Ocphire Corporate Presentation

November 10, 2021
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## Ocuphire Opportunity

**A Late-Stage Clinical Ophthalmic Biotech (Nasdaq Symbol: OCUP)**

<table>
<thead>
<tr>
<th>Late Clinical Stage Company Targeting Large, Unmet Ophthalmic Markets</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nyxol eye drops target multiple chronic and acute front of the eye indications addressing large markets: Reversal of Mydriasis (RM), Presbyopia (P) &amp; Dim Light / Night Vision Disturbances (NVD)</td>
</tr>
<tr>
<td>• APX3330 tablets target chronic back of the eye indications: Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME), a leading cause of blindness in diabetic patients</td>
</tr>
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<table>
<thead>
<tr>
<th>Significant Clinical Data and Regulatory Precedents</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nyxol and APX3330 achieved promising clinical data over multiple Phase 1, 2, and 3 trials</td>
</tr>
<tr>
<td>✓ Nyxol with &gt; 330 patients treated across 9 trials</td>
</tr>
<tr>
<td>✓ APX3330 with &gt; 340 patients treated across 11 trials</td>
</tr>
<tr>
<td>• FDA End of Phase 2 meeting guidance for Nyxol (all indications) in May 2020</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Significant IP Portfolio and Small Molecule CMC Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• US and global issued patents thru 2034 for both assets; new 2039 Nyxol patent issued for presbyopia</td>
</tr>
<tr>
<td>• Stable, small-molecule drugs</td>
</tr>
<tr>
<td>✓ Nyxol = single-use, preservative-free eye drop</td>
</tr>
<tr>
<td>✓ APX3330 = oral pill</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multiple Near-Term Data Catalysts with Capital Efficient Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Initiated 4 late-stage trials (2 Phase 3, 2 Phase 2) with readouts expected in 2021-2022</td>
</tr>
<tr>
<td>✓ Reported positive P3 data in RM in 1Q21 with Nyxol NDA submission targeted late 2022</td>
</tr>
<tr>
<td>✓ Reported positive P2 data in Presbyopia in 2Q21 with plans to advance to P3 in 2022</td>
</tr>
<tr>
<td>• $24 million cash reported at the end of 2Q 2021 sufficient for operations through late 2022</td>
</tr>
<tr>
<td>• Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and Encode Ideas</td>
</tr>
</tbody>
</table>
Large Unmet Opportunities for the Aging Eye

Developing Drugs to Treat Front & Back of the Eye Diseases

**Reversal of Mydriasis**
- U.S. Prevalence: ~100M pupil dilations per year in U.S.
- US Market Opportunity: $325M - $1B

**Presbyopia**
- U.S. Prevalence: ~120M
- US Market Opportunity: $9B - $18B

**Night Vision Disturbances**
- U.S. Prevalence: ~16M adults
- US Market Opportunity: $2B - $4B

**Diabetic Retinopathy**
- U.S. Prevalence: ~7M
- US Market Opportunity: $3B - $7B

**Diabetic Macular Edema**
- U.S. Prevalence: ~750K
- US Market Opportunity: $1B - $3B

**Nyxol® APX3330**

Source: GlobalData Market Research Report, 2020; Company Estimates for Market Size
# Ocuphire Pipeline & Upcoming Milestones

**Multiple Phase 3 & Phase 2 Clinical Data Readouts Anticipated over the Next Year**

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Development Stage</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ocuphire-Focused Development</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Reversal of Mydriasis (RM)</td>
<td>Pre-clinical</td>
<td>Positive Data Readout</td>
</tr>
<tr>
<td>0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops</td>
<td>Presbyopia (P)</td>
<td>Pre-clinical</td>
<td>Positive Data Readout</td>
</tr>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Dim Light or Night Vision Disturbances (NVD)</td>
<td>Pre-clinical</td>
<td>Recruiting</td>
</tr>
<tr>
<td>APX3330 Oral Pill</td>
<td>Diabetic Retinopathy (DR)/ Macular Edema (DME)</td>
<td>Pre-clinical</td>
<td>Recruiting</td>
</tr>
<tr>
<td><strong>Partnering-Focused Development</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APX2009 Intravitreal</td>
<td>DME, Wet Age-Related Macular Degeneration (wAMD)</td>
<td>Pre-clinical</td>
<td>Next steps: IND enabling studies (with partner funding)</td>
</tr>
</tbody>
</table>

**Note:** 0.75% Nyxol (Phentolamine Ophthalmic Solution) is the same as 1% Nyxol (Phentolamine Mesylate Ophthalmic Solution)
## Extensive Development on Both Drug Candidates

**Well-Controlled Phase 1, 2, and 3 Clinical Programs with MIRA-2 Data Leading the NDA Path**

<table>
<thead>
<tr>
<th>Nyxol</th>
<th>APX3330</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>9</strong> Phase 1, Phase 2, and Phase 3 Trials</td>
<td><strong>11</strong> Phase 1 &amp; Phase 2 Trials</td>
</tr>
<tr>
<td><strong>&gt; 330</strong> Subjects Dosed</td>
<td><strong>&gt; 340</strong> Subjects Dosed</td>
</tr>
<tr>
<td>Exposure in Humans <strong>28</strong> Days</td>
<td>Exposure in Humans <strong>365</strong> Days</td>
</tr>
<tr>
<td>Patents to <strong>2034+</strong></td>
<td>Patents to <strong>2034+</strong></td>
</tr>
</tbody>
</table>

**Studied in multiple ocular refractive indications**

505(b)(2) Development Pathway

**Studied in inflammation/hepatitis & cancer patients**

NCE Development Pathway
Nyxol®

RM  Reversal of Mydriasis

P   Presbyopia

NVD Night Vision Disturbances

Phentolamine Mesylate
Nyxol History & MOA

Rationale for Differentiated Product Profile & 505(b)(2) Path

- Nyxol’s active ingredient, phentolamine mesylate (PM), is currently approved for 2 indications
  - Pheochromocytoma (60+ years ago, Regitine®) – intravenous injection
  - Reversal of oral anesthesia (10+ years ago, OraVerse®) – intramuscular injection
- PM has been reformulated as a topical eye drop (Nyxol)
- Nyxol is a first-in-class non-selective $\alpha_1$ and $\alpha_2$ blocker product candidate
  - MOA of relaxing the iris dilator muscle ($\alpha_1$)
  - Redness is an on-target $\alpha_1$ effect on sclera vessels (transient, mild)

Phentolamine Mesylate

Reduces Pupil Size
$\alpha_1$: Iris Dilator Blockade

Dilates Blood Vessels (Vasodilation)
$\alpha_1$: Smooth Muscle Blockade
Nyxol Product Candidate Profile
Novel Alpha 1/2 Blocker Eye Drop for Refractive Indications (505(b)(2) Pathway)

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

Efficacy Data

Improving Vision
- ↓ Pupil Size (moderate miotic)
- ↑ Contrast Sensitivity (night)
- ↑ Near Visual Acuity (light/dark)
- ↑ Distance Visual Acuity

Safety Data

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

Tolerated Topical Effects
- Mild / Transient / Reversible Eye Redness

IOP Unchanged or Decreased
- ↓ Intraocular Pressure (IOP) at Normal Baseline

Chronic daily dosing of Nyxol at bedtime demonstrated no significant daytime redness and durability of effects for more than 24 hours
Nyxol®

- RM: Reversal of Mydriasis
- P: Presbyopia
- NVD: Night Vision Disturbances

Phentolamine Mesylate
Reversal of Mydriasis (RM) – Acute Treatment

Annual Exams and Specialty Visits Involve Dilation to Monitor Eye Health

The Problem

- At many annual eye exams and specialty visits, pupils are pharmacologically dilated, impairing vision for 6-24 hours
- Dilated eyes:
  - heightened sensitivity to light
  - inability to focus
  - reading, working, and driving are difficult
  - halos and glare

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

RM Patient, Age 51

No Current Commercially Available Treatments

~100M eye exams / year in US

Source: GlobalData Market Research Report, 2020
Reversal of Mydriasis (RM) – Acute Treatment

Single Use Indication Leveraging a Precedent Approval Pathway

Nyxol’s Potential Differentiated Solution

- **Regulatory Precedent** with Rev-Eyes (an alpha 1 blocker), approved by the FDA in 1990 but shortly thereafter discontinued (not for safety or efficacy reasons)

- **Clinical Effect** to potentially reduce pupil size and counteract the effect of mydriatic drugs (alpha agonists and cholinergic blockers) used to dilate the pupil

- **Convenient and Stable** eye drop given at the office that may allow vision to return to normal sooner

- **Tolerable** with a minimal side effect profile (unlike cholinergic agonists such as pilocarpine)

Seeking Treatment Findings

| Patients likely to request reversal of dilation | 80% |
| Eye care providers likely to use reversal drops | 70% |

Source: 1.GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (4-7 on a scale of 1-7)
2.GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (6-10 on a scale of 0-10)
**RM MIRA-2 Phase 3 Registration Design**

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

- **MIRA-2**
  - 12 US sites
  - 168 target healthy subjects

**Eligibility Screening**

- Randomization

**Endpoints**

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

- **Secondary:**
  - % of subjects returning to baseline at 30min, 1h, 2h, 3h, 4h, 6h, 24h (overall, by mydriatic agent, by iris color)
  - Mean change in pupil diameter from mydriatic max at all timepoints (overall, by mydriatic agent, by iris color)
  - Accommodation (Tropicamide/Paremyd)
  - Safety and tolerability (redness)

- **0.75% Nyxol**
  - Mydriasis Time -1 Hour
  - Treatment Time 0 (Max Dilation)

- **Mydriatic Agent A, B, or C**
- **Placebo**

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

- **Started and Completed Enrollment in 4Q20 – 185 Subjects**

- **Topline Results Expected in 1Q21 → Reported in March 2021**

Mydriatic Agents 3:1:1 – 2.5% phenylephrine (alpha 1 agonist), 1% tropicamide (cholinergic blocker), Paremyd® (combination)
Primary Endpoint: % of Subjects Study Eye Returning to Baseline PD at 90 Min

\textit{Nyxol Met the Primary & Secondary Endpoints at 90 Min; Additionally at 60 Min & All Subsequent Timepoints}

\textbf{MIRA-2 Phase 3 Trial}

\textbf{Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD)}

\textbf{Nyxol Reduced PD Faster Across All Mydriatic Agents*}

\begin{itemize}
  \item % of Subjects Returning to \( \leq 0.2 \text{ mm of Baseline} \)
  \begin{itemize}
    \item Placebo \( n=91 \)
    \item Nyxol \( n=94 \)
  \end{itemize}

\begin{itemize}
  \item Mean Pupil Diameter
  \begin{itemize}
    \item Placebo \( n=91 \)
    \item Nyxol \( n=94 \)
  \end{itemize}

\end{itemize}

\begin{itemize}
  \item Max pupil dilation, Treatment
  \begin{itemize}
    \item Placebo
    \item Nyxol
  \end{itemize}

\end{itemize}

\begin{itemize}
  \item Mydriatic
    \begin{itemize}
      \item Placebo
      \item Nyxol
    \end{itemize}

\end{itemize}

\begin{itemize}
  \item Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)
\end{itemize}

Source: MIRA-2 Trial, mITT Population (same as Safety Population), *Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)
Secondary Endpoint: Mean Pupil Diameter Over Time by Mydriatic Agent

*Nyxol Reduced Pupil Diameter With All Mydriatic Agents; More Rapidly with Phenylephrine as Expected*

MIRA-2 Phase 3 Trial

**Nyxol More Rapidly Reduced PD in Subjects Across All 3 Mydriatic Agents**

- Phenylephrine
- Tropicamide and Paremyd

- Mean Pupil Diameter

Source: mITT Population, MIRA-2 Trial, Standard Error bars are shown.
Secondary Endpoint: % of Subjects Returning to Baseline PD by Iris Color

Evidence of Efficacy in Subjects with Either Light or Dark Irides, with a More Vigorous Response in Light Irides

MIRA-2 Phase 3 Trial

More Subjects Returned to PD Baseline with Nyxol in Both Light and Dark Irides

Percent of Subjects Returning to ≤ 0.2 mm of Baseline by Iris Color

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Light Irides</th>
<th>Dark Irides</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0%</td>
<td>7%</td>
</tr>
<tr>
<td>1</td>
<td>0%</td>
<td>4%</td>
</tr>
<tr>
<td>1.5</td>
<td>2%</td>
<td>11%</td>
</tr>
<tr>
<td>2</td>
<td>7%</td>
<td>15%</td>
</tr>
<tr>
<td>3</td>
<td>13%</td>
<td>22%</td>
</tr>
<tr>
<td>4</td>
<td>24%</td>
<td>35%</td>
</tr>
<tr>
<td>6</td>
<td>49%</td>
<td>41%</td>
</tr>
</tbody>
</table>

Source: MIRA-2 Trial mITT Population., Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)
Secondary Endpoint: Accommodation And Time Savings

_Nyxol Demonstrates a Faster Return to Baseline Accommodation and Shorter Dilation Time by 4-5 Hours_

**MIRA-2 Phase 3 Trial**

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**Percent of Subjects with Unchanged Accommodation from Baseline (Tropicamide or Paremyd)**

- **Study Eye, PP population**
  - Placebo (n=32)
  - Nyxol (n=35)

  - Placebo: 16% (n=5)
  - Nyxol: 60% (n=21)

  - Placebo: 66% (n=21)
  - Nyxol: 77% (n=27)

  * p<0.05

---

**Percent of Subjects (%)**

- Time Post-Treatment with Nyxol/Placebo (Hours)
  - 0: Placebo 16%, Nyxol 11%
  - 2: Placebo 68%, Nyxol 38%
  - 6: Placebo 66%, Nyxol 77%

---

**Average Time to Return to ≤ 0.2 mm of Baseline PD**

- **Study Eye**
  - Placebo: 2.3 hrs
  - Nyxol: 2.9 hrs

  **Non-Study Eye**
  - Placebo: 5.8 hrs
  - Nyxol: 6.1 hrs

- **Mydriatic Agent**
  - Phenylephrine: Placebo 1.4 hrs, Nyxol 4.8 hrs
  - Tropicamide: Placebo 3.4 hrs, Nyxol 3.6 hrs
  - Paremyd: Placebo 3.6 hrs, Nyxol 7.2 hrs

  **Iridescence Color**
  - Dark Iridescence
    - Placebo: 5.1 hrs
    - Nyxol: 2.8 hrs
  - Light Iridescence
    - Placebo: 1.8 hrs
    - Nyxol: 6.3 hrs

Note: Worsening of accommodation was defined as an amplitude decrease of greater than 1 diopter.
Summary of Positive MIRA-2 Phase 3 Results for Nyxol Eye Drops

**Sustained Efficacy with a Favorable Safety Profile in Reversing Mydriasis with Nyxol**

- **Met primary endpoint at 90 minutes with high statistical significance with 2 drops of Nyxol**
- **Met all key secondary endpoints with high statistical significance**
  - Efficacy for all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Efficacy with only one Nyxol drop in non-study eye
- **Favorable safety profile**
  - No serious AEs, no drop-outs from AEs, no systemic AEs were observed in ≥ 5% of subjects
  - Mild, transient conjunctival hyperemia reported in the first hour and declined steadily thereafter. Baseline mean of 0.7, the mean hyperemia score increased by approximately 1.0 unit on CCLRU scale

Path to Registration

1. Complete a second RM Phase 3 trial with increased subjects ~330 to also meet 24-hour safety population exposure
2. Complete RM trial with 20 subjects ages 3 to 11 per pediatric plan
3. Complete registration batches with 1-year CMC stability and make commercial batches

Submit NDA by Late 2022

**Proposed Indication**

The treatment of pharmacologically induced mydriasis produced by adrenergic (e.g. phenylephrine) or parasympatholytic (e.g. tropicamide) agents, or a combination thereof.
Reversal of Mydriasis (RM) Market Opportunity

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

$325M - $1B+
Estimated US RM Market Opportunity

100M+
General and specialty eye exams per year

> 65% Patients
Report moderate to severe negative impact of dilated exams

$5 - $20
Price range surveyed for cash pay per patient with room for physician markup

> $6B Eye Exam Market
Exams, the third-largest category, grew faster than both prescription lenses and frames

OptoMap: Retinal screening for those wanting to avoid dilations but not a replacement for full dilated eye exam ➔ $40-65 paid by patients

Physician’s Use of Mydriatic Agents

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

Use of phenylephrine, tropicamide, Paremyd®, or combinations of such comprise nearly 95% of dilating eye drops used by eyecare professionals.

1. GlobalData market research report
Nyxol®

- **RM** Reversal of Mydriasis
- **P** Presbyopia
- **NVD** Night Vision Disturbances

Phentolamine Mesylate
2021: The Time for Presbyopia Drops

Headlines From Academia and Industry Articles Thru the Year with an Early First Approval

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

-OIS

Sources: Academic review articles, journals, and publications
Presbyopia – Chronic Opportunity
Aging Population Drives Demand for Alternatives to Reading Glasses & Very Large Market

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
• Growing need for therapies that improve, rather than hinder, quality of life

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

Source: GlobalData Market Research Report, 2020

No Currently Approved Drug Therapies

120 M Patients

Seeking Treatment Findings

| Patients requesting alternative to reading glasses | 40% |
| Patients would consider an eye drop alternative  | 69% |

Market Assumptions:
Total patients - 120 million patients
Price per month - $50+
Patients considering eyedrops - ~50%
Refills (Months) - 3 to 6

~$9-$18B Market Opportunity
Presbyopia – Chronic Opportunity

Nyxol’s Potential Differentiated Solution

- “Pin-hole” effect of Nyxol and low dose pilocarpine may improve near vision by enhancing depth of field as validated by other devices/therapies

- **More durable** combination of two miotics affecting different muscles (iris dilator and sphincter) involved in pupil size modulation

- **Tolerable** use with minimal side effects expected with chronic evening use of Nyxol and daytime use of fractional concentration of pilocarpine

“This would just become part of my daily routine for my eyes to be able to see things up close. How convenient is that?”

*Presbyopic Patient, Age 49*
Product Profile: Nyxol® + Low-Dose Pilocarpine (LDP) Combo

Moderate Action on Iris Dilator and Iris Sphincter Muscles for Near Vision Improvement

0.75% Nyxol

0.4% LDP

Iris Dilator Muscle Inhibition

Iris Sphincter Muscle Activation

- Phentolamine (alpha1/2 antagonist) approved non-ocular injectable indications decade(s) ago 505(b)(2)
- Novel MOA on iris dilator with 24+ hour durability
- Moderate 1+mm pupil reduction
- No daytime redness w/ chronic evening dosing Nyxol
- Well-tolerated with no systemic effects
- Stable, preservative-free, single use vial

1.5 to 2.5 mm PD reduction moves toward the pin-hole (2 to 2.5 mm, up to 3 mm)

- Pilocarpine (cholinergic agonist) approved decades ago
- Known MOA on sphincter muscle with potent miotic effects at approved doses (1%, 2%, 4%)
- Chronic daytime dosing of LDP
- Low concentration avoids known tolerability issues:
  - headache and browache
  - redness
  - accommodative spasm causing loss of distance vision especially at night

Source: 1) Nyxol® data from 8 completed trials; Pilocarpine Product label and Literature
Presbyopia VEGA-1 Phase 2 Design

Randomized, Double-Blind, Placebo-Controlled, Multi-Center One-Week Trial

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

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

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

Phase 2 Enrollment Completed Feb to May 2021 – 150 Subjects Reported Topline Results End of 2Q21
Primary Endpoint: % of Subjects ≥ 15 Letter Gain in Photopic DCNVA at 1 Hour

Primary Endpoint Was Significantly Met for Nyxol + LDP Gaining ≥ 15 Letters Near Vision

VEGA-1 Phase 2 Trial

Primary Endpoint: Percent of Subjects with ≥ 15 Letters DCNVA Improvement from Baseline Binocular (PP Population)

<table>
<thead>
<tr>
<th>Time (Hours)</th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28%</td>
<td>61%</td>
</tr>
</tbody>
</table>

p=0.003

Secondary Endpoint: Percent of Subjects with ≥ 10 Letters DCNVA Improvement from Baseline Binocular (PP Population)

<table>
<thead>
<tr>
<th>Time (Hours)</th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49%</td>
<td>79%</td>
</tr>
</tbody>
</table>

p=0.006

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

Source: VEGA-1 TLR Table 14.2.1.2 %of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters is 3 lines and 10 letters is 2 lines.
Efficacy Endpoints: % of Subjects ≥ 15 Letter DCNVA Gain Across Timepoints

*Nyxol + LDP had Strong Response with ≥ 15 Letter Near Gain from 30 Minutes to 6 Hours*

**VEGA-1 Phase 2 Trial**

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

<table>
<thead>
<tr>
<th>Time (Hours)</th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16%</td>
<td>33%</td>
</tr>
<tr>
<td>0.5</td>
<td>14%</td>
<td>61%</td>
</tr>
<tr>
<td>1</td>
<td>16%</td>
<td>61%</td>
</tr>
<tr>
<td>2</td>
<td>28%</td>
<td>63%</td>
</tr>
<tr>
<td>3</td>
<td>16%</td>
<td>47%</td>
</tr>
<tr>
<td>4</td>
<td>21%</td>
<td>47%</td>
</tr>
<tr>
<td>6</td>
<td>21%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Source: VEGA-1 TLR Table 14.2.1.2 Percent of Subjects with Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters is 3 lines.
2nd Endpoint: % of Subjects ≥ 15 Letter Gain In Near & < 5 Letter Loss In Distance

Phase 3 Approval Endpoint Confirmed Greater Efficacy of Combo over Components at Multiple Timepoints

### VEGA-1 Phase 2 Trial

Percent of Subjects with 15 Letter Improvement in DCNVA and < 5 Letter Loss in BCDVA

<table>
<thead>
<tr>
<th>Time (Hours)</th>
<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>0.5</td>
<td>14%</td>
<td>33%</td>
<td>26%</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>*p=&lt;0.0001</td>
<td>*p=0.03</td>
<td>*p=0.008</td>
<td>*p=0.008</td>
</tr>
<tr>
<td>1</td>
<td>14%</td>
<td>30%</td>
<td>28%</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>*p=&lt;0.0001</td>
<td>*p=0.01</td>
<td>*p=0.004</td>
<td>*p=0.004</td>
</tr>
<tr>
<td>2</td>
<td>14%</td>
<td>20%</td>
<td>14%</td>
<td>26%</td>
</tr>
<tr>
<td></td>
<td>*p=0.0009</td>
<td>*p=0.06</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistics Compared to Nyxol+LDP arm

- Powered for comparison to placebo whereas comparison to component arms were designed to inform the Phase 3 sample size.

Even with a small sample size, combination arm provided statistically meaningful results at 30 min and 2 hours vs. LDP and Nyxol alone arms.

Source: VEGA-1 TLR Table 14.2.2.2 Percent of Subjects with >= 15 Letters of Improvement in Photopic DCNVA and < 5 Letters of Loss in Photopic Binocular BCDVA by Time Point (PP Population)
Secondary Endpoint: Mean Pupil Diameter Over Time

Achieved Pupil Size ~2mm in Nyxol+LDP Consistent with 3-line Improvement in Near Vision

---

VEGA-1 Phase 2 Trial

Best Eye
Mean Pupil Diameter

**p<0.01
***p<0.0001

---

Source: VEGA-1 TLR Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)
Secondary Endpoint: Safety Findings

Nyxol + LDP Combination Was Well Tolerated with a Favorable Safety Profile

- No serious AEs, almost all AEs were mild
- 0% headaches or brow aches reported for Nyxol+LDP arm
- ≤ 5% mild, transient conjunctival hyperemia AEs in Nyxol+LDP arm
- No change in distance vision for Nyxol + LDP arm
  - 0% had ≤ 5 letter distance loss in photopic lighting
  - Only 5% distance loss in mesopic lighting
- No change in IOP

Source: VEGA-1 Study Results (Safety Population, n=150); Only a single subject difference between mITT (n=148) and PP population (n=147)
## Nyxol’s Potential Differentiated Solution

<table>
<thead>
<tr>
<th>Product Attributes*</th>
<th>Nyxol+LDP compared to VUITY™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy (all time-points)</td>
<td>✓+</td>
</tr>
<tr>
<td>Safety: Maintain Distance Vision (especially at night)</td>
<td>✓+</td>
</tr>
<tr>
<td>Safety: Tolerability (no headaches)</td>
<td>✓+</td>
</tr>
<tr>
<td>Durability (at least 6 hours)</td>
<td>✓+</td>
</tr>
<tr>
<td>Fast Onset (within 30 mins)</td>
<td>✓+</td>
</tr>
<tr>
<td>Convenience (daily drops)</td>
<td>✓</td>
</tr>
<tr>
<td>Tunable Pupil Modulation</td>
<td>✓+</td>
</tr>
</tbody>
</table>

ASCRS (July 2021) Abstract# 76645 (Phase 2) and 74336 (Phase 3) and VUITY™ Label
✓+ - Indicates better compared to Vuity
✓ - Indicates comparable to Allergan/AbbVie based on Phase 3 BID dosing (NCT04983589)
Presbyopia Eye Drops Competitive Landscape
Validation of Pupil Modulating Drops Achieving Pin-Hole Effect & Efficacy, Many with Pilocarpine

- Pupil modulation MOA
- Soften lens MOA
- Combination drugs

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

Cholinergic Agonist* (pilocarpine)

Visus (Brimonol®; brimonidine + carbachol)

Lenz (PRX-100; aceclidine)

Orasis (CSF-1; Low dose pilo)

Allergan (AGN-190584; 1.25% pilo)

Eyenovia (MicroLine; 1 or 2% pilo)

Ocuphire (0.75% Nyxol + 0.4% pilo)

Novartis (EV-06)

Other Cholinergic Agonists*

Visus (Brimonol®; brimonidine + carbachol)

Lenz (PRX-100; aceclidine)

Orasis (CSF-1; Low dose pilo)

Allergan (AGN-190584; 1.25% pilo)

Eyenovia (MicroLine; 1 or 2% pilo)

Ocuphire (0.75% Nyxol + 0.4% pilo)

Novartis (EV-06)

Alpha Antagonist & pilocarpine*

NDA

Phase 3

Phase 2

Phase 1

Ocuphire is differentiated by using both the dilator and sphincter muscles moderately to reach a pin-hole pupil size

Next Steps: Advance into Phase 3 Presbyopia Registration Trials in 1H 2022 Towards a Potential NDA Filing in 2023
Nyxol®

- **RM**: Reversal of Mydriasis
- **P**: Presbyopia
- **NVD**: Night Vision Disturbances

Phentolamine Mesylate
Night Vision Disturbances (NVD) – Chronic Opportunity

Imperfections in the Eye Affect Night Vision in Millions

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

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

<table>
<thead>
<tr>
<th>Moderate-to-Severe NVDs</th>
<th>US Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night Myopia</td>
<td>10.8M</td>
</tr>
<tr>
<td>Cortical Cataracts</td>
<td>4.1M</td>
</tr>
<tr>
<td>Post-LASIK</td>
<td>500k</td>
</tr>
<tr>
<td>Post-IOL Implant</td>
<td>300k</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>~16M</strong></td>
</tr>
</tbody>
</table>

Source: GlobalData Market Research Report, 2020
Night Vision Disturbances (NVD) – Chronic Opportunity
Peripheral Optical Imperfections Allowing Pupil Modulation as a Solution

Nyxol’s Potential Differentiated Solution

- **Moderate Decrease in Pupil Size** for scattered light gets blocked by the iris
- **Clinical Effect** to potentially improve low contrast night vision as seen in trials
- **Tolerable** with a minimal side effect profile
- **Convenient and Durable** with chronic once-daily evening dose

“Once there is a drug and a category, that’s when they start looking for the disease.”

*Physician KOL*

<table>
<thead>
<tr>
<th>Seeking Treatment Findings</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients willing to try a new eye drop treatment</td>
<td>67%</td>
</tr>
<tr>
<td>Patients avoiding driving at night</td>
<td>25%</td>
</tr>
</tbody>
</table>
**NVD LYNX-1 Phase 3 Registration Design**

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

**LYNX-1**

- 20 US sites
- ~160 patients with NVD
- Eligibility Screening
- Randomization

- 1:1
- 0.75% Nyxol: daily evening dose (14 days)
- Placebo: daily evening dose (14 days)

**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)

**Phase 3 Initiated in Late 4Q20**

**Top Line Expected Early 2022**
Nyxol Demonstrated Clinical Effect in NVD

Key Endpoints Observed in Multiple Phase 2 Trials

NYX-SNV Phase 2 Trial

Improved Low Contrast Distance Visual Acuity*

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

Source NYX-SNV

Baseline Pupil Diameter: Placebo 4.6mm, Nyxol 4.7mm

Placebo n=16
Nyxol n=32

P=0.029
P=0.04
P=0.16

ORION-1 Phase 2 Trial

Durable > 24-hour Pupil Modulation Effect

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

Baseline Pupil Diameter: Placebo 4.6mm, Nyxol 4.7mm

Source: NYXG-201

Placebo (n = 20)
1% Nyxol (n = 19)

Durable > 24-hour Pupil Modulation Effect

Day 8
Day 15
Day 16

-0.99 -20%  
-1.00 -21%  
-0.88 -19%

-0.07 -2%  
-0.05 -5%  
-0.11 -1%

-1.4 -2.0 -1.6 -1.2 -0.8 -0.4 0 0.4 0.8 1.2 1.6 2.0

14-day Daily Evening Dosing, Last Dose on Day 14

*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

- **DR** Diabetic Retinopathy
- **DME** Diabetic Macular Edema
- **wAMD** Wet Age-Related Macular Degeneration
Diabetic Retinopathy & Macular Edema
Non-Injectable Alternative Therapies are Needed For Earlier Stages of Disease

The Problem

• Diabetic retinopathy (DR) and diabetic macular edema (DME) are a leading cause of vision loss worldwide

• Diabetes damages small blood vessels within the eye causing leakage, oxygen starvation, and abnormal vessel growth

• DR patients are not routinely treated with approved injectable anti-VEGF drugs
  - DR progresses resulting in vision loss

• Current treatment for DME are not satisfactory
  - 25% non-responders
  - 50% partial responders to anti-VEGF drugs

Limited Retina Treatment Options for Diabetics

Large, Unmet Need in Diabetic Eye Diseases (US)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>DR</td>
<td>~7.7M Patients</td>
</tr>
<tr>
<td>DME</td>
<td>~750K Patients</td>
</tr>
</tbody>
</table>

APX3330 History and Ref-1 Inhibition Mechanism

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

- 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
  - Similar oncology origin as approved anti-VEGFs
- MOA uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1

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

APX3330 Down-Regulates VEGF Protein and Anti-Inflammatory Cytokines

In Vivo and In Vitro Evidence of APX Dual Pathway Mechanism of Action

**APX3330 Reduces VEGF Protein in the Brain of Preclinical Models**

- Treatment of APX3330 (10mg/kg, oral gavage) in rats with type 1 diabetes and induced stroke shows a significant decrease of VEGF signaling.
- Increased VEGF is a hallmark of uncontrolled neovascularization and inflammation in diabetic retinopathies; current approved treatments successfully decrease VEGF levels in the eye.

**APX3330 Reduces Pro-inflammatory Cytokines in Murine Cell Lines Involved in Macular Degeneration**

- In vitro APX3330 suppresses pro-inflammatory cytokines in LPS stimulated murine macrophage cell lines known to be involved in macular degeneration:
  - TNF-α is a potent cytokine that enhances secretion of VEGF-A and VEGF-B by human choroidal fibroblast cells. J Cell Physiol. 2011
  - Genetic ablation of IL-6 led to significant suppression of AMD (murine CNV model). Am J Pathol. 2007
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

APX3330

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

Silva et al., 2021

- Silva et al. Oral APX3330 treatment reduces L-CNV lesions in preclinical mouse model and confirms Phase 2 DR/DME clinical dose with sufficient distribution to human retina using PBPK modeling. Presented at the ARVO 2021 Annual Meeting
- Published data on EYLEA

L-CNV Mouse Retina Model

APX3330 Gavage OCT Lesion Volume

EYLEA

Day 7

Day 14

-44%

(c)

- Silva et al. Oral APX3330 treatment reduces L-CNV lesions in preclinical mouse model and confirms Phase 2 DR/DME clinical dose with sufficient distribution to human retina using PBPK modeling. Presented at the ARVO 2021 Annual Meeting
- Published data on EYLEA
Phase 1/2 Clinical Trials: PK Data Supporting the ZETA-1 Trial

APX3330 is Bioavailable and Reaches the Retina via Oral Administration

Does oral administration of APX3330 reach the retina in sufficient concentration?

Mouse

25 mg/kg APX3330 oral gavage measured in mouse retina

Rat

10 mg/kg APX3330 oral gavage measured in rat eye

Human

300 mg BID (600 mg/day total)

Established PBPK model predicts APX3330 reaches sufficient human retinal concentrations

Phase 1 PK Clinical Data

Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels

Human Pharmacokinetics of APX3330 at 120 mg/day

Source: Eisai/Apexian Human PK data

1. Apexian preclinical data
2. Eisai preclinical data
APX3330 Product Candidate Profile for Multiple Retinal Indications

First-in-Class Ref-1 Inhibitor with Favorable Human Safety Data for Retinal Indications

APX3330: Well-tolerated Oral Dose up to 600mg/day

Expected Efficacy Data

Improving Eye Health in Diabetics

↓ Inflammation
↓ Abnormal Angiogenesis

Enhance Compliance & Exposure
Oral pill may reduce the burden of frequent anti-VEGF injections

Safety Data

Few Systemic Adverse Effects
• < 5% Mild Gastrointestinal (diarrhea)
• < 5% Mild Skin Rash (reversible)
• Lack of Significant Acute Neurologic, Cardiovascular, Liver, or Pulmonary toxicity

No Ocular Effects
• No observed ocular AEs

Twice a day dosing of APX3330 being developed to provide steady state effectiveness with a tolerable chronic safety profile
DR/DME ZETA-1 Phase 2b Design

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

ZETA-1

20 US sites

~100 patients with moderate-to-severe NPDR and mild PDR

Eligibility Screening

Randomization

APX3330 600mg

Twice daily oral dose (24 weeks)

Placebo

Twice daily oral dose (24 weeks)

Endpoints

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

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

Exploratory:
- Labs / PK

Phase 2b Start Initiated in April 2021

Top Line Expected in 2022
Innovative Approach for Retinal Diseases with APX Platform

APX3330 May Treat Patients Across the Spectrum of Retinal Diseases

- **Potential First Oral Rx for Retina Diseases**
  - First-line earlier intervention for the diabetic eye
  - Add-on therapy to current anti-VEGF treatments
- **Proven Novel Mechanism**
  - May decrease both inflammation and angiogenesis
- **Convenient Daily Regiment**
- **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
Boards and Milestones
Ocuphire's World-Class Medical Advisory Board

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

Eliot Lazar, MD
Georgetown University

Jay Pepose, MD, PhD
UCLA

Ed Holland, MD
Loyola University Chicago

Marguerite McDonald, MD
Columbia University

Thomas Samuelson, MD
University of Minnesota

Richard Lindstrom, MD
University of Minnesota

Douglas Devries, OD
University of Nevada

Y. Ralph Chu, MD
Northwestern University

Paul Karpecki, OD
Indiana University

Michael Allingham, MD, PhD
University of North Carolina

Gerald Horn, MD
University of Illinois
Co-Founder Ocularis/Nyxol
Past MAB Member

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

Peter Kaiser, MD
Harvard Medical School

David Boyer, MD
Chicago Medical School

David Brown, MD
Baylor University

Jeffrey Heier, MD
Boston University

Retina-Vitreous Associates Medical Group

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

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

Cam Gallagher, MBA
Chair, Board Director

Cam Gallagher, MBA
Chair, Board Director

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

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

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Jay Pepose, MD, PhD
Board Director

Jay Pepose, MD, PhD
Board Director

Cam Gallagher, MBA
Chair, Board Director

James Manuso, PhD/MBA
Board Director

James Manuso, PhD/MBA
Board Director

Richard Rodgers, MBA
Board Director

Richard Rodgers, MBA
Board Director

Susan Benton, MBA
Board Director

Susan Benton, MBA
Board Director
2021 to 2022 Ocuphire Cadence of Milestones
Multiple Data Catalysts On Path To NDA(s)

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

**2022**
- Report Phase 3 Data for NVD
- Report 2nd Phase 3 Data for RM
- Report Pediatric Data in RM
- Submit Nyxol NDA for RM
- Report Phase 2 Data for DR/DME
- Initiate Two Phase 3 Presbyopia Trials
- Initiate Phase 3 Chronic Safety Trial

Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)

Early 2022
Recent FDA Ophthalmology Drug Approvals

*FDA Record Number of Drugs Approved for Front and Back of the Eye in 2021*

<table>
<thead>
<tr>
<th>Company</th>
<th>Drug</th>
<th>Indication</th>
<th>Date</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santen</td>
<td>Cyclosporine Topical Ophthalmic Emulsion</td>
<td>Severe Vernal Keratoconjunctivits</td>
<td>June 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td>Oyster Point Pharma</td>
<td>OC-01 Nasal Spray</td>
<td>Dry Eye Disease</td>
<td>October 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td>Ocular Therapeutics</td>
<td>Dextenz™</td>
<td>Ocular Itching Associated with Allergic Conjunctivitis</td>
<td>October 2021</td>
<td>sNDA Approved</td>
</tr>
<tr>
<td>BAUSCH Health</td>
<td>Xipere™</td>
<td>Macular Edema associated with Uveitis</td>
<td>October 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td>eyenovia</td>
<td>MydCombi™</td>
<td>Fixed combination mydriatic microdose system</td>
<td>October 2021</td>
<td>CRL, now drug/device classification</td>
</tr>
<tr>
<td>Genentech</td>
<td>Susvimo™</td>
<td>Wet-AMD</td>
<td>October 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td>Allergan</td>
<td>Vuity™</td>
<td>Presbyopia</td>
<td>October 28 2021</td>
<td>Approved Two months in advance.</td>
</tr>
</tbody>
</table>

Source: Company websites, 2020 10K annual reports, Q2 2021 quarterly reports
OCUP – Market Snapshot

Sufficient Cash Runway Through 2022

<table>
<thead>
<tr>
<th>Ticker</th>
<th>OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>$4.17</td>
</tr>
<tr>
<td>Close on 11-9-21</td>
<td></td>
</tr>
<tr>
<td>Market Cap</td>
<td>$72 M</td>
</tr>
<tr>
<td>As of 11-9-21</td>
<td></td>
</tr>
<tr>
<td>Shares Outstanding</td>
<td>16.9 M</td>
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<tr>
<td>As of 6-30-21</td>
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<tr>
<td>Cash</td>
<td>$24.2 M</td>
</tr>
<tr>
<td>As of 6-30-21</td>
<td></td>
</tr>
<tr>
<td>Cash Runway</td>
<td>Sufficient through 2022</td>
</tr>
<tr>
<td>Guidance as of 6-30-21</td>
<td></td>
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<tr>
<td>Average Daily Volume</td>
<td>200 K</td>
</tr>
<tr>
<td>As of 11-9-21</td>
<td></td>
</tr>
<tr>
<td>Short Interest</td>
<td>445K; 2.6% of CSO</td>
</tr>
<tr>
<td>As of 10-29-21</td>
<td></td>
</tr>
</tbody>
</table>

Research Analyst Coverage on OCUP

<table>
<thead>
<tr>
<th>Research Analyst Coverage on OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>James Molloy</td>
</tr>
<tr>
<td>Alliance Global Partners</td>
</tr>
<tr>
<td>John Newman</td>
</tr>
<tr>
<td>Canaccord Genuity</td>
</tr>
<tr>
<td>Kristen Kluska</td>
</tr>
<tr>
<td>Cantor Fitzgerald</td>
</tr>
<tr>
<td>Prakhar Agrawal</td>
</tr>
<tr>
<td>Jones Trading</td>
</tr>
</tbody>
</table>
NVD Endpoint: 5% Low Contrast Visual Acuity (LCVA) Chart

*FDA Accepted Endpoint for Contrast Sensitivity Assessment*

**Primary Endpoint of Nyxol LYNX-1 Trial**

Percent of subjects with ≥ 3 lines of improvement in mesopic low contrast best-corrected distance visual acuity (7 days)

* Inclusion Criteria includes subjects with baseline mesopic LCVA of 20/100 or worse
DR/DME Endpoint: Diabetic Retinopathy Severity Scale (DRSS)

*FDA Accepted Endpoint for DR (EYLEA® in PANORAMA Pivotal Trial)*

**Primary Endpoint of APX3330 ZETA-1 Trial**

Percent of patients with a $\geq 2$ step improvement on the DRSS score at week 24

### A 13-point Scale Outlining the Various Stages of Diabetic Retinopathy

<table>
<thead>
<tr>
<th>DRSS Score</th>
<th>Description</th>
<th>Retinal Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (10)</td>
<td>DR Absent</td>
<td>Healthy blood vessels with no bulges</td>
</tr>
<tr>
<td>2 (20)</td>
<td>Microaneurysm only</td>
<td>Small bulges in blood vessel walls as well as other signs in the retina</td>
</tr>
<tr>
<td>3 (35)</td>
<td>Mild NPDR</td>
<td>More changes in the blood vessels in the retina and small spots of blood can become more visible</td>
</tr>
<tr>
<td>4 (43)</td>
<td>Moderate NPDR</td>
<td>More blood vessels in larger areas of the retina show changes</td>
</tr>
<tr>
<td>5, 6 (47, 53)</td>
<td>Moderately Severe NPDR</td>
<td>Many of the blood vessels in the retina show visible changes</td>
</tr>
<tr>
<td>7 – 13 (60, 61, 65, 71, 75, 85, 90)</td>
<td>PDR – Mild, Moderate, and Severe</td>
<td>Increased growth of new, damaged blood vessels</td>
</tr>
</tbody>
</table>

**Patients included in the ZETA-1 Trial**

**Percent of patients with a $\geq 2$ step improvement on the DRSS score at week 24**

**Description**

- **DR Absent**: Healthy blood vessels with no bulges
- **Microaneurysm only**: Small bulges in blood vessel walls as well as other signs in the retina
- **Mild NPDR**: More changes in the blood vessels in the retina and small spots of blood can become more visible
- **Moderate NPDR**: More blood vessels in larger areas of the retina show changes
- **Moderately Severe NPDR**: Many of the blood vessels in the retina show visible changes
- **PDR – Mild, Moderate, and Severe**: Increased growth of new, damaged blood vessels