Glucoma & Anterior Segment
Eyecelerator@AAO 2021

Mina Sooch CEO and Founder

November 11, 2021
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Ocuphire Overview
A Late-Stage Clinical Ophthalmic Biotech (Nasdaq Symbol: OCUP)

**Presbyopia**
U.S. Prevalence: ~128M

**Night Vision Disturbances**
U.S. Prevalence: ~16M adults

**Reversal of Mydriasis**
~100M pupil dilations per year in U.S.

**Nyxol®**
Positive Phase 2 Top-line Data 2Q21
Advance Two Phase 3 in 2022

Phase 3 Recruiting
Phase 3 Top-Line Data early 2022

Positive Phase 3 Top-Line Data 1Q21
2nd Phase 3 Planned 2H21
2nd Phase 3 Top-Line Data early 2022
NDA Submission Late 2022

**Diabetic Retinopathy**
U.S. Prevalence: ~7M

**Diabetic Macular Edema**
U.S. Prevalence: ~750K

**APX3330**
Phase 2 Recruiting
Phase 2 Top-Line Data in 2022
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
Product Profile: Nyxol® + Low-Dose Pilocarpine (LDP) Combo

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

0.75% Nyxol

- 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

0.4% LDP

- 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

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

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

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

VEGA-1

17 US sites
150 presbyopia patients

0.75% Nyxol

Placebo

4 arms

Randomization

Screening

Visit 1
Evening Dosing (3-4 doses)

Visit 2 (3 – 6 Days Later)

Treatment Arms

Baseline → Nyxol → LDP Drop

Nyxol + LDP

Nyxol Alone

Baseline → No Treatment

LDP Alone

Baseline → Placebo → LDP Drop

Placebo Alone

Baseline → Placebo → No Treatment

Endpoints

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

Secondary:

• % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours in photopic lighting comparing Nyxol + LDP vs placebo, Nyxol alone, and LDP alone

• No loss of distance vision

• Pupil diameter at time points

• Safety and tolerability (redness)

Eligibility Criteria

• Males or females ≥ 40 and ≤ 64 years of age

• BCDVA of 0.0 LogMAR (20/20 Snellen equivalent) or better in each eye under photopic conditions

• DCNVA of 0.4 LogMAR (20/50 Snellen equivalent) or worse in photopic conditions in each eye & binocularly

Phase 2 Enrollment Completed Feb to May 2021 – 150 Subjects
Reported Topline Results End of 2Q21

Clinical trial NCT#04675151. DCNVA = distance-corrected near visual acuity. BCDVA = best corrected distance visual acuity
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

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.

**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>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16%</td>
<td>33%</td>
<td>0.09</td>
</tr>
<tr>
<td>0.5</td>
<td>14%</td>
<td>28%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1</td>
<td>16%</td>
<td>61%</td>
<td>0.03</td>
</tr>
<tr>
<td>2</td>
<td>16%</td>
<td>63%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>21%</td>
<td>47%</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>21%</td>
<td>47%</td>
<td>0.02</td>
</tr>
<tr>
<td>6</td>
<td>19%</td>
<td>37%</td>
<td>0.06</td>
</tr>
</tbody>
</table>

- **Primary Endpoint**
- Rapid onset of efficacy
- Durable benefit over 6 hours
- Nyxol alone effect (~12 hr data)
- 33% Placebo Adjusted Response

Rapid onset of efficacy
Secondary Endpoint: Improvement in DCNVA Baseline vs. 1 Hour Post Nyxol+LDP

Nyxol + LDP had a Rapid Improvement on Near Vision for Many Patients

Source: VEGA-1 TLR Table 14.2.24.1 Percent of Subjects with Photopic DCNVA by Time Point (PP Population)
Secondary Endpoint: Intermediate Vision
Nyxol + LDP Had Significant Improvement in Letters Read in DCIVA Compared to Placebo

VEGA-1 Phase 2 Trial

Change from Baseline in Binocular Photopic DCIVA (Letters Read)

Nyxol + LDP Had Significant Improvement in Letters Read in DCIVA Compared to Placebo

Source: VEGA-1 TLR Table 14.2.7.1 Observed Values and Change from Baseline in Photopic DCIVA by Time Point (Letters Read) (PP Population)
Secondary Endpoint: Mean Pupil Diameter Over Time

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

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

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=43)</th>
<th>Nyxol (n=30)</th>
<th>LDP (n=31)</th>
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</thead>
<tbody>
<tr>
<td>Baseline Mean</td>
<td>4.8</td>
<td>4.5</td>
<td>4.3</td>
<td>4.4</td>
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<tr>
<td>0</td>
<td>4.6</td>
<td>4.5</td>
<td>4.4</td>
<td>4.4</td>
</tr>
<tr>
<td>1</td>
<td>4.5</td>
<td>4.5</td>
<td>4.4</td>
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<tr>
<td>6</td>
<td>4.3</td>
<td>4.4</td>
<td>4.4</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Daily Evening Nyxol Dosing 12 hr minimum interval to Time 0

**p<0.01
***p<0.0001

VEGA-1 Phase 2 Trial

Best Eye Mean Pupil Diameter

Nyxol+LDP arm statistically significant compared to all arms

Source: VEGA-1 TLR Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)
Additional VEGA-1 Phase 2 Efficacy Results

Nyxol + LDP Efficacy Data has Potential for Differentiation

• Met the planned Phase 3 primary endpoint of 15 letters (3 lines) near vision gain with less than 5 letters of distance vision loss
  – Statistical significance and/or trend across multiple timepoints for combination treatment vs. each individual component (Nyxol or LDP)

• Met multiple additional key secondary endpoints
  – Nyxol+LDP was numerically better than each component at every timepoint
  – Efficacy data in both light and dark iris colors
  – Near vision efficacy seen monocularly
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
Summary & Next Steps for Ocphure Presbyopia Drops

Advance Into Phase 3 with a Differentiated Product Profile

<table>
<thead>
<tr>
<th>Important Product Attributes</th>
<th>Nyxol+LDP Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>✓</td>
</tr>
<tr>
<td>Safety: Maintain Distance</td>
<td>✓</td>
</tr>
<tr>
<td>Safety: Tolerability</td>
<td>✓</td>
</tr>
<tr>
<td>Durability</td>
<td>✓</td>
</tr>
<tr>
<td>Fast Onset</td>
<td>✓</td>
</tr>
<tr>
<td>Convenient Daily Drops</td>
<td>✓</td>
</tr>
<tr>
<td>Tunable Pupil Modulation</td>
<td>✓</td>
</tr>
</tbody>
</table>

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

**AAO 2021 Presentations**

**AAO Refractive Surgery Day ePoster**

VEGA-1 Presbyopia Presentation by Dr. Jay Pepose
Abstract # 30068457

**AAO Retina Day Scientific ePoster**

ZETA-1 DR/DME Presentation by Dr. Mike Allingham
Abstract # PO332

Advance into Presbyopia Phase 3
With Registration Trials in 1H22
Towards a Potential NDA Filing in 2023

Source: VEGA-1 Clinical Study Results