Ocuphire Corporate Presentation

November 18, 2022

Ocuphire PHARMA

Restore Vision & Clarity
Disclosures and Forward-Looking Statements

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Ocuphire Pharma
Nasdaq: OCUP

Upcoming Catalysts
• NDA Submission for Nyxol for RM (4Q22)
• Initiate VEGA-2 Phase 3 Trial for P (4Q22)
• Topline Results APX3330 ZETA-1 P2b trial for DR/DME (Early 2023)
• Initiate VEGA-3 Phase 3 Trial for P and LYRA-1 Long Term Safety Trial (2023)

Founded in 2018, Acquired 2 Lead Assets for Front & Back of Eye Therapies with Novel MOAs & Patent Coverage to 2034+
• APX3330 oral tablets
  • Diabetic Retinopathy (“DR”) – diabetes retinal (eye) disease
• Nyxol eyedrops
  • Reversal of Mydriasis (“RM”) – eye dilation
  • Presbyopia – age-related blurry near vision
  • Night Vision Disturbance (“NVD”) – halos, glares, starbursts

Four Large Markets (~$20B US total) w/Unmet Needs and Limited to No Competition

Successful Execution of 5 Trials in Last 2 Years with 6 Positive Phase 3 & Phase 2 Data Read-outs for Nyxol in RM, Presbyopia, and NVD

Ocuphire Entered into a Global License Agreement with Famy/Viatris for the Development and Commercialization of Nyxol Eye Drops for RM, P, and NVD

Strong Financial Position to Support Operations and Development into 2025

P = Presbyopia
RM = Reversal of Mydriasis
NVD = Night Vision Disturbances
DR/DME = Diabetic Retinopathy/Diabetic Macular Edema
## Ocuvre Overview

**Two Late-Stage Clinical Assets Addressing Unmet Needs in Multiple Large Markets**

### Refractive

<table>
<thead>
<tr>
<th>Nyxol</th>
<th>Novel a1/α2 Blocker 505(b)(2)</th>
<th>NDA-submission Ready</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12</strong></td>
<td>Completed Phase 1, Phase 2, and Phase 3 Trials</td>
<td><strong>&gt;650</strong> Subjects Dosed</td>
</tr>
<tr>
<td><strong>28</strong> Days</td>
<td>Exposure in Humans</td>
<td>Patent Coverage <strong>2034+</strong></td>
</tr>
<tr>
<td><strong>~100 M</strong></td>
<td>Reversal of Mydriasis</td>
<td><strong>~128 M</strong> Presbyopia</td>
</tr>
<tr>
<td><strong>~36 M</strong></td>
<td>Night Vision Disturbances</td>
<td><strong>~100 M</strong> Prevalence (US)</td>
</tr>
<tr>
<td><strong>2 Phase 3 Positive Data &amp; Ped P3</strong></td>
<td>Development Milestone</td>
<td><strong>~128 M</strong> Prevalence (US)</td>
</tr>
<tr>
<td><strong>Phase 2 Positive Data Single &amp; Combo</strong></td>
<td></td>
<td><strong>~36 M</strong> Prevalence (US)</td>
</tr>
<tr>
<td><strong>1st Phase 3 Positive Data</strong></td>
<td></td>
<td><strong>~36 M</strong> Prevalence (US)</td>
</tr>
</tbody>
</table>

### Retina

<table>
<thead>
<tr>
<th>APX3330</th>
<th>Oral REF-1 Inhibitor New Chemical Entity</th>
<th>Phase 2b Data 4Q22</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>11</strong></td>
<td>Completed Phase 1 and Phase 2 Trials</td>
<td><strong>&gt;340</strong> Subjects Dosed</td>
</tr>
<tr>
<td><strong>365</strong> Days</td>
<td>Exposure in Humans</td>
<td>Patent Coverage <strong>2034+</strong></td>
</tr>
<tr>
<td><strong>~8 M</strong></td>
<td>Diabetic Retinopathy</td>
<td><strong>Phase 2b Last Patient Last Visit Completed Aug 22</strong></td>
</tr>
<tr>
<td><strong>~2.4 M</strong></td>
<td>Diabetic Macular Edema</td>
<td><strong>Phase 2b Last Patient Last Visit Completed Aug 22</strong></td>
</tr>
</tbody>
</table>

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Source: Eisai and Apexian Data; GlobalData Market Research Report, 2020; Company Estimates for US Market Size; Ocuvre internal estimates
## Ocuhpire Pipeline & Clinical Milestones

*Multiple Phase 3 & Phase 2 Clinical Data Readouts Accomplished 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>Diabetic Retinopathy (DR)/Macular Edema (DME)</td>
<td>APX3330 Oral Pill</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ZETA-1 Phase 2b data expected in early 2023 (n=103)</td>
</tr>
<tr>
<td>Reversal of Mydriasis (RM)</td>
<td>Nyxol® Eye Drop</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Positive MIRA-3 Phase 3 data in 1Q 2022 (n=368)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Positive MIRA-4 Pediatric data in 2Q 2022 (n=23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Submit Nyxol NDA for RM in 4Q 2022</td>
</tr>
<tr>
<td>Presbyopia (P)</td>
<td>Nyxol® Eye Drop</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Positive VEGA-1 Nyxol alone data in 1Q 2022 (and in combination with LDP in mid-2021)</td>
</tr>
<tr>
<td></td>
<td>Nyxol® + 0.4% Low Dose Pilocarpine (LDP) Eye Drops</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VEGA Phase 3 program planned to initiate in 4Q 2022 for single agent and combination with LDP</td>
</tr>
<tr>
<td>Dim Light or Night Vision Disturbances (NVD)</td>
<td>Nyxol® Eye Drop</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Positive LYNX-1 Phase 3 data in 2Q 2022 (n=145)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate LYNX-2 2nd Phase 3 Trial</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)
Ocuphire Announces Global Partnership for Nyxol

**Viatris has Agreed to Acquire Two Companies to Create a Leading Global Ophthalmology Franchise**

### Viatris New Ophthalmology Business

<table>
<thead>
<tr>
<th><strong>FamyGen</strong></th>
<th><strong>Oyster Point</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pipeline Portfolio</strong></td>
<td><strong>Approved Product and US Commercial Infrastructure</strong></td>
</tr>
<tr>
<td>MR-140: Reversal of Mydriasis (RM)</td>
<td>Tyrvaya® Nasal Spray for Dry Eye Commercial</td>
</tr>
<tr>
<td>MR-148: Dry Eye Disease</td>
<td></td>
</tr>
<tr>
<td>MR-149: Blepharitis</td>
<td></td>
</tr>
</tbody>
</table>

Ocuphire’s Nyxol Eye Drop

Viatris has agreed to acquire FamyGen and Oyster Point; See Viatris and Ocuphire press releases on November 7, 2022
Key Terms of Global Partnership for Nyxol

*Development and Commercialization Partner Famy/Viatris in US and Key Global Markets*

### Licensing Agreement Economics

- $35 million upfront cash payment
- Funding for all budgeted Nyxol development costs across all 3 indications through FDA approvals in the US
- $130 million in potential additional regulatory or sales milestone payments
  - First potential payment of $10M for RM FDA approval in 2H 2023
- Tiered double digit royalties through 2040 (based on aggregate annual net sales)
  - Low double-digit up to low 20% in US
  - Low double-digit for outside the US

### Viatris is Responsible for:

- Manufacturing and commercial in US
- Development, manufacturing, and commercial outside the US

### Partnership Accomplishes 4 Strategic Objectives

- Continue US Development by Ocuphire for All 3 Nyxol Indications; Ex-US Development Led by Viatris
- Partner for Nyxol Commercialization in US and Globally
- Focus on APX3330 Development
- Strengthen Cash Position into 2025

Viatris has agreed to acquire FamyGen and Oyster Point; See Viatris and Ocuphire press releases on November 7, 2022.
# Ophthalmology is Attractive Biotechnology Sector

*Active Partnering and Constructive FDA Ophthalmology Division*

## Recent Ophthalmic Deal Activity

<table>
<thead>
<tr>
<th>Month</th>
<th>Partners</th>
<th>Deal Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2021</td>
<td>Alcon / Novartis</td>
<td>$355 M</td>
</tr>
<tr>
<td></td>
<td>Simbrinza®</td>
<td></td>
</tr>
<tr>
<td>September 21</td>
<td>Allergan / REGENXBIO</td>
<td>~$1.8 B</td>
</tr>
<tr>
<td>October 21</td>
<td>Théa / Curacle</td>
<td>~$2 B</td>
</tr>
<tr>
<td>December 21</td>
<td>Rayner / Omeros</td>
<td>~$1 B</td>
</tr>
<tr>
<td></td>
<td>OMIDRIA®</td>
<td></td>
</tr>
<tr>
<td>December 21</td>
<td>Novartis / Gyroscope</td>
<td>~$1.5 B</td>
</tr>
<tr>
<td>May 2022</td>
<td>Alcon / Kala</td>
<td>$385 M</td>
</tr>
<tr>
<td>August 22</td>
<td>Alcon / Aerie</td>
<td>$770 M</td>
</tr>
<tr>
<td>November 22</td>
<td>Viatris / Oyster Point &amp; Famy</td>
<td>~$750 M</td>
</tr>
</tbody>
</table>

## New Eye Rx Approvals (since 2021)

<table>
<thead>
<tr>
<th>Company</th>
<th>Rx Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergan</td>
<td>Vuity™</td>
</tr>
<tr>
<td>Roche</td>
<td>Susvimo™</td>
</tr>
<tr>
<td>Oyster Point</td>
<td>Tyrvaya™</td>
</tr>
<tr>
<td>Roche</td>
<td>Vabysmo™</td>
</tr>
<tr>
<td>Bausch Health</td>
<td>Xipere™</td>
</tr>
<tr>
<td>Novartis</td>
<td>Beovu™</td>
</tr>
<tr>
<td>Ocular Therapeutics</td>
<td>Dextenza™</td>
</tr>
<tr>
<td>Samsung Bioepis</td>
<td>Byooviz™</td>
</tr>
<tr>
<td>Santen</td>
<td>Verkazia™</td>
</tr>
<tr>
<td>Coherus</td>
<td>Cimerli™</td>
</tr>
</tbody>
</table>

- *sNDA* Ranibizumab biosimilar
Diabetic Retinopathy

Diabetic Macular Edema

“"I could lose my hearing, I could lose talking but…. It’s frightening to lose my eyesight.”

Patient Diagnosed with DR
Diabetic Retinopathy At a Glance

**Larger Disease to Manage with Growing Diabetes**

- There are **8M** adults in the U.S. with DR\(^1\)
- **1 in 4** people with type 1 and type 2 diabetes
- DR/DME affects about **14M** by 2050
- DR is the leading cause of blindness among working-age adults
- Majority of mild to moderate patients with DR are not treated with anti-VEGF due to injection fear and burden
- If untreated, DR can rob people of their vision prematurely\(^2,3\)
- Global Intravitreal Injection Revenues: **$13B** (2020)
- 56% of patients reported anxiety related to anti-VEGF treatment

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**Source:**
1. American Diabetes Association; International Diabetes Federation; Healthline;
3. Patient survey adapted from Lions International Foundation and International Diabetes Foundation-Europe; Meltzer 2000
Diabetic Patients Usually Present with Complex Co-Morbidities

Diabetic Patients are Young and Face Life-long Systemic and Ocular Complications

- Diabetic retinopathy
- Diabetic neuropathy
- Diabetic nephropathy
- Cardiovascular disease
- Dyslipidemia
- Stroke

Patients with DME have an even greater risk of complications than diabetes patients without DME.


DR is the most common cause of vision loss or blindness in working-age adults usually affecting both eyes.

DME is vision threatening complication caused by DR where excess fluid leaks near fovea and triggers swelling of the macula.

Treating DR leads to control of DME.

DME
APX3330 History and Ref-1 Inhibition Mechanism

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

**Mechanism of Action – Ref-1 Inhibition**

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

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

- Neovascularization
- Steroids

**APX3330**

- 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
APX3330 Product Candidate Profile for Multiple Retinal Indications

*Oral, First-In-Class Ref-1 Inhibitor with Favorable Human Safety Data from 11 Completed Trials*

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**Expected Efficacy Data**

- Novel MOA for treating retina
  - ↓ Inflammation
  - ↓ Abnormal Angiogenesis

- Convenient Oral Dosing for Patient Compliance

- Allow Daily vs. Episodic Exposure
  Oral pill may reduce the burden of frequent anti-VEGF injections

**Favorable Safety Profile**

- Over 300 Subjects (Healthy, Liver, Cancer) Treated, Notably Several Subjects Dosed for ~1 year

- Few Systemic Adverse Effects
  - ~ 5% Mild Diarrhea
  - ~ 5% Mild Skin Rash (reversible)

- No Treatment-Related Organ Toxicity
  (Liver, Cardiovascular {BP, HR}, Kidney, Neurologic, Pulmonary)

- No Ocular Side Effects

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*11 completed Phase 1 and Phase 2 clinical trials by Eisai and Apexian; along with ongoing ZETA-1 trial by Ocuhire (*includes ~103 subject)*
DR/DME ZETA-1 Phase 2b Design

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 in study eye and central DME allowed in fellow eye

**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)
- Best Corrected Distance Visual Acuity (BCDVA) change
- DRSS improvements
- DRSS worsening
- Progression to vision threatening complications
- Rescue subjects
- DME fellow eye status
- Safety and tolerability

**Exploratory:**
- Labs / PK

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103 Subjects Enrolled with Last Patient Last Visit 2H 2022
Top Line Expected in Early 2023
Comprehensive Laboratory Panels Collected in ZETA-1

*Blood, Kidney, and Inflammatory Markers Evaluated*

**Chemistry**
- Albumin
- Alanine aminotransferase (ALT)
- Alkaline Phosphatase
- Aspartate aminotransferase (AST)
- Blood Urea Nitrogen (BUN)
- Creatinine
- Glucose (Random)
- Sodium
- Total bilirubin
- Total protein

**Test Panel Components**
- **Hematology**
  - (CBC without Differential)
  - WBC
  - RBC
  - HGB (Hemoglobin)
  - HCT (Hematocrit)
  - Platelet Count
  - Calcium
  - Carbon Dioxide (Bicarbonate)
  - Chloride

**Cytokine Panel (Biomarker)**
- Interleukin-1 ß (IL-1ß)
- Interleukin-6 (IL-6)
- Interleukin-8 (IL-8)
- Tumor Necrosis Factor α (TNF-α)

**PK and Biomarkers**
- REF-1 ELISA 1

**Kidney Function**
- eGFR
- Creatinine

**DR**

**DME**
## Baseline Characteristics for DR Patients in ZETA-1 Trial

### Typical Demographics, DRSS Scores, and Visual Metrics for Diabetic Patients

#### Demographics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total N = 103</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years):</strong></td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>56 (24-81)</td>
</tr>
<tr>
<td><strong>Sex:</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>50 (49%)</td>
</tr>
<tr>
<td>Female</td>
<td>53 (51%)</td>
</tr>
<tr>
<td><strong>Race:</strong></td>
<td></td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>White</td>
<td>81 (79%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (3%)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²):</strong></td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>31 (21-40)</td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg):</strong></td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>138 (100-180)</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg):</strong></td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>80 (53-109)</td>
</tr>
<tr>
<td><strong>Heart rate (BPM):</strong></td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>77 (51-96)</td>
</tr>
<tr>
<td><strong>Hemoglobin A1c:</strong></td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>8.1 (5.9-12.3)</td>
</tr>
</tbody>
</table>

#### DRSS Scores

<table>
<thead>
<tr>
<th>DRSS Scores</th>
<th>Total N = 103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Eye DRSS n(%)</td>
<td></td>
</tr>
<tr>
<td>DRSS 47 (Moderately Severe NPDR)</td>
<td>39 (38%)</td>
</tr>
<tr>
<td>DRSS 53 (Severe NPDR)</td>
<td>53 (52%)</td>
</tr>
<tr>
<td>DRSS 61 (Mild PDR)</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>DRSS 20-40 (Mild to Moderate NPDR)</td>
<td>29 (28%)</td>
</tr>
<tr>
<td>DRSS 47 (Moderately Severe NPDR)</td>
<td>34 (33%)</td>
</tr>
<tr>
<td>DRSS 53 (Severe NPDR)</td>
<td>22 (21%)</td>
</tr>
<tr>
<td>DRSS 61 (Mild PDR)</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>DRSS 65-85 (Moderate to Severe PDR)</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>Not Graded</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

#### Key Visual Metrics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total N = 103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Eye Screening CST (um):</td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>270 (203-319)</td>
</tr>
<tr>
<td>Fellow Eye Screening CST (um)*:</td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>269 (211-401)</td>
</tr>
<tr>
<td>Study Eye BCVA:</td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>Letters Read: 80 (69-93)</td>
</tr>
<tr>
<td>Fellow Eye BCVA:</td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>Letters Read: 77 (0-91)</td>
</tr>
<tr>
<td>IOP Study Eye and Fellow Eye (mmHg):</td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>15 (8-22)</td>
</tr>
<tr>
<td>Diabetic Status (Years):</td>
<td>mean (range)</td>
</tr>
<tr>
<td></td>
<td>16 (5-58)</td>
</tr>
<tr>
<td>Study Eye with anti-VEGF injections within 6 months prior to Screening</td>
<td>None</td>
</tr>
<tr>
<td>Fellow Eye with anti-VEGF injections within 6 months prior to Screening</td>
<td>15</td>
</tr>
</tbody>
</table>

*Note: 15 fellow eyes were CST>320 microns (center-involved DME eyes)
Masked Safety Findings from Ongoing ZETA-1 Trial

Favorable Safety Profile (as of 9/15/2022) Observed with 600 mg Oral Daily Doses in Diabetic Subjects

- 169 TEAEs in 62/103 Subjects (60%)
  - 30 Treatment-Related
    - 18 Mild
    - 12 Moderate
    - 0 Severe
  - 149 Unrelated
    - 92 Mild
    - 48 Moderate
    - 9 Severe
- 16 SAEs in 12/103 Subjects
  - 0 Treatment-Related
    - liver, heart, kidney, brain, lung, or vital signs
  - 16 Unrelated

- 103 Subjects Enrolled
- 95 Subjects completed thru week 12
- 91 Subjects completed thru week 24
- >7900 Subject-Days of Treatment at 600 mg/day APX3330 Exposure

Oral APX3330 safety profile consistent with that seen in prior trials

1. 12 events in 8 subjects: diarrhea, worsening DME (OD and OS), pruritis, urticaria, blurry vision, decrease in hemoglobin level, ischemic diabetic maculopathy and central vision scotoma (in same subject), photophobia (OD and OS) and hypoesthesia (in same subject)
2. Cellulitis (2 events in same subject), dyskinesia, transient ischemic event, COVID-19 and acute respiratory failure (same subject), progression of multivessel coronary artery disease, cholelithiasis, osteomyelitis, vertigo, chest pain, infection of toe and ulcer of toe and embolism (3 events in same subject), multi-system organ failure, worsening bradycardia
3. DME, Dyspnea, Pre-Syncope.

Note: ZETA-1 Interim Data as of database 9/15/22 with monitoring to be completed before final database lock; assumes 50% subjects on APX3330

1. 12 events in 8 subjects: diarrhea, worsening DME (OD and OS), pruritis, urticaria, blurry vision, decrease in hemoglobin level, ischemic diabetic maculopathy and central vision scotoma (in same subject), photophobia (OD and OS) and hypoesthesia (in same subject)
2. Cellulitis (2 events in same subject), dyskinesia, transient ischemic event, COVID-19 and acute respiratory failure (same subject), progression of multivessel coronary artery disease, cholelithiasis, osteomyelitis, vertigo, chest pain, infection of toe and ulcer of toe and embolism (3 events in same subject), multi-system organ failure, worsening bradycardia
3. DME, Dyspnea, Pre-Syncope.

Note: ZETA-1 Interim Data as of database 9/15/22 with monitoring to be completed before final database lock; assumes 50% subjects on APX3330
Broad Opportunities to Treat Retinal Diseases with APX Platform

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

### 34 Million Diabetics in US

- **Diabetic Retinopathy**
  - Mild NPDR: 6M
  - Moderate to Severe NPDR (DRSS 43-53): 1M
  - PDR (DRSS >60): 1M

- **~8M+** DR Patients

#### Addressable Market

#### US Market Opportunity

- **~$10B+** Market Revenues

### Inflammatory component is common across these retina indications as well & potentially addressable by MOA of Ref-1

- **APX2009 / APX2014 / APX3330** (Local Delivery)

- **APX3330** + Anti-VEGF treatments

**Potential First Oral Rx for Retina Diseases with Multi-Billion Revenue Opportunity**

- **DME** 1M
- **Wet AMD** 2M
- **Dry AMD** 10M+
- **GA** 1M
- **RVO** 2M

---

**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
4. Estimates are provided by the National Eye Institute, FactSheet, Global Data, and Research and Markets. Estimated values are rounded.
5. Estimated prevalence in the U.S.; DME- Diabetic Macular Edema; Age-related Macular Degeneration; Geographic Atrophy; Retinal Vein Occlusion
NYXOL®
EYE DROPS

THREE INDICATIONS

NEW PARTNERSHIP WITH VIATRIS

Reversal of Mydriasis

Presbyopia

Night Vision Disturbance

RM

P

NVD

Nyxol as a Single Drop

Nyxol with LDP Adjunctive Therapy

1

2

NVD

NVD
Pupillary Mechanism

Pupil Modulation is Mediated by Dilator (radial) and Sphincter (constrictor) Muscles
Nyxol’s Differentiated MOA as an Alpha-1 Blocker

No Engagement of Ciliary Muscle ➔ No Headaches and Lower Risk of Retinal Detachment

Phentolamine is the Active Ingredient in Nyxol: a non-selective α1 Antagonist

Phentolamine blocks α1 receptors on the Iris Dilator Muscle

- Decreases pupil size (moderately)
- without affecting the iris sphincter or ciliary muscles
- Allows for 3 indications: RM, Presbyopia and NVD

505(b)(2) Regulatory Pathway Supported by Phentolamine Approval for 2 Indications:

- Regitine® (Pheochromocytoma) – intravenous injection approved in 1952
- OraVerse® (Reversal of oral anesthesia) – intramuscular injection approved in 2008
Nyxol Product Candidate Profile

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

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

<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  

**Well-Tolerated Topical Effects**  
  • Mild, transient, reversible Eye redness (11%)  
  • Mild, instillation site discomfort (11%)  

IOP unchanged or decreased  
Minimal to No headaches | Effects Last ≥ 24 Hours  
Chronic daily dosing of Nyxol at bedtime reduces pupil size for up to 24 to 36 hours |
Summary of Nyxol Trial Results

**Demonstrated Efficacy Response & Well Tolerated Safety Profile Across 3 Indications**

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>Efficacy Data</th>
<th>Key Secondary Endpoint(s)</th>
<th>Safety &amp; Tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Return to baseline pupil diameter at 90 minutes after dilation</td>
<td><strong>Met Phase 3 primary endpoint</strong>&lt;br&gt; MIRA-3: 58% Nyxol vs. 6% placebo&lt;br&gt; MIRA-2: 49% Nyxol vs. 7% placebo (p&lt;0.0001)&lt;br&gt; MIRA-4: 64% Nyxol vs. 25% placebo</td>
<td>Efficacy across all mydriatic agents, iris color, 1 or 2 drops, and all ages (3-80)</td>
<td>▪ No headaches&lt;br&gt;▪ No blurry vision&lt;br&gt;▪ ~5% mild redness&lt;br&gt;▪ No change in IOP&lt;br&gt;▪ No SAEs&lt;br&gt;▪ Most AEs were mild</td>
</tr>
<tr>
<td>≥3 line gain in near vision with loss of no more than 1 line in distance vision</td>
<td><strong>Met planned Phase 3 primary endpoint</strong>&lt;br&gt; VEGA-1: 29% Nyxol vs. 12% placebo at 12 hrs post-Nyxol dose (p=0.02)</td>
<td>Durable near vision (18 hrs) Optimal pupil size Pupillary light reflex</td>
<td></td>
</tr>
<tr>
<td>≥3 lines (eye test) of improvement in mesopic low contrast best-corrected distance visual acuity (mLCVA)</td>
<td><strong>Met Phase 3 primary endpoint</strong>&lt;br&gt; LYNX-1: 13% Nyxol vs. 3% placebo at Day 8 (p&lt;0.05) and 21% in Nyxol vs 3% placebo at Day 15 (p&lt;0.01)</td>
<td>Improvement visual acuity measures (distance and near) in dim light conditions</td>
<td></td>
</tr>
</tbody>
</table>

*Trend toward statistical significance even in smaller POS arm from time 0 to time 6 hours (n=30); larger sample size for all arms planned in Phase 3 program*
Large Market Opportunity for Nyxol Across 3 Indications

**All Products Cash Pay with No Payor Reimbursement or Other Hurdles**

- **Reversal of Mydriasis**: 100M Annual Eye Dilations
  - MIRA Trials Represent 95M Dilation Drops Used in Practice
  - 63M Report Moderate to Severe Impact to Daily Function
  - 80% Patients Likely to Request Drop
  - 50M Dilations
  - US Market Opportunity
  - $500M+
  - Cash Pay
  - Market Research $10 to $20+
  - No Competition

- **Presbyopia**: ~128M Presbyopes in the US
  - Emmetropes
  - Myopes Low
  - Myopes High
  - Hyperopes
  - Pseudophakes
  - 66M
  - 30M
  - 9M
  - 14M
  - 9M
  - 17M
  - 8M
  - 2M
  - 17M (Addressable Market 25%)
  - 33M Patients
  - US Market Opportunity
  - ~$8B*
  - Cash Pay
  - Vuity™ Price $79
  - Pricing similar to Presbyopia
  - No Competition

- **Night Vision Disturbances**: ~38 M US NVD Population
  - Night Myopia
  - Cortical Cataracts
  - Post-Lasik
  - Post-IOL Implant
  - Number of Patients
  - 26M
  - 9M
  - 1M
  - 2M
  - 11M
  - 4M
  - 0.5M
  - 0.3M
  - 7M
  - 2M
  - 0.3M
  - 0.2M
  - ~10 M Patients
  - US Market Opportunity
  - ~$2B*
  - Cash Pay
  - Pricing similar to Presbyopia
  - No Competition

* Assumes 3 refills per annum
Mydriasis or dilated eyes causes:

- heightened sensitivity to light
- inability to focus
- reading, working, and driving difficulty
- halos and glare
- headaches

I visit my retina MD for my monthly injections, where I am dilated. Being dilated every month is a huge burden on my day.
**NDA Submission Targeted For 4Q 2022**

*Multiple Positive Clinical Trials To Support Broad Label*

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**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.

---

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

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

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

**MIRA-4 Pediatric**
- n=23
- Primary Endpoint Met ✓
- Secondary Endpoints Met ✓

**Production of 3 registration batches ✓**
Commercial Strategy With Cash Pay Model

Simple, Value-Driven, Capital-Efficient and Accelerates Adoption

Preservative-Free Single Unit Vial (5-pack)

Viatris US Commercial Partner

Sell Direct to Office

Physician Sells to Patient

Preservative-Free Single Unit Vial (5-pack)

Low Adoption Hurdles:
- No reimbursement or payors/PBMs
- No training, dilations are routine
- No specialty/retail pharmacies
- No competition
- Cash pay is favored by majority of MDs and ODs

20,000 Ophthalmologists
46,000 Optometrists
3,000 Retinal Specialists

58% of physicians would start prescribing Nyxol within 1st year

Source: GlobalData Market Research Survey. 1. please see FAMY/VIATRIS November 7, 2022 Press Release
NYXOL®
FOR
PRESBYOPIA

• Nyxol Alone
• Nyxol with LDP Adjunctive Therapy

88% of patients expressed an interest in presbyopia-correcting drops across all ages and income groups.

Source: Burke Healthcare Research April 2020, n = 1000 presbyopes ages 40-80 years old.

FDA approval of AbbVie Eye Drop a New Moment in Presbyopia
10/29/21
Nyxol® and Nyxol + Low Dose Pilocarpine Presbyopia Eye Drops

Differentiated MOA with Two Potential Product Labels for Functional Near Vision Improvement

0.75% Nyxol

Iris Dilator Muscle Inhibition

Iris Sphincter and Ciliary Muscles Activation

0.4% LDP

Nyxol as a Single Agent for Presbyopia

Single Durable Drop

Evening drop

Daytime drop

Optimal Pupil Target is 2-3 mm

Source: Nyxol® data from 12 completed trials; Pilocarpine product label and literature
Presbyopia Eye Drops Competitive Landscape

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

- Nyxol alone potential differentiation:
  1) New MOA class (iris dilator muscle)
  2) Favorable safety and tolerability (e.g.: no headaches, no accommodative spasm, no risk of retinal detachment)
  3) 24-hour durability
  4) Broad range of patients including high myopes
  5) Improvement in night vision disturbances

- Nyxol+LDP may offer added efficacy and tunability

Other Cholinergic Agonists*

- Phase 1
  - Ocuphire
  - Nyxol (0.75% phentolamine)
  - Lenz
  - Aceclidine; Aceclidine + brim

- Phase 2
  - Orasis
  - CSF-1 (Low dose pilo)
  - Visus
  - Brimochol® (carbachol + brim)

- Phase 3
  - Allergan
  - Vuity™; (1.25% pilo)
  - Eyenovia
  - MicroLine (2% pilo)

Cholinergic Agonist* (pilocarpine)

Other Cholinergic Agonists* (pilocarpine)
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
Management, Medical Advisors, Board

Milestones

Investment Summary
Ocuphire Management Team

Decades of Biotech and Drug Development Experience

Mina Sooch, MBA
President & CEO
and Founder

Charlie Hoffmann, MBA
VP, Corporate Development
and Operations

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

Mitch Brigell, PhD
Head, Clinical Development
and Strategy

Bindu Manne
Head, Market Development
and Commercialization

Chris Ernst
Global Head, QA
and Manufacturing

Laura Gambino
Director, Project Management

Ronil Patel, MS
VP, Business Development
and Market Strategy

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

Amy Rabourn, CPA
VP, Finance

Drey Coleman
VP, Clinical Operations

Barbara Withers, PhD
VP, Clinical and
Regulatory Strategy
Ocuphire's World-Class Medical Advisory Board

Leading KOLs in Refractive, Retina, and Medical Optometry

**Chief Medical Advisor, Ocuphire**
Jay Pepose, MD, PhD
UCLA School of Medicine

**OculVision**
Chu Vision

**Refractive Specialist**
Zaina Al-Mohtaseb, MD
Baylor College of Medicine

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

**Refractive Specialist**
Mitch Jackson, MD
University of Chicago

**Refractive/Glaucoma Specialist**
Thomas Samuelson, MD
University of Minnesota

**Retinal Specialist**
James Katz, MD
University of Illinois

**Retinal Specialist**
Marguerite McDonald, MD
Columbia University

**Retinal Specialist**
Eliot Lazar, MD
Georgetown University

**Retinal Specialist**
Inder Paul Singh, MD
The Chicago Medical School

**Retinal Specialist**
Inder Paul Singh, MD
Chicago Medical School

**Retinal Specialist**
David Boyer, MD
Chicago Medical School

**Retinal Specialist**
David Brown, MD
Baylor University

**Retinal Specialist**
Jeffrey Heier, MD
Boston University

**Retinal Specialist**
Caroline Baunal, MD
University of Toronto Medical School

**Retinal Specialist**
Peter Kaiser, MD
Harvard Medical School

**Retinal Specialist**
Laura Storey, MD
Boston University Medical School

**Retinal Specialist**
Michael Allingham, MD, PhD
University of North Carolina

**Retinal Specialist**
David Boyer, MD
Chicago Medical School

**Retinal Specialist**
David Lally, MD
Vanderbilt University

**Retinal Specialist**
Inder Paul Singh, MD
Chicago Medical School

**Retinal Specialist**
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Boston University

**Retinal Specialist**
Caroline Baunal, MD
University of Toronto Medical School

**Retinal Specialist**
Peter Kaiser, MD
Harvard Medical School

**Retinal Specialist**
Laura Storey, MD
Boston University Medical School

**Retinal Specialist**
Michael Allingham, MD, PhD
University of North Carolina

**Retinal Specialist**
David Lally, MD
Vanderbilt University

Co-Founder
Mark Kelley, PhD
Indiana University

**Co-Founder**
Apexian/APX3330

**Optometry**
Paul Karpecki, OD
Indiana University

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

**Optometry**
Leslie O'Dell, OD
Salus University

**Optometry**
Selina McGee, OD
Northeastern State University

**Optometry**
Justin Schweitzer, OD
Pacific University College of Optometry

**Co-Founder**
Indiana Eye Center

**EYE CARE INSTITUTE**

**Co-Founder**
New England Retina Consultants

**Co-Founder**
Tel-Aviv Sourasky Medical Center

**Co-Founder**
OculVision

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

**Co-Founder**
Inder Paul Singh, MD
Chicago Medical School

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

**Co-Founder**
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*

**Cam Gallagher, MBA**
Chair, Board Director

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

**Sean Ainsworth, MBA**
Lead Independent Director,
Board Director

**James Manuso, PhD/MBA**
Board Director

**Jay Pepose, MD, PhD**
Board Director

**Richard Rodgers, MBA**
Board Director

**Susan Benton, MBA**
Board Director

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

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Jay Pepose, MD, PhD
Board Director

Richard Rodgers, MBA
Board Director

Susan Benton, MBA
Board Director
<table>
<thead>
<tr>
<th>Track Record of Achieving Milestones ➔ Exciting News Cadence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Positive Data Readouts and Partnership with Multiple Catalysts Ahead</td>
</tr>
</tbody>
</table>

### 2021 – 1H 2022
- **Positive** Nyxol 1st Phase 3 Data for RM (MIRA-2)
- **Positive** Nyxol+LDP Phase 2 Data for Presbyopia (VEGA-1)
- **Positive** Nyxol Phase 2 Data for Presbyopia (VEGA-1)
- **Positive** Nyxol 2nd Phase 3 Data for RM (MIRA-3)
- **Positive** Nyxol Pediatric Phase 3 Data for RM (MIRA-4)
- **Positive** Nyxol 1st Phase 3 Data for NVD (LYNX-1)

### 2H 2022 – 2023
- Establish Nyxol Commercial Partnership
- Submit Nyxol NDA for RM
- Initiate Nyxol VEGA-2 Phase 3 Presbyopia Trials
- Report APX3330 Phase 2b Data for DR (ZETA-1)
- Report Nyxol Phase 3 Presbyopia Data
- **Potential Nyxol NDA Approval for RM**

**Ongoing Partnering Discussions with Leading Ophthalmic Companies for APX3330 (including Europe and Asia)**
Founded in 2018, Acquired 2 Lead Assets for Front & Back of Eye Therapies with Novel MOAs & Patent Coverage to 2034+

- APX3330 oral tablets
  - Diabetic Retinopathy ("DR") – diabetes retinal (eye) disease
- Nyxol eyedrops
  - Reversal of Mydriasis ("RM") – eye dilation
  - Presbyopia – age-related blurry near vision
  - Night Vision Disturbance ("NVD") – halos, glares, starbursts

Four Large Markets (~$20B US total) w/Unmet Needs and Limited to No Competition

Successful Execution of 5 Trials in Last 2 Years with 6 Positive Phase 3 & Phase 2 Data Read-outs for Nyxol in RM, Presbyopia, and NVD

Ocuphire Entered into a Global License Agreement with Famy/Viatris for the Development and Commercialization of Nyxol Eye Drops for RM, P, and NVD

Strong Financial Position to Support Operations and Development into 2025
Appendix: Nyxol Data
## Summary of MIRA FDA Registration Trial Designs
Randomized, Double-Masked, Placebo-Controlled, Parallel, Multi-Center, One-Day Trials

<table>
<thead>
<tr>
<th>Source: In order from left to right</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIRA-2 Registration Trial NCT# 04620213</td>
</tr>
<tr>
<td>MIRA-3 Registration Trial NCT# 05134974</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>MIRA-2 1st Phase 3</th>
<th>MIRA-3 2nd Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Sites</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Subjects Enrolled</td>
<td>185</td>
<td>368</td>
</tr>
<tr>
<td>Eligibility</td>
<td>Healthy ≥ 12 years old</td>
<td>Healthy ≥ 12 years old</td>
</tr>
<tr>
<td>Randomization</td>
<td>1:1</td>
<td>2:1</td>
</tr>
<tr>
<td>Mydriatic Agents</td>
<td>2.5% Phenylephrine, 0.5% Tropicamide and Paremyd</td>
<td>2.5% Phenylephrine, 0.5% Tropicamide and Paremyd</td>
</tr>
<tr>
<td>Positive Data Readout</td>
<td>1Q 2021</td>
<td>1Q 2022</td>
</tr>
</tbody>
</table>

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

**Secondary Endpoints**
- % of subjects returning to baseline PD at 0min to 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

**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**

**Total Subjects Enrolled**
- >550

**Total Exposure To Nyxol**
- >330

Source: Ocuhire Pharmaceuticals
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)

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

Time Post-Treatment with Nyxol/Placebo (Hours)

MIRA-2 Phase 3 Trial

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

- Placebo n=91
- Nyxol n=94

Time Post-Treatment with Nyxol/Placebo (Hours)

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).
Planned NDA Package Incorporates Positive Data from MIRA Trials
Nyxol Significantly Reduced PD in Subjects Ages 3 & Over with Favorable Safety and Tolerability

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 (age 3-17) trial 64% Nyxol vs. 25% placebo
- Met key endpoints with high statistical significance in MIRA-2 & MIRA-3
  - Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Efficacy with 1 or 2 drops
  - Over 60% subjects returned to baseline accommodation at 2-3 hours
  - Accelerated return to normal distance-corrected near visual acuity

Safety
- No deaths, serious AEs, or withdrawals due to AEs
- All treatment related AEs were mild in severity
- The only AE occurring in ≥ 5% of subjects treated with Nyxol was mild and transient conjunctival hyperemia 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
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
Visit 2
Evening Dosing (4 doses)
(Day 5)

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

Randomization
Screening

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:
- Primary endpoint for Nyxol alone vs placebo
- % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours
- % of subjects achieving 20/40 or better vision
- 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
- DCNVA of 20/50 Snellen equivalent or worse in photopic conditions in each eye & binocularly
- BCDVA of 20/20 Snellen equivalent or better in each eye under photopic conditions
- No limitation on axial length or diopters for myopia patients

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
**Summary of Positive VEGA-1 Phase 2 Results**

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

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Durability*</th>
<th>Functional Vision (20/40 or better)</th>
<th>Sustained Reduction in Pupil Diameter</th>
<th>Benefit in a Breadth of Patients</th>
<th>Safety &amp; Tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met planned P3 endpoint at 12 hours post-Nyxol (29%; p=0.02)</td>
<td>Durable near vision gain through 18 hours</td>
<td>56% at 12 hours post-Nyxol</td>
<td>18+ hours (post-dose of Nyxol)</td>
<td>▪ Ages 40-64</td>
<td>▪ No headaches</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>▪ No myopia exclusions</td>
<td>▪ No blurry vision</td>
</tr>
<tr>
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<td>▪ Light and dark irides</td>
<td>▪ ~5% mild redness</td>
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<td>▪ No change in IOP</td>
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<td>▪ No SAEs, most AEs were mild</td>
</tr>
<tr>
<td>Met primary endpoint at 1 hour post-LDP (60%; p=0.004)</td>
<td>Durable near vision gain through 18 hours with enhanced near vision gain for at least 6 hours</td>
<td>84% at 13 hours post-Nyxol and 1 hour post-LDP</td>
<td>18+ hours (post-dose of Nyxol)</td>
<td>▪ Ages 40-64</td>
<td>▪ No headaches</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>▪ Light and dark irides</td>
<td>▪ No blurry vision</td>
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</tr>
</tbody>
</table>

*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*
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

<table>
<thead>
<tr>
<th>Placebo (n=74)</th>
<th>Nyxol (n=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12%</td>
<td>29%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=43)</th>
<th>Nyxol (n=30)</th>
<th>LDP (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14%</td>
<td>61%</td>
<td>33%</td>
<td>26%</td>
</tr>
</tbody>
</table>

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
NVD LYNX-1 Phase 3 Registration Design
Randomized, Double-Masked, Placebo-Controlled Two-Week Trial

ELIGIBILITY
Screening*
Randomization

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

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)

Primary Endpoint

Day 0 Assessments
Primary Endpoint
Day 8 Assessments
Day 15 Assessments

0.75% Nyxol
daily evening dose (14 days)

Placebo
daily evening dose (14 days)

Day 0
Day 8
Day 15

Phase 3 Initiated in Dec 2020; 145 Patients Enrolled
Top Line Results Reported May 19, 2022

Note: Inclusion Criteria includes subjects with baseline mesopic LCVA of 20/63 or worse
Summary of Positive LYNX-1 Phase 3 Results For Nyxol Eye Drops

Source: mITT Population, LYNX-1Trial

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
- 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