doses (1%, 2%, 4%)
- Low concentration avoids known safety issues:
  - Headache, brow ache, and redness
  - Accommodative spasm causing loss of distance vision especially at night

Potential Two Drop Solution
Nyxol + LDP for Presbyopes Who Need More Power

Source: Nyxol® data from 9 completed trials; Pilocarpine product label and literature
Presbyopia VEGA-1 Phase 2 Trial

Completed Randomized, Double-Masked, Placebo-Controlled, Multi-Center One-Week Trial

VEGA-1

17 US sites
150 presbyopic patients

0.75% Nyxol

Baselines

Nyxol

LDP Drop
Nyxol Alone
LDP Alone
Placebo Alone

Evening Dosing (3-4 doses)

Visit 1

Visit 2 (3 – 6 Days Later)

Treatment Arms

Randomization
Screening

0.75% Nyxol

Endpoints

Primary: % of subjects with ≥ 3 lines of improvement in distance-corrected near visual acuity comparing Nyxol + LDP vs placebo alone at 1 hour

Secondary:
• % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours in photopic lighting comparing Nyxol + LDP vs placebo, Nyxol alone, and LDP alone
• No loss of distance vision
• Pupil diameter at time points
• Safety and tolerability (redness)

Eligibility Criteria

• Males or females ≥ 40 and ≤ 64 years of age
• BCDVA of 0.0 LogMAR (20/20 Snellen equivalent) or better in each eye under photopic conditions
• DCNVA of 0.4 LogMAR (20/50 Snellen equivalent) or worse in photopic conditions in each eye & binocularly

Phase 2 Enrollment Completed Feb to May 2021 – 150 Subjects Reported Topline Results in June 2021 and Jan 2022

Clinical trial NCT#04675151. DCNVA = distance-corrected near visual acuity. BCDVA = best corrected distance visual acuity
VEGA-1: Nyxol+LDP Met Primary & Secondary Endpoints

60% Patients with Nyxol+LDP had ≥ 15 Letter Near Gain with Fast Onset & Durable Responses

VEGA-1 Phase 2 Trial

Percent of Subjects with ≥ 15 Letters Binocular Photopic DCNVA Improvement from Baseline

Note: PP population differs from mITT by only one subject; results were essentially identical.
VEGA-1: Planned P3 Efficacy Endpoint Met by Nyxol and Nyxol+LDP

Nyxol Single Drop and LDP Combination Provide Statistically Significant 3-line Near Vision Gain

**Percent of Subjects with ≥ 15 Letter Gain In Near & < 5 Letters Loss In Distance Vision in Photopic Binocular DCNVA**

**Time 0=12 Hours Post-Nyxol Dose**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=74)</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>Nyxol (n=73)</td>
<td>29%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Percent of Subjects with ≥ 15 Letter Gain In Near & < 5 Letters Loss In Distance Vision in Photopic Binocular DCNVA**

**Time 30 Minutes**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=43)</td>
<td>14%</td>
<td>0.03</td>
</tr>
<tr>
<td>Nyxol+LDP (n=43)</td>
<td>60%</td>
<td>0.008</td>
</tr>
<tr>
<td>Nyxol (n=30)</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>LDP (n=31)</td>
<td>26%</td>
<td></td>
</tr>
</tbody>
</table>

53% of subjects achieved ≥ 10 letter improvement in DCNVA at 12 hours (p=0.005 vs placebo) and a similar trend at other time points.

79% of subjects achieved ≥10 letter improvement in DCNVA at 1 Hour (p=0.005 vs placebo) and a similar trend at other time points.
VEGA-1: Improvement in Functional Near Vision

Nyxol and Nyxol with LDP Both Provide Durable Improvement in Functional Near Vision

Similar trend was seen at all timepoints
Baseline Inclusion: Photopic DCNVA of 20/50 or worse
Source: VEGA-1 TLR Table 14.2.24.1 Percent of Subjects with Photopic DCNVA by Time Point (PP Population)
What is the Optimal Pupil Size?

Literature Highlights: New Drops to Treat Presbyopia Achieve Optimal Pupil Diameter of 2-3 mm

“A fixed 2- to 3-mm small pupil or a 30% pupil miosis can both produce near visual acuity gains without significant losses to distance acuity or image quality, and therefore can be considered as optimal for a presbyope experiencing a wide range of light levels.”

- Optometry and Vision Science, November 2016

Effect of Target Luminance on Optimum Pupil Diameter for Presbyopic Eyes

“The impact of pupillary modulation on the functional depth of field differs among patients with refractive error versus those who are truly emmetropic.”

- Cataract & Refractive Surgery Today (CRST), January 2022

Source: Xu et al, OVS 2016; Pepose & Xu CRST article 2022, Effect of Target Luminance on Optimum Pupil Diameter for Presbyopic Eyes
VEGA-1: Mean Pupil Diameter Over Time

Achieved Optimal Pupil Size in Nyxol+LDP and Nyxol Alone Consistent with Near Vision Gains

**p<0.01
***p<0.0001

VEGA-1 Phase 2 Trial

Best Eye (PP Population)
Mean Photopic Pupil Diameter

Optimal Pupil Size between 2-3 mm

Nyxol+LDP arm statistically significant compared to all arms
Both components maintained dynamic pupillary response

Source: VEGA-1 TLR Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)
Summary Of Positive VEGA-1 Phase 2 Results

*Nyxol and Nyxol + LDP has Demonstrated Efficacy Response & Well Tolerated Safety Profile*

Well-Controlled, Multi-Center Phase 2 Trial Evaluating Nyxol & Nyxol+LDP

1. Nyxol as a Single Drop
   - Single Durable Drop
   - Met planned P3 endpoint at 12 hours (29%; p=0.02)
   - Durable near vision gain at 12 and 18 hours
   - 56% (12 hours post-dose)
   - Sustained PD reduction at least 18 hours
   - Ages 40-64
   - 20/50 or worse DCNVA
   - Light and dark irides

2. Nyxol with LDP Adjunctive Therapy
   - Two Drops Tunable Option
   - Met primary endpoint at 1 hour (60%; p=0.004)
   - Durable near vision gain through at least 6 hours
   - 84% (1-hour post-dose)
   - Sustained PD reduction at least 6 hours
   - Ages 40-64
   - 20/50 or worse DCNVA
   - Light and dark irides

Efficacy

Durability

Functional Vision (20/40 or better)

Reduction in PD

Breadth of Patients Showed Efficacy

Efficacy

Safety

- No serious AEs, most AEs were mild
- No headaches, no brow aches, and no blurry vision AEs were reported
- No loss in distance vision under photopic and mesopic lighting
- ~5% mild, transient redness
- No change in IOP

Nyxol and Nyxol+LDP Pooled Safety Findings

PP Population, VEGA-1 Trial

*Trend toward statistical significance even in smaller Nyxol arm from time 0 to time 6 hours (n=30); larger sample size for all arms planned in Phase 3 program*
Two Treatment Options for Spectrum of Presbyopic Patients

Two NDA Submissions Targeted in 2023: Nyxol Alone and Nyxol+LDP

Pursuing Product Labels for 1 Drop and 2 Drop Options for the Treatment of Presbyopia

Nyxol as a Single Agent for Presbyopia

- Single Durable Drop

Nyxol with LDP as Adjunctive Therapy for Presbyopia

- Two Drops Tunable Option

Initiating VEGA Phase 3 Program in Mid-2022 for Both Labels
Potential ‘Best in Class’ Presbyopia Drop(s)

**Nyxol and Nyxol+LDP Combination Data Differentiate on Efficacy, Safety, and Durability**

**Product Attributes***

<table>
<thead>
<tr>
<th>1) Efficacy (&gt; 3-Line Gain w/o loss of 1 line in DCNVA - Primary Endpoint Responders)*</th>
<th><strong>VUITY™</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>26-31% (3 hours)</td>
<td>No Significant Loss</td>
</tr>
<tr>
<td>&gt;5% Headaches</td>
<td>&gt;5% redness</td>
</tr>
<tr>
<td>18% at 6 hours</td>
<td></td>
</tr>
</tbody>
</table>

**Placebo Adjusted Values for Vuity™ were 15-23% in Gemini 1 & 2; Placebo Adjusted Nyxol was 16% and Nyxol+LDP was 33% (all stat significant)**

| **Caveats of cross-trial comparisons for VUITY™ and Nyxol/LDP. Differences include age, severity of near vision loss, lighting conditions, doses, timing, and # of patients** |

<table>
<thead>
<tr>
<th><strong>Nyxol</strong></th>
<th><strong>Nyxol+LDP</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>29% (12 hours)</td>
<td>60% (1 hour)</td>
</tr>
<tr>
<td>No Significant Loss</td>
<td>No Significant Loss</td>
</tr>
<tr>
<td>No Headaches</td>
<td>No Headaches</td>
</tr>
<tr>
<td>&lt;5% mild redness</td>
<td>~5% mild redness</td>
</tr>
<tr>
<td>37% at 18 hours</td>
<td>37% at 6 hours</td>
</tr>
</tbody>
</table>

*Nyxol’s Potential Differentiated Solution*
Presbyopia Eye Drops Competitive Landscape

*act on sphincter and ciliary muscles in dose-dependent manner

Allergan (VUITY™; 1.25% pilo)  
Orasis (CSF-1; Low dose pilo)  
Visus (Brimochol®; carbachol+brim)  
Lenz (aceclidine; aceclidine+brim)  
Novartis (EV-06)

NDA

Other Cholinergic Agonists*

Cholinergic Agonist* (pilocarpine)

Phase 1  
Phase 2  
Phase 3

Nyxol Creates a New, Differentiated MOA Class; Nyxol+LDP Offers Tunability Option

Ocuphire  
Eyenovia (MicroLine; 2% pilo)

Alpha Antagonist

Alpha Antagonist & pilocarpine*

Ocuphire (Nyxol)

Nyxol is differentiated as a new MOA class (iris dilator muscle) to reach an optimal pupil size
Presbyopia is a Burgeoning Market Opportunity

Large Disease Category with Global Spend on Reading Glasses; Tens of Millions of Likely Early Users in US

The Problem

- Lens loses ability to change shape when viewing objects up close as we age
- Dependence on reading glasses for intermittent and prolonged use, but unable to see near and far at same time
- Aesthetics and inconvenience

100% of adults over the age of 40 years are at risk of developing presbyopia

Emmetropes
- Naturally occurring clear vision
- No refractive error/post-LASIK

Hyperopes
- Poor near vision (starting at age 40)

Pseudophakes
- Cataract surgery for artificial lens (monofocal, multifocal IOLs)

Myopes
- Poor distance vision

~128M Presbyopes in the US

66 M

Emmetropes

14 M

Hyperopes

9 M

Pseudophakes

39 M

Myopes

~50 M Patients Likely To Be Early Users of Presbyopia Eyedrops

Assume 50% use eye drops*

Source:
### Key Findings from GlobalData Market Research on Presbyopia

*Insights Very Consistent with Presbyopia Eye Drop Market Research Surveys*

<table>
<thead>
<tr>
<th>120+ Million</th>
<th>90%</th>
<th>70%</th>
<th>40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presbyopia patients in the US</td>
<td>presbyopia patients wear reading glasses ≥ once per day</td>
<td>patients would consider an eye drop as an alternative to reading glasses</td>
<td>patients have asked their physicians about alternatives to reading glasses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>51%</th>
<th>67%</th>
<th>70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>physicians would offer eye drops as a first-line presbyopia treatment</td>
<td>physicians indicated interest in Nyxol+LDP</td>
<td>patients considered the 2 drops/bottle dosing to be moderately-to-very convenient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$\geq$ $50$/mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Willing to Pay</td>
</tr>
<tr>
<td>Vuity™ is priced at $79 for a 30-day supply</td>
</tr>
</tbody>
</table>

**Physician Perspective**

- N=120

**Patient Perspective**

- n=134
**Vuity™ is the First FDA-Approved Eyedrop for Presbyopia**

*Approval Sets the Stage for Market Development by Large Pharma to Build a Large Market*

**FDA Approval of Vuity™ positive for the presbyopia space**

Opportunities for new entrants with differentiated product attributes in a newly established segment with physicians and patients/consumers

~50 M Patients Likely To Be Early Users of Presbyopia Eyedrops

3-6 refills per year assumed

Private Cash Pay (Vuity™ fill List Price)

~$10B - $20B

Estimated US Presbyopia Market Opportunity

~2 Billion Presbyopes Globally for Even Larger Market Potential

Source:
I’m no longer comfortable driving at night, especially with my son in the car. I have a hard time playing beach volleyball in the evenings due to the bright lights at the courts.

Post-LASIK, Age 42
Market Opportunity in Dim Light or Night Vision Disturbances

No Approved Treatments with Ripe Opportunity for Growth

The Problem

- Peripheral imperfections scatter light when pupils enlarge in dim light, causing halos, starbursts, and glare that impair vision
- The imperfections may be caused by LASIK surgery, IOL implants, certain types of cataracts (cortical), and natural reasons (especially with age)
- Symptoms cannot be properly corrected by any type of lens (reading glasses, contact lenses) or surgical procedures

No Approved Treatments

- Moderate-Severe NVD
  ~16 M

Seeking Treatment Findings

- Night Myopia
  11 M
- Cortical Cataracts
  4 M
- Post-Lasik
  0.5 M
- Post-IOL Implant
  0.3 M

- Patients willing to try a new eye drop treatment | 67%

$2B - $4B

Estimated US NVD Market Opportunity

Pupil reduction with Nyxol may offer a potential solution to peripheral optical imperfections

GlobalData Market Research Report, 2020; Photos are illustrative
NVD LYNX-1 Phase 3 Registration Design

Ongoing Randomized, Double-Masked, Placebo-Controlled Two-Week Trial

LYNX-1

- 20 US sites
- 140 - 160 patients with NVD

Eligibility Screening → Randomization

0.75% Nyxol

daily evening dose (14 days)

Day 0

PLACEBO

Day 15 Assessments

Phase 3 Initiated in Dec 2020; Enrolled 145 Patients Jan 2022

Top Line Expected 2Q 2022

Endpoints

Primary: % of subjects with $\geq 3$ lines of improvement in mesopic low contrast best-corrected distance visual acuity (Day 8)

Secondary (Days 8 & 15):
- Pupil diameter
- Visual acuity measures (distance and near)
- Safety and tolerability (redness)
Nyxol Demonstrated Clinical Effect in NVD
Key Endpoints Observed in Multiple Phase 2 Trials; 24 to 36 Hour Durable Pupil Modulation

**NYX-SNV Phase 2 Trial**

**Improved Low Contrast Distance Visual Acuity***

<table>
<thead>
<tr>
<th>% of Eyes with Mesopic Low Contrast Visual Acuity Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 line</td>
</tr>
<tr>
<td>≥ 2 lines</td>
</tr>
<tr>
<td>≥ 3 lines</td>
</tr>
</tbody>
</table>

Source NYX-SNV

**ORION-1 Phase 2 Trial**

**Durable > 24-hour Pupil Modulation Effect**

<table>
<thead>
<tr>
<th>Pupil Diameter Change from Baseline in Mesopic Conditions (Study Eye)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Pupil Diameter: Placebo 4.6mm, Nyxol 4.7mm</td>
</tr>
</tbody>
</table>

Source: NYXG-201

<table>
<thead>
<tr>
<th>Day</th>
<th>Pupil Diameter Change from Baseline (mm and %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 8</td>
<td>-0.99 -20%</td>
</tr>
<tr>
<td>Day 14</td>
<td>-0.07 -2%</td>
</tr>
<tr>
<td>Day 15</td>
<td>-1.00 -21%</td>
</tr>
<tr>
<td>Day 16</td>
<td>-0.88 -19%</td>
</tr>
</tbody>
</table>

*NYX-SNV trial was small and not designed for a statistical 3-line improvement in low-contrast visual acuity; the ~20% effect was used for powering and sizing of Phase 3 trial.
APX3330

ORAL TABLET

DR  Diabetic Retinopathy

DME  Diabetic Macular Edema
Clinical Unmet Need in Diabetic Retinal Diseases

*Increasing Prevalence of DR with No Early Intervention Options*

### The Problem

- **DR/DME are major causes of vision loss in working aged adults**
- **Diabetic population expected to increase dramatically worldwide**
  - Losing vision is one of diabetic patients' top concerns
- **Approved therapies for DR are effective but require IVT injection**
- **DR patients are not routinely treated with approved injectable anti-VEGF drugs until they develop center-involved DME or PDR**
  - DR progresses resulting in vision loss
- **Early, noninvasive intervention targeting DR represents a therapeutic unmet need**

### Growing Incidence of Diabetes and DR

<table>
<thead>
<tr>
<th>Diabetes</th>
<th>34 M US &gt;450 M WW</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR</td>
<td>7 M US &gt;150 M WW</td>
</tr>
</tbody>
</table>

### US Projected Market in DR

$10+B Oral Rx Revenues

### DR/DME affects about 1 in 4 people with type 1 and type 2 diabetes

### Oral Alternatives To Injectable Therapies Are Needed For Earlier Stages Of Disease

Source:
1. American Diabetes Association; International Diabetes Federation; Healthline; *Ocphire internal analysis and assumptions*
3. Patient survey adapted from Lions International Foundation and International Diabetes Foundation-Europe; Meltzer 2000
APX3330 History and Ref-1 Inhibition Mechanism

Ref-1 Involved in Multiple Key Pathways that Contribute to Diabetic Retinopathy and DME

Mechanism of Action – Ref-1 Inhibition

- **Hypoxia**
  - Ref-1
  - HIF-1α
  - VEGF (Signaling Cascade)

- **Inflammation**
  - Ref-1
  - NF-κB
  - TNF-α
  - Chemokines
  - Other Growth Factors (Signaling Cascade)

- **Anti-VEGF**
- **Neovascularization**
- **Steroids**

- **Lucentis®**
- **EYLEA®**

**Ref-1 (reduction-oxidation effector factor-1) is a novel target discovered by Dr. Mark R. Kelley at Indiana University School of Medicine**

**APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of Ref-1**

**APX3330 previously developed by Eisai for multiple hepatic inflammatory indications and later by Apexian for advanced solid tumors in 11 Phase 1 and 2 trials**
  - Similar oncology origin as approved anti-VEGFs

**MOA uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1**

**Extensively studied in over 20 in-vitro and animal studies with favorable efficacy and safety**
In vitro Validation of APX3330 Mechanism of Action

APX3330 reduces VEGF protein expression in preclinical stroke model

APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages

APX3330 increases DNA oxidative repair and neuronal protection

Source:
1. Tao Yan et al. APX3330 Promotes Neurorestorative effects after stroke in type one diabetic rats. Aging and Disease. Vol 9, Oct 2018
2. Apurinic/Apyrimidinic endonuclease 1 regulates inflammatory response in macrophages.
Preclinical Data: Oral APX3330 Blocks Neovascularization

Lesion Volume Decrease with Oral APX3330 in Murine Laser CNV Model Similar to EYLEA® Data

- Efficacy was also seen after single intravitreal injection of 20µM APX3330 in mouse L-CNV model**
- Efficacy was also seen after dosing intraperitoneal injection of 50 mg/kg twice daily, 5 days on/2 days off, for 2 weeks in mouse L-CNV model***
- Efficacy was also seen after single intravitreal injection of 20µM APX3330 in Vldlr −/− mice model****

Source:
1. Silva et al. ARVO 2021 Annual Meeting
2. *Published data on EYLEA. This study was performed independently from APX3330 study and is a cross-study comparison.
3. **Li 2014; ***Pasha 2018; ****Jiang 2011 (Vldlr −/−: Very Low-Density Lipoprotein receptor knock-out mice)
Phase 1/2 Clinical Trials: PK Data Supporting the ZETA-1 Trial

APX3330 is Bioavailable and Reaches the Retina via Oral Administration

Plasma levels with 120 and 240 mg/day APX3330 dosing is multiple times higher than plasma concentrations for mouse efficacy ➔ planned clinical dose is 600 mg/day

Oral administration of APX3330 reaches the retina

Mouse

25 mg/kg APX3330 oral gavage measured in mouse retina

Rat

10 mg/kg APX3330 oral gavage measured in rat eye

Human

300 mg BID (600 mg/day total)

Established PBPK model predicts APX3330 reaches sufficient human retinal concentrations

Source:
Eisai PK clinical data APX_CLN_0002 (left panel)
1. Apexian preclinical data
2. Eisai preclinical data
3. Silva et al. Presented at the ARVO 2021 Annual Meeting
ZETA-1 Clinical Trial is Sponsored by Ocuphire Pharma https://clinicaltrials.gov/ct2/show/NCT04692688?term=ZETA-1&draw=2&rank=1

Ongoing, Randomized, Double-Blind, Placebo-Controlled 24-Week Trial (Similar To Eylea P3 DR Trial)

Top Line Expected in 2H 2022

Endpoints

Primary: % of subjects with a ≥ 2 step improvement on the DRSS (Diabetic Retinopathy Severity Scale) score at week 24

Secondary:
- Central subfield thickness (CST)
- BCDVA (ETDRS)
- DRSS change at week 12
- Rescue subjects
- Safety and tolerability

Exploratory:
- Labs / PK

Phase 2b Enrolled 103 DR Patients from April 2021 to March 2022

25 US sites

90-100 participants with moderately severe-to-severe NPDR or mild PDR

Noncentral DME is permitted

Eligibility Screening Randomization

APX3330 600mg/day (BID)

1:1

Week 0 Week 4 Week 12 Week 24

Primary Endpoint

Placebo BID

NPDR = non-proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
PDR = proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
ZETA-1 Clinical Trial is Sponsored by Ocuphire Pharma https://clinicaltrials.gov/ct2/show/NCT04692688?term=ZETA-1&draw=2&rank=1
Why DRSS is an Important Endpoint?

**FDA Accepted Endpoint for EYLEA® in PANORAMA Pivotal DR Trial - 2 Step Improvement on the DRSS Score at Week 24**

**Diabetic Retinopathy Severity Scale (DRSS)**

<table>
<thead>
<tr>
<th>ETDRS Severity Level</th>
<th>Steps</th>
<th>Non-proliferative disease</th>
<th>Proliferative disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETDRS Severity Level</td>
<td>ETDRS</td>
<td>Very Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>20</td>
<td>35</td>
<td>43</td>
</tr>
<tr>
<td>85</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PANORAMA: Reduction of DRSS Significantly reduces the incidence of Vision Threatening DR**

**Proportion of Patients Developing a VTC or CI-DME through Week 100**

Kaplan-Meier Analysis

- **VTC (PDR/ASNV) or CI-DME**
  - 79% vs. 79%
  - 30.6% vs. 77%
  - 35.4% vs. 74%
- **VTC**
  - 17.9% vs. 9.1%
  - 20.5% vs. 6.9%
  - 11.3% vs. 14.4%

Risk of vision-threatening events increases with worsening step progression

VTC = Vision threatening complication defined as PDR/ASNV
CI-DME = center involved DME

*Nominal p < 0.001 vs. sham*
Masked Safety Findings from Ongoing ZETA-1 Trial

**Favorable Safety Profile (as of 1/12/2022) Observed with 600 mg Oral Daily Doses in DR Subjects**

- **68** Randomized Subjects
- **>3700** Subject-Days at 600mg/day of Exposure (50% on APX3330)
- **28** Subjects with AEs (52 total events)
- **6** SAEs (all unrelated to study medication)
- Favorable safety profile consistent with 11 prior APX3330 trials

- 52 TEAEs in 28 subjects
  - 6/52 AEs were considered probably or possibly related to study medication
    - 4 Mild (vertigo, rash, pruritus, frequent bowel movements); 2 moderate (diarrhea*, DME**
    - 46/52 AEs were ‘not’ or ‘unlikely’ related (32 mild, 14 moderate)
- 6 SAEs in 6 subjects
  - None of these treatment emergent events were related to study medication
    - Cellulitis, dyskinesia, transient ischemic event, COVID-19, progression of multivessel coronary artery disease, cholecystitis
- Only 2 subjects have withdrawn from study due to AEs*/*
- No major organ toxicities (liver, heart, kidney, brain, lung) or vital sign abnormalities (blood pressure or heart rate) were observed

*Note: ZETA-1 Interim Data as of database 1/12/22. Complete monitoring will be performed before final database lock.

*vasovagal near syncope same subject considered unrelated to study medication and **DME same subject possibly study medication related (APX3330 or placebo)
### APX3330 Product Candidate Profile for Multiple Retinal Indications

**Oral, First-In-Class Ref-1 Inhibitor with Favorable Human Safety Data**

<table>
<thead>
<tr>
<th>Expected Efficacy Data</th>
<th>Favorable Safety Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improving Eye Health in Diabetics</strong></td>
<td>&gt;5800 Subject-exposure days* at ≥600 mg/day dose</td>
</tr>
<tr>
<td>↓ Inflammation</td>
<td>Few Systemic Adverse Effects</td>
</tr>
<tr>
<td>↓ Abnormal Angiogenesis</td>
<td>• &lt; 5% Mild Gastrointestinal (diarrhea)</td>
</tr>
<tr>
<td>Enhance Compliance &amp; Exposure</td>
<td>• &lt; 5% Mild Skin Rash (reversible)</td>
</tr>
<tr>
<td>Oral pill may reduce the burden of frequent anti-VEGF injections</td>
<td>No Organ Toxicity (Liver, Cardiovascular {BP, HR}, Kidney, Neurologic, Pulmonary)</td>
</tr>
<tr>
<td></td>
<td>No Ocular Effects</td>
</tr>
<tr>
<td></td>
<td>• No observed ocular AEs</td>
</tr>
</tbody>
</table>

*Phase 1 and Phase 2 clinical trials by Eisai, Apexian and Ocuphire (*includes ~34 subjects from ongoing ZETA-1 study)
Broad Opportunities to Treat Retinal Diseases with APX Platform

APX3330 May Treat Patients Across Retinal Diseases as Single Agent or Adjunctive Therapy

Potential Differentiated Solution

• Potential First Oral Rx for Retina Diseases
  – First-line earlier intervention for the diabetic eye
  – Add-on therapy to current anti-VEGF treatments to reduce intravitreal injection burden

• Proven Novel Mechanism
  – May decrease both inflammation and angiogenesis

• Convenient Daily Regimen

• Favorable Oral Safety Profile
  – As seen in 11 completed Phase 1 and Phase 2 clinical trials

• Improve Patient Compliance
  – Potentially alleviate the frequent burden of injections

Inflammatory component is common across these retina indications and potentially addressable by the MOA of Ref-1

Current anti-VEGF treatments

APX2009
APX2014
APX3330
(Local Delivery)
Large Global Market Opportunity in Retinal Disease

Retinal Global Markets Served by Anti-VEGF Injections Alone are Greater than $10B+ Today

Global Disease Prevalence (Patients)

- 93 M DR and DME combined¹
- 28 M RVO²
- 5 M GA³
- 196 M AMD⁴ (wet/dry)

Anti-VEGF Injectable Global Revenue⁶

- $5+B GA Revenues³
- $20 B Projected Global Revenue 2030
- $13 B Global Revenues 2020

Source:
5. Ocophile internal analysis and assumptions
6. Market Scope 2020
Team/Boards, Milestones, and Financial Data
Ocuphire's World-Class Medical Advisory Board

Fortunate for the Insights of Leading KOLs & Drug Candidate Co-Founders

- **James Katz, MD**
  - University of Illinois

- **Jay Pepose, MD, PhD**
  - UCLA School of Medicine

- **Thomas Samuelson, MD**
  - University of Minnesota

- **Marguerite McDonald, MD**
  - Columbia University

- **Elion Medical**
  - Eliot Lazar, MD
  - Georgetown University

- **Mark Kelley, PhD**
  - Indiana University
  - Co-Founder Apexian/APX3330

- **Michael Allingham, MD, PhD**
  - University of North Carolina

- **Peter Kaiser, MD**
  - Harvard Medical School

- **Jeffrey Heier, MD**
  - Boston University

- **Douglas Devries, OD**
  - University of Nevada

- **David Brown, MD**
  - Baylor University

- **Mitch Jackson, MD**
  - University of Chicago

- **Ed Holland, MD**
  - Loyola University Chicago

- **Jack Holladay, MD**
  - University of Texas

- **Y. Ralph Chu, MD**
  - Northwestern University

- **David Lally, MD**
  - Vanderbilt University

- **Michael Allingham, MD, PhD**
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Ocuphire Board of Directors

Seasoned Directors with Decades of Drug Development, M&A/Financings, and Ophthalmology
Track Record of Achieving Milestones ➔ Exciting 2022 News Cadence

Multiple Late-Stage Data Catalysts Expected in 2022 for Potential First NDA Approval in 2023

2021

- Report Positive Phase 3 Data for RM (MIRA-2)
- Report Positive Nyxol+LDP Phase 2 Data for Presbyopia (VEGA-1)
- New Patent Claims for Presbyopia
- ASCRS 2021 Presentation for MIRA-2 & VEGA-1
- Manufacture 3xRegistration Batches for Nyxol Blow-Fill-Seal (BFS) Eye Drops
- Initiate 2nd Phase 3 RM AND Pediatric RM trial

2022

- Report Positive Nyxol Alone Phase 2 Data for Presbyopia
- Report 2nd Phase 3 Data for RM (MIRA-3)
- Report Pediatric Data for RM (MIRA-4)
- Report Phase 3 Data for NVD (LYNX-1)
- Submit Nyxol NDA for RM
- Report Phase 2 Data for DR/DME (ZETA-1)
- Initiate VEGA Phase 3 Presbyopia Program

Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)
OCUP – Market Snapshot
Active Trading Volume and Sufficient Cash Runway Into 2Q 2023

<table>
<thead>
<tr>
<th>Ticker</th>
<th>OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>$2.80 As of 4-15-22</td>
</tr>
<tr>
<td>Market Cap</td>
<td>$53 M As of 4-15-22</td>
</tr>
<tr>
<td>Shares Outstanding</td>
<td>19.0 M As of 10K (3-24-21)</td>
</tr>
<tr>
<td>Cash</td>
<td>$24.5 M As of 12-31-21 (audited)</td>
</tr>
<tr>
<td>Cash Runway</td>
<td>Sufficient into 2Q 2023</td>
</tr>
<tr>
<td>Average Daily Volume</td>
<td>~215 K As of 4-15-22 (YTD Avg)</td>
</tr>
<tr>
<td>Short Interest</td>
<td>302 K; 1.6% of Float As of 4-15-22</td>
</tr>
</tbody>
</table>

Research Analyst Coverage on OCUP

<table>
<thead>
<tr>
<th>Research Analyst</th>
<th>Firm Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Newman</td>
<td>Canaccord Genuity</td>
</tr>
<tr>
<td>Kristen Kluska</td>
<td>Cantor Fitzgerald</td>
</tr>
<tr>
<td>James Molloy</td>
<td>Alliance Global Partners</td>
</tr>
<tr>
<td>Soumit Roy</td>
<td>Jones Trading</td>
</tr>
<tr>
<td>Matthew Caufield</td>
<td>H. C. Wainwright</td>
</tr>
</tbody>
</table>
www.ocuphire.com
ir@ocuphire.com

Click here to view Ocuphire Pharma’s Investor R&D Day Recording
What’s Important for RM?

Nyxol Has the Potential to be the Only FDA-Approved Treatment Option to Reverse Dilation

**Efficacy Signal**
- Statistically significant percent of subjects on Nyxol compared to placebo returning to baseline (within 0.2 mm) photopic pupil diameter (PD) at 90 min demonstrated in 2 well-controlled, multi-center clinical trials
- Precedent set with RevEyes Approval

**Safety**
- Well-tolerated drop
- No ocular or systemic AEs or SAEs

**Label Expansion**
- Opportunity to expand label with ongoing pediatric trial in patients 3 years and up given safety shown in dental reversal approval for phentolamine

**FDA Guidance**

**Physician/Patients**

**Efficacy Signal**
- Compelling magnitude of response compared to placebo with statistical significance
- More rapid response with Nyxol vs. placebo
- Works in all iris colors
- Works across all commonly used mydriatic agents

**Safety**
- No systemic side-effects such BP, HR, headache
- Mild, transient hyperemia is acceptable and common in Rx drops

**Patient Experience**
- Patients desire more rapid return to normal activities
- Patients actively asking for ‘reversal’ drops
- Patients want a comfortable experience post-dilation
- Patients more likely to maintain their annual exams if option to reverse dilation is presented
What’s Important for Presbyopia?

Nyxol+LDP has the Potential to be “Best in Class” Presbyopia Eyedrop

**Efficacy Signal**

Percent of subjects with ≥3-line improvement in near vision with less than 5 letters of distance loss in Nyxol+LDP combo compared to Nyxol alone and LDP alone as demonstrated in 2 well-controlled, multi-center clinical trials.

**Safety**

No loss of distance (included in efficacy)
Maintain night distance vision
Well-tolerated

**Broad Label Opportunity**

For Vuity™, FDA did not limit the use of the product to clinical trial parameters such as:
- age
- lighting conditions (photopic or mesopic)
- monocular or binocular
- phakic status

**Efficacy Signal**

- Achieve “functional near vision” and intermediate vision
- Achieve optimal pupil size
- Durability
- Dynamic/responsive pupil

**Safety**

- No loss of distance vision
- No headaches or brow aches
- Reliable night distance vision
- No stinging or burning
- Minimal redness

**Patient Experience**

- Tunability - ability to customize treatment based on patient’s lifestyle needs
- Favorable tolerability for continued use and Rx refills
What’s Important for DR/DME?
APX3330 Has the Potential to be 1st Line of Therapy for DR Patients

Efficacy Signal
Percent of patients on APX3330 with a ≥ 2 step improvement on the DRSS score at week 24 compared to placebo in 2 well-controlled, multi-center clinical trials

Safety
Approval depends on a product's benefit outweighing its risks in the intended population as demonstrated in multi-center, 2 years clinical trial

Non-Invasive Treatment Option
FDA does not require comparative arm of approved anti-VEGF injections such as Eylea for DR

Efficacy Signal
- Clinically meaningful decrease in diabetic retinopathy severity with APX3330
- Early intervention with oral may reduce progression to vision threatening DR into DME

Safety
- No major organ toxicities
- Well-tolerated (e.g., AEs acceptable if mild and infrequent for oral)

Non-Invasive Treatment Option
- Eylea®, although approved, is currently not used as standard of care because of the treatment burden for asymptomatic DR patients
- Ability to be prescribed by all eye care doctors
- Oral option increases global access, especially in underserved regions