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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, 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 > 550 patients treated across 10 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 2Q22
- 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 / ANGEL / Allergan
$355M

September 2021
REGN / BIO
$1.75B

October 2021
Théa / THUCURACLE
~$2B

December 2021
~$1B

New Product Approvals

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

Aging Population
Active Partnering in 2021
Lower Cost, Quick Enrolling, Short Duration Clinical Trials
Favorable Regulatory Environment

October 2021
December 2021
December 2021
December 2021

~$1.5B
~$1B
$670M

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
Nyxol® & APX3330: Development History and Patents

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

**Nyxol®**
- Novel α1/α2 Blocker
- 505(b)(2)

**APX3330**
- Oral REF-1 Inhibitor
- New Chemical Entity

**US Market Opportunity**

**Refractive**
- Completed Phase 1, Phase 2, and Phase 3 Trials
- >550 Subjects Dosed
- Exposure in Humans: 28 Days
- Patent Coverage: 2034+

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

**Presbyopia**
- Exposure in Humans: 28 Days
- Patent Coverage: 2034+

**Diabetic Retinopathy**
- Oral Rx Revenues: $10+B

**Diabetic Macular Edema**
- Oral Rx Revenues: $10+B

**Diabetes**
- Oral Rx Revenues: $10+B

**Night Vision Disturbances**
- Exposure in Humans: 28 Days
- Patent Coverage: 2034+

Source: Eisai and Apexian Data; GlobalData Market Research Report, 2020; Company Estimates for US Market Size; *Ocuphire internal estimates
## 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></td>
<td>MIRA-2 ✓ MIRA-3 ✓</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>Presbyopia (P)</td>
<td>Nyxol® Eye Drop</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VEGA-1 ✓</td>
<td>❑ VEGA Phase 3 program planned to initiate in mid-2022</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></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>✓ Recent Positive Trial Data Ongoing Trial</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™

<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>
<tr>
<td>Nyxol blocks α1 receptors only found on the Iris Dilator Muscle</td>
<td></td>
</tr>
<tr>
<td>Decreases Pupil Size (Moderate Miosis) without Affecting the Ciliary Muscle</td>
<td></td>
</tr>
</tbody>
</table>

Iris Dilator Muscle

Iris Sphincter 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>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 |

Nyxol: 0.75% Phentolamine Ophthalmic Solution  
Preservative Free, EDTA Free, and Stable

**Favorable Safety Profile**

- No Systemic Effects
- No Changes in Blood Pressure
- No Changes in Heart Rate

**Well-Tolerated Topical Effects**

- Mild, Transient, Reversible Eye Redness

- IOP Unchanged or Decreased
- Minimal to No Headaches

**Durable**

- Effects Last ≥ 24 Hours
- Chronic daily dosing of Nyxol at bedtime reduces pupil size for up to 24 to 36 hours
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%
- Phenylephrine Alone 16%
- Tropicamide and Phenylephrine 18%
- Paremyd 9%
- Cyclopentolate 5%

*Note - Tropicamide and Cyclopentolate have same MOA*

---

NO REVERSAL DROPS COMMERCIALY 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
  - \((\alpha_1\) agonist)
  - Sympathetic (primarily \(\alpha_1\)) 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 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

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

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

- 16 US sites
- 368 subjects

**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 0 min, 30 min, 1 h, 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

*MIRA* - 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>Placebo (n=124)</th>
<th>Nyxol (n=244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>4%</td>
<td>42%</td>
</tr>
<tr>
<td>1</td>
<td>2%</td>
<td>58%</td>
</tr>
<tr>
<td>1.5</td>
<td>6%</td>
<td>66%</td>
</tr>
<tr>
<td>2</td>
<td>7%</td>
<td>79%</td>
</tr>
<tr>
<td>3</td>
<td>14%</td>
<td>86%</td>
</tr>
<tr>
<td>4</td>
<td>17%</td>
<td>91%</td>
</tr>
<tr>
<td>6</td>
<td>36%</td>
<td>72%</td>
</tr>
<tr>
<td>24</td>
<td>89%</td>
<td>89%</td>
</tr>
</tbody>
</table>

**MIRA-2 Phase 3 Trial**

<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>28%</td>
</tr>
<tr>
<td>1.5</td>
<td>7%</td>
<td>49%</td>
</tr>
<tr>
<td>2</td>
<td>14%</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>17%</td>
<td>80%</td>
</tr>
<tr>
<td>4</td>
<td>36%</td>
<td>82%</td>
</tr>
<tr>
<td>6</td>
<td>86%</td>
<td>45%</td>
</tr>
<tr>
<td>24</td>
<td>91%</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.
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>Study Eye</th>
<th>Fellow Eye</th>
<th>Placebo</th>
<th>Nyxol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>n=115</td>
<td>n=230</td>
<td>2.1, p=&lt;0.001</td>
<td>6.3hrs</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>n=66</td>
<td>n=137</td>
<td>1.3, p=&lt;0.001</td>
<td>5.6hrs</td>
</tr>
<tr>
<td>Tropicamide</td>
<td>n=26</td>
<td>n=46</td>
<td>4.0, p=&lt;0.001</td>
<td>7.6hrs</td>
</tr>
<tr>
<td>Paremyd</td>
<td>n=23</td>
<td>n=47</td>
<td>2.7, p=&lt;0.001</td>
<td>7.1hrs</td>
</tr>
<tr>
<td>Dark Irides</td>
<td>n=59</td>
<td>n=122</td>
<td>2.3, p=&lt;0.001</td>
<td>5.7hrs</td>
</tr>
<tr>
<td>Light Irides</td>
<td>n=56</td>
<td>n=108</td>
<td>2.0, p=&lt;0.001</td>
<td>7.0hrs</td>
</tr>
</tbody>
</table>

Source: MIRA-3 Table 14.2.3.2 (PP Population).
MIRA-3: 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)

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

Baseline Near Vision

Max dilation; Treatment
Mydriatic

Change from Baseline (Letters Read)

Time Post-Treatment with Nyxol/Placebo
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 < 0.001)
  - 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
  - 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

- 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

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.

---

**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

---

**Preservative-Free Single Unit Vial (5-pack)**

---

**Ongoing**

---

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

---

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

\[
\text{Estimated US RM Market Opportunity} \approx \$500+M
\]

Source: GlobalData Market Research Survey
Calculation: 100M Annual Eye Dilations \times 65\% \times 80\% \times \$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><strong>Traditional Ophthalmic Launch</strong></th>
<th><strong>Ocuphire’s Nyxol RM Launch</strong></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 Ocuhire; GlobalData market research

Retina
- 3,000 Retinal Specialists

Ophthalmology
- 20,000 Ophthalmologists

Optometry
- 46,000 Optometrists
NYXOL®
for
PRESBYOPIA

“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
“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

Optimal Pupil Target is 2-3 mm

Potential One Drop Solution
Nyxol with Durable Functional Near Vision

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

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

Daytime drop

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

Placebo

Randomization
Screening

Visit 1
Evening Dosing
(3-4 doses)
Visit 2
(3 – 6 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

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

- **Placebo (n=43)**
  - 0 hours: 16%
  - 0.5 hours: 14%
  - 1 hour: 28%
  - 2 hours: 16%
  - 3 hours: 21%
  - 4 hours: 21%
  - 6 hours: 19%

- **Nyxol+LDP (n=43)**
  - 0 hours: 33%
  - 0.5 hours: 16%
  - 1 hour: 60%
  - 2 hours: 60%
  - 3 hours: 47%
  - 4 hours: 47%
  - 6 hours: 37%

**Note:** PP population differs from mITT by only one subject; results were essentially identical.

**Rapid onset of efficacy**

**Durable benefit over 6 hours**
VEGA-1: Planned P3 Efficacy Endpoint Met by Nyxol and Nyxol+LDP
\textit{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 $\geq 15$ Letter Gain In Near & $<$ 5 Letters Loss In Distance Vision in Photopic Binocular DCNVA

\textit{Time 0=12 Hours Post-Nyxol Dose}

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

2. Nyxol with LDP Adjunctive Therapy

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

\textit{Time 30 Minutes}

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent of Subjects</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=43)</td>
<td>14%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Nyxol+LDP (n=43)</td>
<td>60%</td>
<td>p=0.03</td>
</tr>
<tr>
<td>Nyxol (n=30)</td>
<td>33%</td>
<td>p=0.008</td>
</tr>
<tr>
<td>LDP (n=31)</td>
<td>26%</td>
<td></td>
</tr>
</tbody>
</table>

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

79\% of subjects achieved \(\geq 10\) 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

1. Nyxol as a Single Drop for Presbyopia
2. Nyxol with LDP Adjunctive Therapy

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?

"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
VEGA-1: Mean Pupil Diameter Over Time

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

**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>Single Durable Drop</td>
<td>Two Drops Tunable Option</td>
</tr>
</tbody>
</table>

#### Efficacy

- **Efficacy**
  - Met planned P3 endpoint at 12 hours (29%; \(p=0.02\))
  - Met primary endpoint at 1 hour (60%; \(p=0.004\))
  - Durable near vision gain at 12 and 18 hours
  - Durable near vision gain through at least 6 hours
  - 56% (12 hours post-dose)
  - 84% (1-hour post-dose)

- **Functional Vision** (20/40 or better)
  - Sustained PD reduction at least 18 hours
  - Sustained PD reduction at least 6 hours

- **Reduction in PD**
  - **Breadth of Patients Showed Efficacy**
    - Ages 40-64
    - 20/50 or worse DCNVA
    - Light and dark irides

#### 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

---

*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*

<table>
<thead>
<tr>
<th>Product Attributes*</th>
<th>VUITY™</th>
<th>Nyxol</th>
<th>Nyxol+LDP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy (≥ 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>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>Tolerability: Headaches and Conjunctival Hyperemia</td>
<td>&gt;5% Headaches &gt;5% redness</td>
<td>No Headaches &lt;5% mild redness</td>
<td>No Headaches ~5% mild redness</td>
</tr>
<tr>
<td>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

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

- **Pupil modulation MOA**
- **Soften lens MOA**
- **Combination drugs**

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

**Other Cholinergic Agonists***

- Novartis (EV-06)
- Ocuphire (Nyxol)
- Lenz (aceclidine; aceclidine+brim)
- Orasis (CSF-1; Low dose pilo)
- Visus (Brimochol®; carbachol+brim)
- Eyenovia (MicroLine; 2% pilo)
- Allergan (VUITY™; 1.25% pilo)
- Ocuphire (Nyxol + 0.4% pilo)
- Lenz (aceclidine; aceclidine+brim)
- Orasis (CSF-1; Low dose pilo)
- Visus (Brimochol®; carbachol+brim)
- Eyenovia (MicroLine; 2% pilo)
- Allergan (VUITY™; 1.25% pilo)

**Alpha Antagonist & pilocarpine***

**Alpha Antagonist**

- Allergan
- Ocuphire

**Cholinergic Agonist*** (pilocarpine)

**Phase 1**

**Phase 2**

**Phase 3**

**NDA**

*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

~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

~44 M Patients Likely To Be Early Users of Presbyopia Eyedrops

Source:
Key Findings from GlobalData Market Research on Presbyopia

Insights Very Consistent with Presbyopia Eye Drop Market Research Surveys

120+ Million
Presbyopia patients in the US

90%
Presbyopia patients wear reading glasses ≥ once per day

70%
Patients would consider an eye drop as an alternative to reading glasses

40%
Patients have asked their physicians about alternatives to reading glasses

51%
Physicians would offer eye drops as a first-line presbyopia treatment

67%
Physicians indicated interest in Nyxol+LDP

≥ $50/mo
Patient Willing to Pay

Vuity™ is priced at $79 for a 30-day supply

70%
Patients considered the 2 drops/bottle dosing to be moderately-to-very convenient

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

~44 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

---

**求医欲求治疗的发现**

- 愿意尝试新眼药水治疗的患者比例：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
Ongoing Randomized, Double-Masked, Placebo-Controlled Two-Week Trial

**LYNX-1**

- 20 US sites
- 140 - 160 patients with NVD
- Eligibility Screening
- Randomization
- Daily evening dose (14 days) - 0.75% Nyxol
- Placebo

**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)

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

**Top Line Expected 2Q 2022**
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*

% of Eyes with Mesopic Low Contrast Visual Acuity Improvement

Source NYX-SNV

ORION-1 Phase 2 Trial

Durable > 24-hour Pupil Modulation Effect

Pupil Diameter Change from Baseline in Mesopic Conditions (Study Eye)

Source NYXG-201

*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

Diabetic Retinopathy

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

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

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

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

$10+B

Oral Rx Revenues
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)

- 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 Levels and Inflammatory Cytokines; Provides Neuronal Protection

APX3330 reduces VEGF protein expression in preclinical stroke model

Control

APX3330

VEGF

0.1mm

APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages

TNF-α

IL-6

Increasing APX3330 dose

APX3330 increases DNA oxidative repair and neuronal protection

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 Gavage OCT

Lesion Volume

Silva et al. 2021

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

25 mg/kg APX3330 oral gavage measured in mouse retina

10 mg/kg APX3330 oral gavage measured in rat eye

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)

ZETA-1

25 US sites
90-100 participants with moderately severe-to-severe NPDR or mild PDR
Noncentral DME is permitted

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

APX3330 600mg/day (BID)

Placebo BID

1:1

Week 0
Week 4
Week 12
Week 24

Top Line Expected in 2H 2022

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

Eligibility Screening
Randomization

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?

**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>Very Mild</th>
<th>Mild</th>
<th>Mod</th>
<th>Sev.</th>
<th>Mild</th>
<th>Mod</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steps</td>
<td>10</td>
<td>20</td>
<td>35</td>
<td>43</td>
<td>47</td>
<td>53</td>
<td>61</td>
</tr>
</tbody>
</table>

**Non-proliferative disease**

**Proliferative disease**

**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**
  - 17.9%*
  - 20.8%
  - VTC
  - 11.3%*
  - 14.4%
  - CI-DME

- **% reduction in likelihood of developing the event over time**

*Nominal p < 0.001 vs. Sham

**Risk of vision-threatening events increases with worsening step progression**
## 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**

<table>
<thead>
<tr>
<th>APX3330 Masked Safety Data</th>
<th>68 Randomized Subjects</th>
<th>&gt;3700 Subject-Days at 600mg/day of Exposure (50% on APX3330)</th>
<th>28 Subjects with AEs (52 total events)</th>
<th>6 SAEs (all unrelated to study medication)</th>
<th>Favorable safety profile consistent with 11 prior APX3330 trials</th>
</tr>
</thead>
</table>

- 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

*vasovagal near syncope same subject considered unrelated to study medication and **DME same subject possibly study medication related (APX3330 or placebo)

Note: ZETA-1 Interim Data as of database 1/12/22. Complete monitoring will be performed before final database lock.
# 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>&lt;br&gt;↓ Inflammation&lt;br&gt;↓ Abnormal Angiogenesis</td>
<td><strong>&gt;5800 Subject-exposure days* at ≥600 mg/day dose</strong></td>
</tr>
<tr>
<td><strong>Enhance Compliance &amp; Exposure</strong>&lt;br&gt;Oral pill may reduce the burden of frequent anti-VEGF injections</td>
<td><strong>Few Systemic Adverse Effects</strong>&lt;br&gt;• &lt; 5% Mild Gastrointestinal (diarrhea)&lt;br&gt;• &lt; 5% Mild Skin Rash (reversible)</td>
</tr>
<tr>
<td></td>
<td><strong>No Organ Toxicity</strong> (Liver, Cardiovascular {BP, HR}, Kidney, Neurologic, Pulmonary)</td>
</tr>
<tr>
<td></td>
<td><strong>No Ocular Effects</strong>&lt;br&gt;• No observed ocular AEs</td>
</tr>
</tbody>
</table>

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*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

DR
DME
Wet AMD
Dry AMD
RVO
GA

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

APX3330
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)

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

Anti-VEGF Injectable Global Revenue⁶

- **$10+B** Oral Rx Revenues⁶
- **$5+B** GA Revenues³
- **$20 B** Projected Global Revenue 2030
- **$13 B** Global Revenues 2020

Source:
5. Ocuphire internal analysis and assumptions
6. Market Scope 2020

4% CAGR
- Aging
- Access
- Diabetes
- New Rx Products
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

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

Ronil Patel, MS
Senior Director BD and
Market Strategy

Bindu Manne
Head, Market Development
and Commercialization

MBA

Drey Coleman
VP, Clinical Operations

Chris Ernst
Global Head, QA
and Manufacturing

Laura Gambino
Director, Project Management

Mitch Brigell, PhD
Head, Clinical Development
and Strategy

Barbara Withers, PhD
VP, Clinical and
Regulatory Strategy

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VP, Clinical and
Regulatory Strategy

Chris Ernst
Global Head, QA
and Manufacturing
Ocuphire's World-Class Medical Advisory Board
Fortunate for the Insights of Leading KOLs & Drug Candidate Co-Founders

- **Oculocare's World-Class Medical Advisory Board**

**CEI**
- **CEI Cincinnati Eye Institute**
- **Refractive Specialist**
- **James Katz, MD**
  University of Illinois

**OCLI**
- **OCLI**
- **Refractive Specialist**
- **Marguerite McDonald, MD**
  Columbia University

**ChuVision**
- **Refractive Specialist**
- **Y. Ralph Chu, MD**
  Northwestern University

**arcscan**
- **Refractive Specialist**
- **Jack Holladay, MD**
  University of Texas

**eCON Medical**
- **Refractive Specialist**
- **Eliot Lazar, MD**
  Georgetown University

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

**New England Retina Consultants**
- **Retinal Specialist**
- **David Lally, MD**
  Vanderbilt University

**Duke Eye Center**
- **Retinal Specialist**
- **Michael Allingham, MD, PhD**
  University of North Carolina

**Ophthalmic Consultants of Boston**
- **Retinal Specialist**
- **Jeffrey Heier, MD**
  Boston University

**Cleveland Clinic**
- **Retinal Specialist**
- **Peter Kaiser, MD**
  Harvard Medical School

**Retina Vitreous Associates**
- **Retinal Specialist**
- **David Boyer, MD**
  Chicago Medical School

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

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

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

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

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

**University of Illinois**
- **Profile Image**
- **Jay Pepose, MD, PhD**
  UCLA School of Medicine

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

**University of Kentucky**
- **Profile Image**
- **Paul Karpkeck, OD**
  Indiana University

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

**Indiana University**
- **Profile Image**
- **Mark Kelley, PhD**
  Indiana University
  Co-Founder Apexian/APX3330
Ocuphire Board of Directors

Seasoned Directors with Decades of Drug Development, M&A/Financings, and Ophthalmology
Multiple Late-Stage Data Catalysts Expected in 2022 for Potential First NDA Approval in 2023

Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)
## OCUP – Market Snapshot

*Active Trading Volume and Sufficient Cash Runway Through 2Q 2023*

<table>
<thead>
<tr>
<th>Ticker</th>
<th>OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Price</strong></td>
<td>$3.40</td>
</tr>
<tr>
<td><strong>Market Cap</strong></td>
<td>$64.2 M</td>
</tr>
<tr>
<td><strong>Shares Outstanding</strong></td>
<td>18.8 M</td>
</tr>
<tr>
<td><strong>Cash</strong></td>
<td>$24.5 M (unaudited)</td>
</tr>
<tr>
<td><strong>Cash Runway</strong></td>
<td>Sufficient into 2Q 2023</td>
</tr>
<tr>
<td><strong>Average Daily Volume</strong></td>
<td>204 K</td>
</tr>
<tr>
<td><strong>Short Interest</strong></td>
<td>176 K; 1.0% of Float</td>
</tr>
</tbody>
</table>

*Source: FactSet*

<table>
<thead>
<tr>
<th>Research Analyst Coverage on OCUP</th>
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</thead>
<tbody>
<tr>
<td>John Newman</td>
</tr>
<tr>
<td>Canaccord Genuity</td>
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<tr>
<td>Kristen Kluska</td>
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<td>Cantor Fitzgerald</td>
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<td>James Molloy</td>
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<td>Alliance Global Partners</td>
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<td>Soumit Roy</td>
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<td>Jones Trading</td>
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<tr>
<td>Matthew Caufield</td>
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<tr>
<td>H. C. Wainwright</td>
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</tbody>
</table>
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

FDA Guidance

Physician/Patients

Patient Experience
- Tunability - ability to customize treatment based on patient’s lifestyle needs
- Favorable tolerability for continued use and Rx refills

No loss of distance (included in efficacy)
What’s Important for DR/DME?

APX3330 Has the Potential to be 1\textsuperscript{st} Line of Therapy for DR Patients

**Efficacy Signal**

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

**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**

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

**Safety**

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

**Non-Invasive Treatment Option**

FDA does not require comparative arm of approved anti-VEGF injections such as Eylea for DR.

**Non-Invasive Treatment Option**

- Eylea\textsuperscript{®}, 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