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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 (P), 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/NVD/P/DR/DME. 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 Ocufire 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 Ocufire’s product candidates, including the scalability of Ocufire’s product candidates and (x) the maintenance of Ocufire’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 > 650 patients treated across 12 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 6 positive Phase 3 & Phase 2 data read-outs for Nyxol in RM, Presbyopia, and NVD
- 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
- $19.2 million cash reported at 3-31-22 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
Ophthalmology – An Attractive Biotech Sector

Demographics, M&A, Regulatory Approvals and Efficient Trials Favor Ophthalmic Drugs

Deal Activity

- April 2021: $355M
- October 2021: ~$2B
- December 2021: ~$1.5B
- January 2022: $670M
- December 2021: $1.75B

New Product Approvals

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

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

Aging Population

Active Partnering in 2021

Lower Cost, Quick Enrolling, Short Duration Clinical Trials

Favorable Regulatory Environment

Lower Cost, Quick Enrolling, Short Duration Clinical Trials

*SNDA

~$2B

~$1B

$1.75B

$670M

$355M

~$1.5B

$2B

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
Ocuphire Overview

Two Assets Addressing Unmet Needs in Multiple Large Markets

**Refractive**

- **Nyxol®**
  - Novel α1/α2 Blocker 505(b)(2)
  - NDA-Filing Ready
  - Completed Phase 1, Phase 2, and Phase 3 Trials
  - >650 Subjects Dosed
  - Exposure in Humans: 28 Days
  - Patent Coverage: 2034+
  - US Market Opportunity: ~$500 M
    - ~100 M eye dilations

- **APX3330**
  - Oral REF-1 Inhibitor New Chemical Entity (NCE)
  - Phase 2b Enrolled
  - Completed Phase 1 and Phase 2 Trials
  - >340 Subjects Dosed
  - Exposure in Humans: 365 Days
  - Patents to 2034+

**Retina**

- **Diabetic Retinopathy (DR)**
  - US Market Opportunity: $10+B
  - ~8 M patients

- **Diabetic Macular Edema (DME)**
  - US Market Opportunity: $2B - $4B
  - ~16 M patients

- **Presbyopia**
  - ~128 M patients
  - $10B - $20B

- **Night Vision Disturbances (NVD)**
  - ~8 M patients
  - $2B - $4B

**US Market Opportunity**

- $2B - $4B
- ~16 M patients

- $10B - $20B
- ~128 M patients

- ~$500 M
- ~100 M eye dilations

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

<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 the Active Ingredient in Nyxol: a Non-selective α1 & α2 Antagonist

- **Blocking α1**
  - Reduces Pupil Size
  - Nyxol blocks α1 receptors only found on the Iris Dilator Muscle
  - Decreases Pupil Size (Moderate Miosis)
  - without Affecting the Ciliary Muscle

- **Blocking α1**
  - Dilates Blood Vessels

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

**Nyxol: 0.75% Phentolamine Ophthalmic Solution**
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

**Physician’s Use of Mydriatic Agents**

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

*Note - Tropicamide and Cyclopentolate have same MOA*

**NO REVERSAL DROPS COMMERCIA LLY AVAILABLE**

1. GlobalData Market Research Survey; Oraverse and Regitine Label
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\(^1\)
- Induces accommodation spasm and reduction in distance vision\(^2\)
- Induced anterior shift of the lens can increase the risk of acute angle-closure glaucoma\(^2\)
- High incidence of brow ache and headache following installation\(^3\)

* 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
Reversal of Mydriasis Unmet Need & Landscape

With No Commercially Available Treatment, Nyxol is Uniquely Positionered 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

Source – Optos plc Pricing
MIRA-3 Phase 3 Registration Trial Design

*Randomized, Double-Masked, 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)
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>4%</td>
</tr>
<tr>
<td>1</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>1.5</td>
<td>6%</td>
<td>58%</td>
</tr>
<tr>
<td>2</td>
<td>7%</td>
<td>66%</td>
</tr>
<tr>
<td>3</td>
<td>14%</td>
<td>79%</td>
</tr>
<tr>
<td>4</td>
<td>17%</td>
<td>86%</td>
</tr>
<tr>
<td>6</td>
<td>36%</td>
<td>91%</td>
</tr>
<tr>
<td>24</td>
<td>72%</td>
<td>89%</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=91</th>
<th>Nyxol n=94</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>1</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>1.5</td>
<td>7%</td>
<td>49%</td>
</tr>
<tr>
<td>2</td>
<td>11%</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>18%</td>
<td>80%</td>
</tr>
<tr>
<td>4</td>
<td>30%</td>
<td>82%</td>
</tr>
<tr>
<td>6</td>
<td>45%</td>
<td>45%</td>
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<tr>
<td>24</td>
<td>66%</td>
<td>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.
# 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 2\textsuperscript{nd} 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 $\geq$ 12 years of age</td>
<td>Healthy $\geq$ 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 Nyxol**: $>330$

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.

In addition, 32 subjects were enrolled in positive MIRA-1 Phase 2 trial, a randomized, double-masked, placebo-controlled, crossover, multi-center trial as well as MIRA-4 pediatric safety trial of 23 children.

Source: In order from left to right
MIRA-2 Trial NCT# 04620213
MIRA-3 Trial NCT# 05134974

RM
Summary of Three Positive Late-Stage MIRA Clinical Trials

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

**Efficacy**
- Pivotal trials met primary endpoint of return to baseline PD at 90 minutes after dilation
  - MIRA-3 Phase 3 (58% Nyxol vs. 6% placebo, p<0.0001)
  - MIRA-2 Phase 3 (49% Nyxol vs 7% placebo; p<0.0001)
- MIRA-4 pediatric trial achieved 64% Nyxol vs. 25% Placebo (p<0.0001)
- Met key secondary endpoints with high statistical significance
  - Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Efficacy with 1 or 2 drops
  - Accelerated return to normal distance-corrected near visual acuity
- Saving of ~4 hours in time to return to normal pupil diameter

**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 and instillation site discomfort (11% Nyxol vs. 0% placebo)
- 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, MIRA-3 and MIRA-4 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)**

**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

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

**Ongoing**
Submit NDA by late 2022, with expected approval review of 10 months

**RD**

Target Label Indication

Nyxol®
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
- 80% of Patients Likely to Request Drop
- Patient Willingness to Pay $10 - $20+
- 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 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

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

Components of an Efficient Launch

- Retina
  - 3,000 Retinal Specialists

- Ophthalmology
  - 20,000 Ophthalmologists

- Optometry
  - 46,000 Optometrists

Sources: ASRS; AMA; AAO; Women in Optometry (WO); AOA Excel and Jobson Medical Information; Physician Interviews Conducted by Ocuhire; 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

Headlines from Academia and Industry Articles with an Early First Approval for Vuity™

“The correction of presbyopia remains ophthalmology’s ‘Holy Grail’…”

-OIS

Sources: Academic review articles, journals, and publications between July 2021 to December 2021
Nyxol® and Nyxol + Low Dose Pilocarpine Presbyopia Eye Drops

Differentiated MOA with Two Potential Product Labels 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

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

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

Daytime drop
- 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

Optimal Pupil Target is 2-3 mm

Nyxol as a Single Agent for Presbyopia
Single Durable Drop

Nyxol with LDP as Adjunctive Therapy for Presbyopia
Two Drops Tunable Option

Source: Nyxol® data from 12 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

Visit 1
Evening Dosing (4 doses)
Visit 2 (5 Days Later)

Treatment Arms

Baseline → Nyxol → LDP Drop → Nyxol + LDP
Baseline → Nyxol → No Treatment → Nyxol Alone
Baseline → Placebo → LDP Drop → LDP Alone
Baseline → Placebo → No Treatment → Placebo Alone

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

![Graph showing percent of subjects with ≥ 15 Letter Gain at various time points with statistical significance noted.]

- **Rapid onset of efficacy**
- **Durable benefit over 6 hours**

**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

1. Nyxol as a Single Drop for Presbyopia

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 at Visit 2

- Placebo (n=74): 12%
- Nyxol (n=73): 29%

p=0.02

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

2. Nyxol with LDP Adjunctive Therapy

Percent of Subjects with ≥ 15 Letter Gain In Near & < 5 Letters Loss In Distance Vision in Photopic Binocular DCNVA
Time 30 Minutes at Visit 2

- Placebo (n=43): 14%
- Nyxol+LDP (n=43): 60%
- Nyxol (n=30): 33%
- LDP (n=31): 26%

p<0.0001
p=0.03
p=0.008

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

Nyxol+LDP is statistically superior to Nyxol alone and LDP alone
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?

Literture 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

Photopic Lighting (100 -1000 lux)
Natural Pupil Size ~ 4 mm

VSTOF (Constricted/natural)

NEAR Vision

Optimum 2.0-3.0 mm

DISTANCE Vision

% Constricted Pupil Size of Natural Pupil

0% 20% 40% 60% 80% 100%

Natural Pupil

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*

---

**Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)**

<table>
<thead>
<tr>
<th>Time (Hours)</th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=43)</th>
<th>Nyxol (n=30)</th>
<th>Placebo + LDP (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.5</td>
<td>4.5</td>
<td>4.5</td>
<td>4.6</td>
</tr>
<tr>
<td>0</td>
<td>4.3</td>
<td>4.3</td>
<td>4.4</td>
<td>4.4</td>
</tr>
<tr>
<td>1</td>
<td>3.2</td>
<td>3.2</td>
<td>3.3</td>
<td>3.3</td>
</tr>
<tr>
<td>2</td>
<td>2.4</td>
<td>2.5</td>
<td>2.5</td>
<td>2.7</td>
</tr>
<tr>
<td>3</td>
<td>2.3</td>
<td>2.3</td>
<td>2.7</td>
<td>3.1</td>
</tr>
<tr>
<td>4</td>
<td>2.1</td>
<td>2.5</td>
<td>3.1</td>
<td>3.3</td>
</tr>
<tr>
<td>5</td>
<td>2.9</td>
<td>2.7</td>
<td>2.7</td>
<td>3.3</td>
</tr>
<tr>
<td>6</td>
<td>3.6</td>
<td>3.3</td>
<td>3.3</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- **p<0.01**
- ***p<0.0001**

---

- **Nyxol+LDP arm statistically significant compared to all arms**
- Both components maintained dynamic pupillary response
- Optimal Pupil Size between 2-3 mm

---

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

<table>
<thead>
<tr>
<th>Nyxol as a Single Drop</th>
<th>Nyxol with LDP Adjunctive Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td><strong>Efficacy</strong></td>
</tr>
<tr>
<td>Met planned P3 endpoint at 12 hours (29%; p=0.02)</td>
<td>Met primary endpoint at 1 hour (60%; p=0.004)</td>
</tr>
<tr>
<td>Durable near vision gain at 12 and 18 hours</td>
<td>Durable near vision gain through at least 6 hours</td>
</tr>
<tr>
<td>56% (12 hours post-dose)</td>
<td>84% (1-hour post-dose)</td>
</tr>
<tr>
<td>Sustained PD reduction at least 18 hours</td>
<td>Sustained PD reduction at least 6 hours</td>
</tr>
<tr>
<td><strong>Durability</strong></td>
<td><strong>Safety</strong></td>
</tr>
<tr>
<td><strong>Functional Vision (20/40 or better)</strong></td>
<td><strong>Safety</strong></td>
</tr>
<tr>
<td><strong>Reduction in PD</strong></td>
<td><strong>Safety</strong></td>
</tr>
<tr>
<td><strong>Breadth of Patients Showed Efficacy</strong></td>
<td><strong>Safety</strong></td>
</tr>
<tr>
<td><em>Ages 40-64</em></td>
<td>• No serious AEs, most AEs were mild</td>
</tr>
<tr>
<td><em>20/50 or worse DCNVA</em></td>
<td>• No headaches, no brow aches, and no blurry vision AEs were reported</td>
</tr>
<tr>
<td><em>Light and dark irides</em></td>
<td>• No loss in distance vision under photopic and mesopic lighting</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>• ~5% mild, transient redness</td>
</tr>
<tr>
<td><strong>Pooled Safety Findings</strong></td>
<td>• No change in IOP</td>
</tr>
</tbody>
</table>

*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*
Potential ‘Best in Class’ Presbyopia Drop(s)

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

<table>
<thead>
<tr>
<th>Product Attributes*</th>
<th>VUITY™</th>
<th>Nyxol</th>
<th>Nyxol+LDP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Efficacy (&gt; 3-Line Gain w/o loss of 1 line in DCNVA - Primary Endpoint Responders)*</td>
<td>26-31% (3 hours)</td>
<td>29% (12 hours)</td>
<td>60% (1 hour)</td>
</tr>
<tr>
<td>2) Safety: Loss of Distance in Mesopic</td>
<td>No Significant Loss</td>
<td>No Significant Loss</td>
<td>No Significant Loss</td>
</tr>
<tr>
<td>3) Tolerability: Headaches and Conjunctival Hyperemia</td>
<td>&gt;5% Headaches</td>
<td>No Headaches</td>
<td>No Headaches</td>
</tr>
<tr>
<td></td>
<td>&gt;5% redness</td>
<td>&lt;5% mild redness</td>
<td>~5% mild redness</td>
</tr>
<tr>
<td>4) Durability (% responders at the longest timepoint)</td>
<td>18% at 6 hours</td>
<td>37% at 18 hours</td>
<td>37% at 6 hours</td>
</tr>
</tbody>
</table>

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.

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).

Source: Nyxol Data: ASCRS (July 2021) Abstract# 76845 (Phase 2) and VEGA-1; Abstract 74336 (Phase 3). VUITY™ Data FDA Label and AAO 2021 Presentation.
Presbyopia Eye Drops Competitive Landscape

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

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

Pupil modulation MOA
Soften lens MOA
Combination drugs

Cholinergic Agonist*
(pilocarpine)

Other Cholinergic Agonists*

Visus
(Brimochol®; carbachol+brim)

Orasis
(CSF-1; Low dose pilo)

Eyenovia
(MicroLine; 2% pilo)

Lenz
(aceclidine; aceclidine+brim)

Novartis
(EV-06)

Ocuphire
(Nyxol)

Ocuphire
(Nyxol + 0.4% pilo)

Allergan
(VUITY™; 1.25% pilo)

Alpha Antagonist & pilocarpine*

Alpha Antagonist

NDA

Phase 3

Phase 2

Phase 1

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

Corporate Websites, Grzybowski, A, Markeviciute A, Zemaitiene R. A Review of Pharmacological Presbyopia Treatment. 2020
Presbyopia is a Burgeoning Market Opportunity

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

The Problem

- Lens loses ability to view objects up close as we age
- Dependence on reading glasses for intermittent and prolonged use, with inability 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 presbyopia³

FDA Approval of Vuity™ positive for the presbyopia eyedrop market

Private Cash Pay Vuity™ List Price $79

~$10B - $20B Estimated US Presbyopia Market Opportunity

~128M Presbyopes in the US

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

Assume 50% use eye drops*

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

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

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

Seeking Treatment Findings

- 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
NVD LYNX-1 Phase 3 Registration Design

Randomized, Double-Blind, Placebo-Controlled Two-Week Trial

**LYNX-1**
- 19 US sites
- 140 - 160 patients with NVD

**Eligibility Screening**
- Randomization

**Endpoints**

**Primary:** % of subjects with ≥ 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)

**Assessments**
- Day 0 Assessments
- Day 8 Assessments
- Day 15 Assessments

**Top Line Results Reported May 19, 2022**

**Phase 3 Initiated in Dec 2020; 145 Patients Enrolled**

*Note: Inclusion Criteria includes subjects with baseline mesopic LCVA of 20/63 or worse*
LYNX-1: Nyxol Met Primary Endpoint
Significantly Higher % of Nyxol Treated Subjects Gained ≥15 Letter and ≥10 Letter From Baseline

LYNX-1 Phase 3 Trial

Source: LYNX-1 topline data
LYNX-1: Improvement in Distance Vision

Nyxol Provides Meaningful Low Contrast Vision Benefit Across Lighting Conditions at Day 15

LYNX-1 Phase 3 Trial

Percent of Subjects with ≥10 Letter Improvement in mLCCA, pLCCA at Day 15

Study Eye (PP Population)

<table>
<thead>
<tr>
<th>Visual Acuity Metric</th>
<th>Placebo (n=71)</th>
<th>Nyxol (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mLCCA (Mesopic)</td>
<td>24%</td>
<td>47%</td>
</tr>
<tr>
<td>pLCCA (Photopic)</td>
<td>7%</td>
<td>30%</td>
</tr>
</tbody>
</table>

p<0.05

FDA Accepted Endpoint For Contrast Sensitivity Assessment Tested in Dim Light (Mesopic) and Bright Light (Photopic) Conditions

5% Low Contrast Visual Acuity (LCVA) Chart

Source: LYNX-1 topline data
Summary of Positive LYNX-1 Phase 3 Results For Nyxol Eye Drops

Data Support a Favorable Benefit/Risk Profile For Subjects with NVD

**Efficacy**

- Met primary endpoint at Day 8 with 13% of subjects gaining 15 or more ETDRS letters of mesopic low contrast distance visual acuity vs. 3% on placebo (p<0.05)
- Nyxol's 3 line efficacy increased after 14 days of evening dosing, with 21% responders compared to 3% on placebo (p<0.01)
- Nyxol statistically significantly reduced pupil diameter by a mean of ~1 mm on Day 8 and Day 15
- Significant improvements in low contrast distance vision under photopic conditions were also observed
- Efficacy was seen with light and dark irides
- Nyxol demonstrated benefit in mesopic high contrast near vision

**Safety**

- No deaths or serious AEs
- AEs occurring in >5% of Nyxol treated subjects included: Instillation site irritation (9% vs 0% placebo), Installation site pain (13% vs 0% placebo), Dysgeusia (11% vs 0% placebo) and conjunctival hyperemia (9% vs 3% placebo)
- 84% of the AEs considered related to Nyxol were mild
- No statistical difference in conjunctival hyperemia between treatment arms with evening dosing at Day 8 and Day 15

Source: mITT Population, LYNX-1Trial
APX3330
ORAL TABLET

Diabetic Retinopathy
Diabetic Macular Edema
Clinical Unmet Need in Diabetic Retinal Diseases

Growing Incidence of Diabetes and DR

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

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

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; *Ocuphire 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)
  - APX3330
- Inflammation
  - Ref-1
  - NF-κB
  - TNF-α
  - Chemokines
  - Other Growth Factors (Signaling Cascade)
- Neovascularization
- Steroids
- Anti-VEGF

- 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 Levels and Inflammatory Cytokines; Provides Neuronal Protection

APX3330 reduces VEGF protein expression in preclinical stroke model

Control  APX3330

APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages

APX3330 increases DNA oxidative repair and neuronal protection

VEGF

APX3330 enhances Ref-1 endonuclease activity in dorsal root ganglion neurons

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

L-CNV Mouse Retina Model

Lesion Size and Corresponding Fluorescent Stains in L-CNV Models Treated with APX3330 at 25 mg/kg oral gavage

APX3330

Vehicle 25 mg/kg 50 mg/kg

L-CNV Mouse Retina Model

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
**DR/DME ZETA-1 Phase 2b Design**

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

---

**Endpoints**

**Primary:** % of subjects with a $\geq$ 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

---

**ZETA-1**

25 US sites

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

Noncentral DME is permitted

Eligibility Screening → Randomization → 1:1

APX3330 600mg/day (BID)

Placebo BID

Week 0 → Week 4 → Week 12 → Week 24

Primary Endpoint

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

Top Line Expected in 2H 2022

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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](https://clinicaltrials.gov/ct2/show/NCT04692688?term=ZETA-1&draw=2&rank=1)
Why DRSS is an Important Endpoint?

**Eylea® Panorama study**

**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>
</tr>
</thead>
<tbody>
<tr>
<td>Non-proliferative disease</td>
<td>10 20 35 43 47 53 61 65 71 75 85</td>
</tr>
<tr>
<td>Proliferative disease</td>
<td>1 2 3 4 5 6 7 8 9 10 11</td>
</tr>
</tbody>
</table>

**ETDRS Severity**
- Very Mild
- Mild
- Mod
- Sev.
- Very Sev.
- Mild
- Mod
- High Risk

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

- Kaplan-Meier Analysis
- VTC (PDR/ASNV) or Cl-DME
- VTC
- Cl-DME

**Risk of vision-threatening events increases with worsening step progression**
Masked Safety Findings from Ongoing ZETA-1 Trial

Favorable Safety Profile (as of 4/27/2022) Observed with 600 mg Oral Daily Doses in Diabetic Subjects

103 Subjects Enrolled

70% Subjects completed thru Week 12

>30% Subjects completed thru Week 24

110 TEAEs in 46/103 Subjects (45%)

22 Treatment-Related
17 Mild
5 Moderate
Diarrhea, DME¹, pruritus, urticaria and blurry vision
0 Severe

88 Unrelated
57 Mild
25 Moderate
6 Severe

0 Major Organ Toxicities (Liver, heart, kidney, brain, lung or vital sign abnormalities e.g., blood pressure or heart rate)

7 SAE in 7/103 Subjects
0 Treatment Related
7 Unrelated²

>5600 Subject-Days of at 600mg/day APX3330 Exposure

Oral APX3330 Safety Profile Consistent with That Seen in Prior Trials

1. DME possibly study medication related (APX3330 or placebo)
2. Cellulitis (2 events in same subject), dyskinesia, transient ischemic event, COVID-19, progression of multivessel coronary artery disease, cholecystitis

Note: ZETA-1 Interim Data as of database 4/27/22 with complete monitoring before final database lock; assumes 50% subjects on APX3330
### 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><em><em>&gt;7700 Subject-exposure days</em> at ≥600 mg/day dose</em>*</td>
</tr>
<tr>
<td>↓ Inflammation</td>
<td><strong>Few Systemic Adverse Effects</strong></td>
</tr>
<tr>
<td>↓ Abnormal Angiogenesis</td>
<td>• &lt; 5% Mild Gastrointestinal (diarrhea)</td>
</tr>
<tr>
<td></td>
<td>• &lt; 5% Mild Skin Rash (reversible)</td>
</tr>
<tr>
<td><strong>Enhance Compliance &amp; Exposure</strong></td>
<td><strong>No Organ Toxicity</strong> (Liver, Cardiovascular {BP, HR}, Kidney, Neurologic, Pulmonary)</td>
</tr>
<tr>
<td>Oral pill may reduce the burden of frequent anti-VEGF injections</td>
<td><strong>No Ocular Effects</strong></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 ~103 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

Current anti-VEGF treatments

APX2009
APX2014
APX3330 (Local Delivery)

Inflammatory component is common across these retina indications and potentially addressable by the MOA of Ref-1
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 combined
- 5 M GA
- 28 M RVO
- 196 M AMD (wet/dry)

Antivascular Endothelial Growth Factor (Anti-VEGF) Injectable Global Revenue

- $10+B Oral Rx Revenues
- $5+B GA Revenues
- $20 B Projected Global Revenue 2030
- $13 B Global Revenues 2020

Source:
5. Ocuphire internal analysis and assumptions
6. Market Scope 2020
Team/Boards, Milestones, and Financial Data
Ocuphire Management Team

Decades of Biotech and Drug Development Experience

Mina Sooch, MBA
President & CEO and Founder

Amy Rabourn, CPA
VP, Finance

Charlie Hoffmann, MBA
VP Corporate Development and Operations

Tuck School of Business at Dartmouth

SynDev

Goldman Sachs

MICHIGAN ROSS

Daniela Oniciu, PhD
Global Head, R&D, Chemistry and Product Development

UF

Genspire Therapeutics

ESPERION

Cerenis Therapeutics

Novartis

SIRCION Therapeutics

UCF

Akebia Therapeutics

Aerpio

Pfizer

Revolvus

Verta

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

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  - Co-Founder Apexian/APX3330

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  - Vanderbilt University

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- **Retinal Specialist**
  - Jeffrey Heier, MD
  - Boston University
Ocuphire Board of Directors

Seasoned Directors with Decades of Drug Development, M&A/Financings, and Ophthalmology

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Chair, Board Director

Mina Sooch, MBA
Vice-Chair, Board Director
President & CEO

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Jay Pepose, MD, PhD
Board Director

James Manuso, PhD/MBA
Board Director

Richard Rodgers, MBA
Board Director

Susan Benton, MBA
Board Director
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>$2.12</td>
</tr>
<tr>
<td>Market Cap</td>
<td>$41 M</td>
</tr>
<tr>
<td>Shares Outstanding</td>
<td>19.3 M</td>
</tr>
<tr>
<td>Cash</td>
<td>$19.2 M</td>
</tr>
<tr>
<td>Cash Runway</td>
<td>Sufficient into 2Q 2023</td>
</tr>
<tr>
<td>Average Daily Volume</td>
<td>~145 K</td>
</tr>
<tr>
<td>Short Interest</td>
<td>397K; ~2% of Float</td>
</tr>
</tbody>
</table>

As of 6-10-22
As of 6-10-22
As of 10Q (5-13-21)
As of 3-31-22 (unaudited)
Guidance as of 10K (3-24-22)
30-day trailing average
As of 5-31-22

Research Analyst Coverage on OCUP

<table>
<thead>
<tr>
<th>Name</th>
<th>Firm</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>Sean Kim</td>
<td>Jones Trading</td>
</tr>
<tr>
<td>Matthew Caufield</td>
<td>H. C. Wainwright</td>
</tr>
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</table>
Restore Vision & Clarity

www.ocuphire.com
ir@ocuphire.com

Ocuphire Pharma

Click here to view Ocuphire Pharma’s Investor R&D Day Recording