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Agenda and Participants

Second Phase 3 RM Trial Topline Readout as Planned in 1Q22

• Highlights and Overview
• Topline MIRA-3 Phase 3 Clinical Trial Results for Nyxol in Reversal of Mydriasis (RM)
• Reversal of Mydriasis Market Opportunity
• Upcoming Milestones
• Q&A

Participants
Mina Sooch, MBA, President and CEO
Jay Pepose, MD, PhD, Medical Advisory Board and Board Member
Mitch Brigell, PhD, Head of Clinical Development
Susan Benton, MBA, Corporate Board Member
Bindu Manne, Head of Market Development and Commercialization
Charlie Hoffmann, MBA, VP of Corporate Development and Operations
Amy Rabourn, MAcc, VP of Finance
Highlights and Overview
Key Takeaways from Nyxol’s MIRA-3 2nd Phase 3 RM Trial

MIRA-3 Met Primary Endpoint
- Key Secondary Endpoints Met Statistical and Clinical Significance

Completed 2 Confirmatory FDA Registration Trials in RM
- **MIRA-3**
  - 58% vs. 6% p<0.0001
- **MIRA-2**
  - 49% vs. 7% p<0.0001

On Track to File Nyxol NDA in RM in Late 2022

MIRA-2 and MIRA-3 topline data.
### Addressing Unmet Needs in Large Markets

**Significant Preclinical & Clinical Data Supporting MOA, Efficacy and Safety**

<table>
<thead>
<tr>
<th>Refractive</th>
<th>Retina</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nyxol®</strong></td>
<td><strong>APX3330</strong></td>
</tr>
<tr>
<td>Novel α1/α2 Blocker 505(b)(2)</td>
<td>Oral REF-1 Inhibitor New Chemical Entity (NCE)</td>
</tr>
</tbody>
</table>

#### Refractive
- **10** Completed Phase 1, Phase 2, and Phase 3 Trials
- **>600** Subjects Dosed
- **Exposure in Humans**
  - **28 Days**
- **Patent Coverage**
  - **2034+**

#### Retina
- **11** Completed Phase 1 and Phase 2 Trials
- **>340** Subjects Dosed
- **Exposure in Humans**
  - **365 Days**
- **Patents to**
  - **2034+**

### US Market Opportunity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reverse of Mydriasis</td>
<td>~$500 M</td>
</tr>
<tr>
<td>Presbyopia</td>
<td>$10B - $20B</td>
</tr>
<tr>
<td>Night Vision Disturbances</td>
<td>$2B - $4B</td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td>$10+B Oral Rx Revenues*</td>
</tr>
<tr>
<td>Diabetic Macular Edema</td>
<td></td>
</tr>
</tbody>
</table>

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## Ocuphire 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>✓ MIRA-3</td>
<td></td>
<td>✓ Reported 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>❑ MIRA-4 Pediatric safety study data expected in 2Q 2022 (n=23)</td>
</tr>
<tr>
<td></td>
<td>Nyxol® + Low-Dose (0.4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>❑ VEGA Phase 3 program planned to initiate in mid-2022</td>
</tr>
<tr>
<td></td>
<td>Pilocarpine Eye Drops</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></td>
<td>Nyxol® Eye Drop</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></td>
<td>APX3330 Oral Pill</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>❑ Seeking partner funding for IND enabling studies and further development</td>
</tr>
<tr>
<td></td>
<td>APX2009 (Intravitreal or Local Delivery)</td>
<td></td>
<td></td>
<td></td>
<td>✓ Recent Positive Trial Data</td>
<td>✓ Ongoing Trial</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** 0.75% Nyxol (Phentolamine Ophthalmic Solution) is the same as 1% Nyxol (Phentolamine Mesylate Ophthalmic Solution)
Nyxol’s Differentiated MOA as an Alpha-1 Blocker

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

<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>

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><strong>Efficacy Data</strong></th>
<th><strong>Favorable Safety Profile</strong></th>
<th><strong>Durable</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nyxol Improves Vision by Decreasing Pupil (~1-1.5mm)</td>
<td>No Systemic Effects</td>
<td></td>
</tr>
<tr>
<td>↑ Near Vision</td>
<td>No Changes in Blood Pressure</td>
<td>Effects Last ≥ 24 Hours</td>
</tr>
<tr>
<td>↑ Distance Vision</td>
<td>No Changes in Heart Rate</td>
<td>Chronic daily dosing of Nyxol</td>
</tr>
<tr>
<td>↑ Contrast Sensitivity (night)</td>
<td>Well-Tolerated Topical Effects</td>
<td>at bedtime reduces pupil size</td>
</tr>
<tr>
<td></td>
<td>Mild, Transient, Reversible Eye Redness</td>
<td>for up to 24 to 36 hours</td>
</tr>
<tr>
<td></td>
<td>IOP Unchanged or Decreased</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.
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

Physician’s Use of Mydriatic Agents

- Tropicamide Alone 52%
- Tropicamide and Phenylephrine 18%
- Phenylephrine Alone 16%
- Paremyd 9%
- Cyclopentolate 5%
- Paremyd and Phenylephrine 18%

Note - Tropicamide and Cyclopentolate have same MOA

NO REVERSAL DROPS COMMERCIALY AVAILABLE
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)
Sympathetic (primarily α1)
innervation stimulates
the iris dilator muscles

Tropicamide
(anti-cholinergic)
Parasympathetic
innervation stimulates
the iris sphincter and
ciliary muscle

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.

Nyxol® is the only eye drop in clinical development for multiple indications with a MOA that does not affect the ciliary muscle

1 Pilocarpine FDA Label (2017)
2. Optician (2012)- Mydriatic Drugs: Practical Considerations
MIRA-3 Topline Phase 3 Results

Randomized, Parallel Arm, Double-Masked, Placebo-Controlled Study of the Safety and Efficacy of Nyxol (0.75% Phentolamine Ophthalmic Solution) to Reverse Pharmacologically-Induced Mydriasis in Healthy Subjects
MIRA-3 Phase 3 Registration Trial Design

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

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

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

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)
# Demographics

_Treatment and Placebo Arms Were Balanced in MIRA-3 Phase 3 Registration Trial_

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Nyxol n=244</th>
<th>Placebo n=124</th>
<th>Total n=368</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years): Mean (Range)</strong></td>
<td>34 (12-80)</td>
<td>36 (12-80)</td>
<td>35 (12-80)</td>
</tr>
<tr>
<td><strong>Sex: Male n (%)</strong></td>
<td>92 (37.7%)</td>
<td>59 (47.6%)</td>
<td>151 (41.0%)</td>
</tr>
<tr>
<td></td>
<td>152 (62.3%)</td>
<td>65 (52.4%)</td>
<td>217 (59.0%)</td>
</tr>
<tr>
<td><strong>Race: White n (%)</strong></td>
<td>182 (74.6%)</td>
<td>93 (75.0%)</td>
<td>274 (74.5%)</td>
</tr>
<tr>
<td></td>
<td>38 (15.6%)</td>
<td>21 (16.9%)</td>
<td>59 (16.0%)</td>
</tr>
<tr>
<td></td>
<td>22 (9.0%)</td>
<td>9 (7.3%)</td>
<td>31 (8.4%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>1 (0.8%)</td>
<td>7 (1.9%)</td>
</tr>
<tr>
<td></td>
<td>^includes American Indian or Alaska Native; Native Hawaiian or Other Pacific Islander</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Light Iris Color: n (%)</strong></td>
<td>113 (46.3%)</td>
<td>58 (46.8%)</td>
<td>171 (46.5%)</td>
</tr>
<tr>
<td><strong>Dark Iris Color: n (%)</strong></td>
<td>131 (53.7%)</td>
<td>66 (53.2%)</td>
<td>197 (53.5%)</td>
</tr>
</tbody>
</table>

Notes: 
- **32 pediatric subjects 12-17 years old were enrolled in the trial.**
- Race is more than 100% given subjects could check more than one category.
- Demographics represent all randomized population (ARP) of 368 which is the same as Safety Population and Modified-Intent-to-Treat (mITT).
- Per Protocol (PP) Population is 345, excludes 23 subjects who did not dilate more than 0.2 mm 1 hour after receiving mydriatic drop.

Source: MIRA-3 Table 14.1.2.1 (ARP) (mITT).
## Baseline Characteristics Study Eye

*Treatment and Placebo Arms Were Balanced Across Ocular Measures in the MIRA-3 Trial*

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Nyxol n=248</th>
<th>Placebo n=120</th>
<th>Total n=368</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Pupil Diameter</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (mm)</td>
<td>5.1</td>
<td>4.9</td>
<td>5.1</td>
</tr>
<tr>
<td><strong>Max Dilated Pupil Diameter</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (mm)</td>
<td>7.2</td>
<td>7.1</td>
<td>7.2</td>
</tr>
<tr>
<td><strong>Accommodation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (diopters)</td>
<td>7.4</td>
<td>7.6</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>BCDVA letters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55 letters = 20/20</td>
<td>57</td>
<td>57</td>
<td>57</td>
</tr>
<tr>
<td><strong>DCNVA letters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70 letters = 20/20</td>
<td>65</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td><strong>IOP (mmHg)</strong></td>
<td>16.2</td>
<td>16.1</td>
<td>16.1</td>
</tr>
</tbody>
</table>

Source: MIRA-3 Table 14.1.2.1 (ARP) (mITT).
Primary Endpoint: 58% of Subjects’ Study Eye Returned to Baseline at 90 Min

Nyxol Statistically Better Than Placebo Starting At 1 Hour And All Subsequent Timepoints

Source: MIRA-3 Table 14.2.1.1 (mITT). Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd).
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**

Percent of Subjects Returning to ≤ 0.2 mm of Baseline PD Study Eye (mITT)

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Placebo (n=124)</th>
<th>Nyxol (n=244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>4%</td>
<td>96%</td>
</tr>
<tr>
<td>1</td>
<td>2%</td>
<td>98%</td>
</tr>
<tr>
<td>1.5</td>
<td>6%</td>
<td>94%</td>
</tr>
<tr>
<td>2</td>
<td>7%</td>
<td>93%</td>
</tr>
<tr>
<td>3</td>
<td>14%</td>
<td>86%</td>
</tr>
<tr>
<td>4</td>
<td>17%</td>
<td>89%</td>
</tr>
<tr>
<td>6</td>
<td>36%</td>
<td>72%</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MIRA-2 Phase 3 Trial**

Percent of Subjects Returning to ≤ 0.2 mm of Baseline PD Study Eye (mITT)

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Placebo (n=124)</th>
<th>Nyxol (n=244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>3%</td>
<td>97%</td>
</tr>
<tr>
<td>1</td>
<td>1%</td>
<td>99%</td>
</tr>
<tr>
<td>1.5</td>
<td>7%</td>
<td>93%</td>
</tr>
<tr>
<td>2</td>
<td>7%</td>
<td>93%</td>
</tr>
<tr>
<td>3</td>
<td>11%</td>
<td>89%</td>
</tr>
<tr>
<td>4</td>
<td>18%</td>
<td>86%</td>
</tr>
<tr>
<td>6</td>
<td>30%</td>
<td>72%</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></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).
Comparison of One Drop (Fellow Eye) with Two Drops (Study Eye)

Similar 52% of Subjects Return to Baseline at 90 Minutes with a Single Drop of Nyxol

MIRA-3 Phase 3 Trial

Percent of Subjects Returning to ≤ 0.2 mm of Baseline PD Fellow Eye (mITT)

Source: MIRA-3 Table 14.2.1.1 (mITT). Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd).
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.
Mean Pupil Diameter Over Time by Mydriatic Agents

Nyxol Reduced PD With All Mydriatic Agents; More Rapidly with Phenylephrine as Expected

MIRA-3 Phase 3 Trial

Source: MIRA-3 Table 14.2.2.3. (mITT). The p-values are change from max pupil dilation treatment compared to placebo. Standard Error bars are shown.
Mean Pupil Diameter Over Time by Eye Color

Nyxol Reduced Pupil Diameter Rapidly in Both Light and Dark Irides

MIRA-3 Phase 3 Trial

Mean PD - Study Eye (mITT)

Source MIRA-3 Table 14.2.2.5-(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.
Mean Time to Return to Baseline PD

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

**Overall**
- **Study Eye**
  - Placebo: 2.1 hours, p=<0.001
  - Nyxol: 2.3 hours, p=<0.001
- **Fellow Eye**
  - Placebo: 2.5 hours, p=<0.001
  - Nyxol: 2.7 hours, p=<0.001

**Mydriatic Agent (study eye)**
- **Phenylephrine**
  - Placebo: 1.3 hours, p=<0.001
  - Nyxol: 1.5 hours, p=<0.001
- **Tropicamide**
  - Placebo: 2.7 hours, p=<0.001
  - Nyxol: 4.0 hours, p=<0.001
- **Paremyd**
  - Placebo: 3.4 hours, p=<0.001
  - Nyxol: 4.4 hours, p=<0.001

**Irides (study eye)**
- **Dark Irides**
  - Placebo: 2.3 hours, p=<0.001
  - Nyxol: 5.7 hours, p=<0.001
- **Light Irides**
  - Placebo: 2.0 hours, p=<0.001
  - Nyxol: 5.6 hours, p=<0.001

*Source: MIRA-3 Table 14.2.3.2 (PP Population).*
Maximum Pupil Dilation Results in Loss of Near Vision

Nyxol Returns Near Vision to Baseline Levels Statistically Faster Compared to Placebo

MIRA-3 Phase 3 Trial

DCNVA Letters Read
Study Eye (mITT)

Baseline Near Vision

Change from Baseline (Letters Read)

Time Post-Treatment with Nyxol/Placebo

-10 -8 -6 -4 -2 0 2

Nyxol (n=244)
Placebo (n=124)

MIRA-3 Table 14.3.6.1.1 (Safety Population) (mITT). DCNVA- Distance-Corrected Near Visual Acuity.
Summary of Safety Findings

Nyxol was Well Tolerated with a Favorable Safety Profile

• There were no deaths, serious AEs, or withdrawals due to AEs
• 48 of 244 (20%) Nyxol treated subjects reported 101 AEs
  – All treatment related AEs were mild in severity
• The only AE occurring in ≥ 5% of subjects treated with Nyxol, was conjunctival hyperemia (11% Nyxol vs. 0% placebo)
  – Less than 1% of subjects reported instillation site discomfort, pain, or irritation
• Conjunctival hyperemia was observed to be mild and transient
• 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

Source: MIRA-3 Table 14.3.1.1; MIRA-3 Table 14.3.1.2.2; MIRA-3 Table 14.3.3.2 (Safety Population).
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

• Met primary endpoint at 90 minutes with 58% of subjects returning to pre-dilation pupil diameter vs. 6% of placebo treated subjects ($p < 0.0001$)

• Saving of ~4 hours in time to return to normal pupil diameter

• Met key secondary endpoints with high statistical significance
  – Efficacy seen at all timepoints from 60 minutes to 24 hours
  – Similar efficacy for one drop and 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

• Favorable safety and tolerability profile
  – No serious AEs, no drop-outs from AEs
  – No systemic or ocular AEs were observed in $\geq 5\%$ of subjects, except for 11% mild, transient conjunctival hyperemia

• NDA planned for late 2022
Plans to NDA for Nyxol in RM
MIRA Program Evaluating Nyxol for the Reversal of Mydriasis

Efficient Clinical Programs have Positioned Ocuphire to Target NDA Filing in Late 2022

- **MIRA-1**
  - 2019
  - Phase 2b
  - n=32 crossover
  - Primary Endpoint Met ✓
  - Secondary Endpoints Met ✓

- **MIRA-2**
  - 2021
  - Phase 3
  - n=185
  - Primary Endpoint Met ✓
  - Secondary Endpoints Met ✓

- **MIRA-3**
  - 2022
  - Phase 3
  - n=368
  - Primary Endpoint Met ✓
  - Secondary Endpoints Met ✓

- **MIRA-4**
  - 2022
  - Pediatric Safety
  - n=23
  - Fully Enrolled 3-11 years old

- **RM NDA Filing**
  - 2022
  - NDA Submission
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**
Enrolled 23 subjects ages 3 to 11 per agreed FDA initial pediatric study plan

**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

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**Ongoing**
Reversal of Mydriasis Market Opportunity
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

100M Annual Eye Dilations

Current Landscape:

- Rare off-label use of cholinergic agonists (e.g., pilocarpine) given ciliary muscle safety issues\(^1,2\)
- Optomap\textsuperscript{\textregistered} is offered by optometrists to avoid dilations for ~$50 cash-pay, however images may provide limited view of retina and disease pathology\(^3\)

Nyxol’s MOA Uniquely Suited As A Reversal Drop For Dilations

Source
1. Optician (2012)-Mydriatic Drugs: Practical Considerations
2. Pilocarpine FDA Label (2017)
3. Optos plc Pricing
Bottom-Up Calculation of Annual Dilated Eye Exams

~100 M Annual Dilated Eye Exams are Performed in the US

<table>
<thead>
<tr>
<th>Providers</th>
<th>Number of Providers (X)</th>
<th>Average Number of Weekly Exams (Y)</th>
<th>Estimated % Patients Dilated (Z)</th>
<th>Total (X<em>Y</em>Z) * 48 wk/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optometrists</td>
<td>46,000</td>
<td>59</td>
<td>40%</td>
<td>~52 M</td>
</tr>
<tr>
<td>Ophthalmologists</td>
<td>18,000</td>
<td>88</td>
<td>50%</td>
<td>~38 M</td>
</tr>
<tr>
<td>Retina Specialists</td>
<td>3,000</td>
<td>150</td>
<td>50%</td>
<td>~10 M</td>
</tr>
</tbody>
</table>

Demand Side Validation

Supply Side Validation: Based on the ~2 million total units of mydriatic agents sold in 2020, we calculated the total number of dilated eye exams to be ~125 million patients, consistent with demand side estimates.

IQVIA 2020 sales data; KOL Interview; GlobalData market research; and AOA Excel and Jobson Medical Information

'Bottom-Up Calculation' assumes 48 total work weeks in a year

Supply side validation assumed each unit (bottle) has ~10 mL fill volume and each patient gets 2-4 drops
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
- 80% of Patients Likely to Request Drop
- Patient Willingness to Pay $10 - $20+
- MIRA Trials Represent 95% of Dilation Drops Used in Practice
- 65% Report Moderate to Severe Impact to Daily Function

~$500+M
Estimated US RM Market 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

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

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 Ocuhire; GlobalData market research
Upcoming Milestones
**Track Record of Achieving Milestones ➔ Exciting 2022 News Cadence**

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

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

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**Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)**
Q&A

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