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Late Clinical Stage Company Targeting Large, Unmet Ophthalmic Markets

- Nyxol eye drops target multiple chronic and acute front of the eye indications addressing large markets: Dim Light / Night Vision Disturbances (NVD), Reversal of Mydriasis (RM), & Presbyopia (P)
- 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

Significant Clinical Data and Regulatory Precedents

- Nyxol and APX3330 achieved promising clinical data over multiple Phase 1, 2, and 3 trials
  - Nyxol with > 330 patients treated across 9 trials
  - APX3330 with > 340 patients treated across 11 trials
- FDA End of Phase 2 meeting guidance for Nyxol (all indications) in May 2020

Significant IP Portfolio and Small Molecule CMC Advantages

- US and global issued patents thru 2034 for both assets; new 2039 Nyxol patent issued for presbyopia
- Stable, small-molecule drugs
  - Nyxol = single-use, preservative-free eye drop
  - APX3330 = oral pill

Multiple Near-Term Data Catalysts with Capital Efficient Plan

- Initiated 4 late-stage trials (2 Phase 3, 2 Phase 2) with readouts expected 1Q21 thru early 2022
  - Reported positive P3 data in RM in 1Q21 with Nyxol NDA submission targeted late 2022
  - Reported positive P2 data in Presbyopia in 2Q21 with plans to advance to P3
- Recent $15M offering combined with cash on hand sufficient to run operations through late 2022
- Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and Encode Ideas
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

Amy Rabourn, CPA
VP Finance

Ronil Patel, MS
Senior Director BD and
Market Strategy

Mitch Brigell, PhD
Head Clinical Development
and Strategy

Daniela Oniciu, PhD
Head CMC and Global
Clinical Supply

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Head Clinical
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Chris Ernst
Quality Assurance Lead
Large Unmet Opportunities for the Aging Eye

Developing Drugs to Treat Front & Back of the Eye Diseases

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

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

Presbyopia
U.S. Prevalence: ~120M

$4-10B US Markets

Diabetic Retinopathy
U.S. Prevalence: ~7M

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

APX3330

Nyxol®

Source: GlobalData Market Research Report, 2020
# Ocuphire Pipeline & Upcoming Milestones

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

<table>
<thead>
<tr>
<th>Ocuphire-Focused Development</th>
<th>Ocuphire-Focused Development</th>
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</thead>
<tbody>
<tr>
<td><strong>Product Candidate</strong></td>
<td><strong>Development Stage</strong></td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td><strong>Pre-clinical</strong></td>
</tr>
<tr>
<td><strong>0.75% Nyxol® Eye Drop</strong></td>
<td><strong>Reversal of Mydriasis (RM)</strong></td>
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<tr>
<td><strong>0.75% Nyxol® Eye Drop</strong></td>
<td><strong>Dim Light or Night Vision Disturbances (NVD)</strong></td>
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<tr>
<td><strong>0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops</strong></td>
<td><strong>Presbyopia (P)</strong></td>
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<tr>
<td><strong>APX3330 Oral Pill</strong></td>
<td><strong>Diabetic Retinopathy (DR)/ Macular Edema (DME)</strong></td>
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<thead>
<tr>
<th>Partnering-Focused Development</th>
<th>Partnering-Focused Development</th>
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</thead>
<tbody>
<tr>
<td><strong>APX2009 Intravitreal</strong></td>
<td><strong>Development Stage</strong></td>
</tr>
<tr>
<td><strong>DME, Wet Age-Related Macular Degeneration (wAMD)</strong></td>
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*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>9</td>
<td>11</td>
</tr>
<tr>
<td>Phase 1, Phase 2, and Phase 3 Trials</td>
<td>Phase 1 &amp; Phase 2 Trials</td>
</tr>
<tr>
<td>&gt;330 Subjects Dosed</td>
<td>&gt;340 Subjects Dosed</td>
</tr>
<tr>
<td>Exposure in Humans</td>
<td>Exposure in Humans</td>
</tr>
<tr>
<td>28 Days</td>
<td>365 Days</td>
</tr>
<tr>
<td>Patents to</td>
<td>Patents to</td>
</tr>
<tr>
<td>2034+</td>
<td>2034+</td>
</tr>
<tr>
<td>Studied in ocular refractory diseases (NVD) &amp; elderly glaucoma patients</td>
<td>Studied in inflammation/hepatitis &amp; cancer patients</td>
</tr>
</tbody>
</table>

- 505(b)(2) Development Pathway
- 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 α1 and α2 blocker product candidate
  – MOA of relaxing the iris dilator muscle (α1)
  – Redness is an on-target α1 effect on sclera vessels (transient, mild)
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, Aged 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

**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)

**MIRA-2**

- 12 US sites
- 168 target healthy subjects

**1:1**

- **Mydriasis**
  - Time: -1 Hour
  - Treatment: Time 0 (Max Dilation)

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

- **Placebo**

- **0.75% Nyxol**
  - (2 drops study eye, 1 drop fellow eye)

- **Nyxol drop(s)**

- **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

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

MIRA-2 Phase 3 Trial

Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD)

% of Subjects Returning to ≤ 0.2 mm of Baseline

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Placebo n=91</th>
<th>Nyxol n=94</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>1</td>
<td>1%</td>
<td>28%</td>
</tr>
<tr>
<td>1.5</td>
<td>2%</td>
<td>7%</td>
</tr>
<tr>
<td>2</td>
<td>11%</td>
<td>49%</td>
</tr>
<tr>
<td>3</td>
<td>59%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>80%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>6</td>
<td>90%</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

Nyxol Reduced PD Faster Across All Mydriatic Agents*

Mean Pupil Diameter

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Mean Pupil Diameter (Study Eye) (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>Nyxol n=94</td>
</tr>
<tr>
<td>0</td>
<td>Placebo n=91</td>
</tr>
<tr>
<td>0.5</td>
<td>Max pupil dilation, Treatment</td>
</tr>
<tr>
<td>1</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>1.5</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>2</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>6</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

*Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

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**

**Mean Pupil Diameter**

**Phenylephrine**

- Nyxol n=56
- Placebo n=55

**Tropicamide or Paremyd**

- Nyxol n=38
- Placebo n=36

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

Light Irides

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Placebo n=45</th>
<th>Nyxol n=45</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>2%</td>
<td>7%</td>
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<tr>
<td>1.5</td>
<td>7%</td>
<td>24%</td>
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<tr>
<td>2</td>
<td>13%</td>
<td>93%</td>
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<tr>
<td>3</td>
<td>24%</td>
<td>96%</td>
</tr>
<tr>
<td>4</td>
<td>49%</td>
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</tr>
<tr>
<td>6</td>
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</table>

Dark Irides

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Placebo n=46</th>
<th>Nyxol n=49</th>
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</thead>
<tbody>
<tr>
<td>0.5</td>
<td>7%</td>
<td>0%</td>
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<tr>
<td>1</td>
<td>4%</td>
<td>31%</td>
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<tr>
<td>1.5</td>
<td>11%</td>
<td>56%</td>
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<td>2</td>
<td>15%</td>
<td>71%</td>
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<tr>
<td>3</td>
<td>22%</td>
<td>96%</td>
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<tr>
<td>4</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>41%</td>
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</tr>
</tbody>
</table>

Source: MIRA-2 Trial mITT Population, Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)
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
  – Mild, transient conjunctival hyperemia reported in the first hour and declined steadily thereafter
  – No serious AEs, no drop-outs from AEs, no systemic AEs were observed in ≥ 5% of subjects

• Validates Nyxol mechanism of action, therapeutic effect (of 1+mm diameter reduction), and safety profile in the other two indications of presbyopia and night vision disturbances

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

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

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

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.

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1. GlobalData market research report

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Nyxol®

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

Phentolamine Mesylate
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.*

*Physician KOL*

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**No Currently Approved Drug Therapies**

**Seeking Treatment Findings**

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

---

Source: GlobalData Market Research Report, 2020
Presbyopia – Chronic Opportunity

Pupil Modulation Eye Drops May Replace Reading Glasses

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

- Iris Dilator Muscle Inhibition

0.4% LDP

- 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’ (1.6 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 daily dosing of LDP, a more moderate miotic
- 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-Blinded, Placebo-Controlled, Multi-Center One-Week Trial

VEGA-1

17 US sites

150 presbyopic patients

0.75% Nyxol

Baseline

Nyxol

LDP Drop

Nyxol + LDP

Baseline

Nyxol

No Treatment

Nyxol Alone

Baseline

Placebo

LDP Drop

LDP Alone

Baseline

Placebo

No Treatment

Placebo Alone

Visit 1

Evening Dosing (3-4 doses)

Visit 2 (3 – 6 Days Later)

Treatment Arms

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 and mesopic 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 Reporting Topline Results as Guided by 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*

**Primary Endpoint:** Percent of Subjects with ≥ 15 Letters DCNVA Improvement from Baseline

- Placebo (n=43)
- Nyxol+LDP (n=43)

**Secondary Endpoint:** Percent of Subjects with ≥ 10 Letters DCNVA Improvement from Baseline

- Placebo (n=43)
- Nyxol+LDP (n=43)

*p=0.003* for Placebo Adjusted Responders

*p=0.006* for Nyxol+LDP Adjusted Responders

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.
Secondary Endpoint: % of Subjects ≥ 15 Letter DCNVA Gain At All Timepoints

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

VEGA-1 Phase 2 Trial

Percent of Subject with ≥ 15 Letters DCNVA Improvement from Baseline

Binocular

<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>28%</td>
</tr>
<tr>
<td>1</td>
<td>28%</td>
<td>61%</td>
</tr>
<tr>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>16%</td>
<td>61%</td>
</tr>
<tr>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>21%</td>
<td>63%</td>
</tr>
<tr>
<td>3.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>21%</td>
<td>47%</td>
</tr>
<tr>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>19%</td>
<td>37%</td>
</tr>
</tbody>
</table>

- **Durable benefit over 6 hours**
- **Similar Efficacy was Observed In:**
  - Study Eye and Fellow Eye
  - Light and Dark Irides
- **Rapid onset of efficacy**

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 $\geq$ 15 Letter Gain In Near & $\leq$ 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 $\leq$ 5 Letter Loss in BCDVA Binocular

<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% p=0.03</td>
<td>26% p=0.008</td>
<td>28%</td>
</tr>
<tr>
<td>1</td>
<td>26% p=0.01</td>
<td>42% p=0.02</td>
<td>30%</td>
<td>42%</td>
</tr>
<tr>
<td>2</td>
<td>39% p=0.06</td>
<td>63% p=0.0009</td>
<td>14%</td>
<td>20%</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

Source: VEGA-1 TLR Table 14.2.2.2 Percent of Subjects with $\geq$ 15 Letters of Improvement in Photopic DCNVA and $< 5$ Letters of Loss in Photopic Binocular BCDVA by Time Point (PP Population)

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

Mean Pupil Diameter (mm)

Daily Evening Nyxol Dosing 12 hr minimum interval to Time 0

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)
Secondary Endpoint: Safety Findings

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

<table>
<thead>
<tr>
<th>Placebo Alone n=45</th>
<th>Nyxol Alone n=30</th>
<th>LDP Alone n=31</th>
<th>Nyxol+LDP n=44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Treatment Emergent Adverse Events (n)</td>
<td>4</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>TEAEs by Severity (n [%])</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1 (2.2%)</td>
<td>6 (20%)</td>
<td>6 (19.4%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (2.2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>AEs Occurring in ≥ 5% of subjects (n [%])</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instillation Site Pain (Mild)</td>
<td>1 (2.2%)</td>
<td>3 (10%)</td>
<td>2 (6.5%)</td>
</tr>
<tr>
<td>Instillation Site Erythema (Mild)</td>
<td>0 (0%)</td>
<td>3 (10%)</td>
<td>2 (6.5%)</td>
</tr>
<tr>
<td>Conjunctival Hyperemia (Mild)</td>
<td>0 (0%)</td>
<td>2 (6.7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Eye Disorders (Mild)</td>
<td>1 (2.2%)</td>
<td>2 (6.7%)</td>
<td>4 (12.9%)</td>
</tr>
</tbody>
</table>

- No deaths, 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
- Distance vision: 100% Nyxol + LDP arm had ≤ 5 letter distance loss in photopic lighting (95% in mesopic)
- No change in IOP
Presbyopia Eye Drops Competitive Landscape
Validation of Pupil Modulating Drops Achieving Pin-Hole Effect & Efficacy, Many with Pilocarpine

Cholinergic Agonist* (pilocarpine)

Other Cholinergic Agonists*

Visus (Brimochol®; brimonidine + carbachol)
Lenz (PRX-100; aceclidine)

Orasis (CSF-1; Low dose pilo)
Allergan (AGN-190584; 1.25% pilo)
Eyenovia (MicroLine; 1 or 2% pilo)

Orasis (CSF-1; Low dose pilo)
Novartis (EV-06)

Visus (Brimochol®; brimonidine + carbachol)
Lenz (PRX-100; aceclidine)

Ocuphire (0.75% Nyxol + 0.4% pilo)

Novartis (EV-06)

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

Pupil modulation MOA
Soften lens MOA
Combination drugs

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

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

Corporate Websites, Grzybowski, A, Markeviciute A, Zemaitiene R. A Review of Pharmacological Presbyopia Treatment. 2020
Potential ‘Best in Class’ Presbyopia Drops

Differentiated Product Profile and MOA Uniquely Using Both Dilator & Sphincter Muscle

Nyxol+LDP Combination Product Profile

Potential ‘Best in Class’ Presbyopia Drops
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, aged 42

No Currently Approved Therapies

<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>Total</td>
<td>~16M</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>

Before

After
NVD LYNX-1 Phase 3 Registration Design

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

**LYNX-1**

15 US sites
~160 patients with NVD

Eligibility Screening → Randomization ➔ 1:1 ➔ 0.75% Nyxol

daily evening dose (14 days)

0.75% Nyxol

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 3Q21**
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*

% of Eyes with Mesopic Low Contrast Visual Acuity Improvement

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo n=16</th>
<th>Nyxol n=32</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 line</td>
<td>31%</td>
<td>69%</td>
</tr>
<tr>
<td>≥ 2 lines</td>
<td>6%</td>
<td>34%</td>
</tr>
<tr>
<td>≥ 3 lines</td>
<td>0%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Source: NYX-SNV

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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo (n = 20)</th>
<th>1% Nyxol (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last Dose</td>
<td>p = 0.0002</td>
<td>p = 0.0001</td>
</tr>
<tr>
<td>14-day Daily</td>
<td>p = 0.0004</td>
<td></td>
</tr>
<tr>
<td>Evening Dosing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1 line</td>
<td>-0.99 -20%</td>
<td>-1.00 -21%</td>
</tr>
<tr>
<td>≥ 2 lines</td>
<td>-0.07 -2%</td>
<td>-0.05 -5%</td>
</tr>
<tr>
<td>≥ 3 lines</td>
<td>-0.11 -1%</td>
<td>-0.88 -19%</td>
</tr>
</tbody>
</table>

Source: NYXG-201

*NYX-SNV trial was small and not designed for a statistical 3-line improvement in low-contrast visual acuity; the ~20% effect was used for powering and sizing of Phase 3 trial
APX3330

- **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, especially in working age adults in developed countries

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

• DR patients are not commonly treated with approved injectable anti-VEGF drugs given earlier stage of retinal disease and many are asymptomatic

• DR progresses in steps and may result in vision loss if left untreated

• Current treatment for DME: 25% non-responders and 50% partial responders to anti-VEGF drugs

APX3330 History and Ref-1 Inhibition Mechanism

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

- APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of Ref-1
- Ref-1 (reduction-oxidation effector factor-1) is a novel target discovered and characterized by Dr. Mark R. Kelley at Indiana University School of Medicine
- 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

APX3330 Down-Regulates VEGF Protein and Anti-Inflammatory Cytokines

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

- 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 VEGF Protein in the Brain of Preclinical Models

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]
APX3330 Generally Well Tolerated with Clinical Signals

Observations from Pre-Clinical Studies and 11 Clinical Trials of APX3330

L-CNV Mouse Retina Model

APX3330 Reduces Neovascularization Similar to Eylea in Preclinical Models

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

Silva et al, 2021

Phase 1 Clinical Trials

Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels

Human Pharmacokinetics of APX3330 at 120 mg/day

300 mg BID (600 mg/day total) dosing strategy for APX3330 is predicted to reach retinal AUC concentrations of 15.4 μg/mL; Significant APX3330 reaches human retina, folds greater than mice who were given APX3330 25 mg/kg (actual 2hr conc. in retina 0.1 μg/mL)

1. 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
APX3330 Product Candidate Profile

First-in-Class Ref-1 Inhibitor Phase 2 Ready for Retina Diabetic Indications

APX3330: 600mg Oral Dose

Expected Efficacy Data

Improving Eye Health in Diabetics
↓ Inflammation
↓ Hypoxia Signaling
↓ Abnormal Angiogenesis

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

Safety Data

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

No Topical 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 2 Design

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

ZETA-1

15 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)
- Safety and tolerability

Exploratory:
- Labs / PK

Phase 2 Start Initiated in April 2021

Top Line Expected Early 2022

NPDR = non-proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
PDR = proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
Diabetic Retinopathy & Macular Edema

APX3330 to Treat Patients Before Vision Loss Occurs

APX3330’s Potential Differentiated Solution

- **Potential First Oral Therapy** to be used as an earlier intervention for the diabetic eye before vision symptoms appear or as add-on therapy to current anti-VEGF treatment

- **Proven Novel Mechanism** that may decrease both inflammation and VEGF activity

- **Convenient** option for patients to potentially alleviate the burden of injections and increase compliance

- **Tolerable** as seen in 11 completed Phase 1 and Phase 2 clinical trials
Boards and Milestones
Prestigious Ocular Medical Advisory Board

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

[Image of various medical professionals and logos, each with their name and affiliation.]

- Richard Lindstrom, MD
  University of Minnesota

- Paul Karpecki, OD
  Indiana University

- Jack Holladay, MD
  University of Texas

- Thomas Samuelson, MD
  University of Minnesota

- Gary Novak, PhD
  UC Davis

- Jeffrey Heier, MD
  Boston University

- Michael Allingham, MD, PhD
  University of North Carolina

- Marguerite McDonald, MD
  Columbia University

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

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

- Richard Messmann, MD
  Wayne State University
  CMO Apexian/APX3330

- Eliot Lazar, MD
  Georgetown University

- Ed Holland, MD
  Loyola University Chicago

- Marguerite McDonald, MD
  Columbia University

- David Boyer, MD
  Chicago Medical School

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  University of North Carolina

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  Columbia University

- David Boyer, MD
  Chicago Medical School

- Jeffrey Heier, MD
  Boston University
Ocuphire Board of Directors

Seasoned Directors with Decades of Drug Development, M&A/Financings, and Ophthalmology
# 2021 to 2022 Ocuphire Cadence of Milestones

*Multiple Data Catalysts On Path To NDA(s)*

<table>
<thead>
<tr>
<th>2020</th>
<th>1H 2021</th>
<th>2H 2021</th>
<th>2022*</th>
<th>2023*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completion of APX3330 License</td>
<td>Enrollment of Phase 3 RM Trial</td>
<td>ASCRS 2021 Presentation for MIRA-2 &amp; VEGA-1</td>
<td>Report 2nd Ph3 RM Trial</td>
<td>Report Phase 3 Data for Presbyopia Trials</td>
</tr>
<tr>
<td>ARVO 2020 Presentation for MIRA-1 &amp; ORION-1</td>
<td>Initiate Phase 2 Presbyopia Trial</td>
<td>Initiate 2nd P3 RM and Pediatric RM trial for NDA</td>
<td>Report Pediatric RM Trial</td>
<td>Potential NDA for Nyxol in RM</td>
</tr>
<tr>
<td>FDA EOP2 Meeting May 2020</td>
<td>Report Positive Phase 3 Data for RM</td>
<td>Enrollment of Phase 3 NVD Trial</td>
<td>Report Phase 2 Data for DR/DME</td>
<td>Potential Commercial Launch of Nyxol in US</td>
</tr>
<tr>
<td>Completion of Transaction (Nasdaq: OCUP) and concurrent $20M financing</td>
<td>Initiate Phase 2 DR/DME Trial</td>
<td>Report Phase 3 Data for NVD</td>
<td>Initiate 2 Phase 3 Presbyopia Trials</td>
<td>Submit Nyxol NDA filing for Nyxol for Presbyopia in 2023</td>
</tr>
<tr>
<td>Initiate Phase 3 RM Trial</td>
<td>Enrollment of Phase 2 Presbyopia Trial</td>
<td>Enrollment of Phase 2 DR/DME Trial</td>
<td>Initiate Chronic Ph3 Safety Trial (Nyxol /LDP)</td>
<td></td>
</tr>
<tr>
<td>Initiate Phase 3 NVD Trial</td>
<td>New Patent Claims</td>
<td>Industry Conferences &amp; Publications</td>
<td>Complete 1 year CMC stability on 3xreg batches</td>
<td></td>
</tr>
<tr>
<td>Complete Nyxol Market Research</td>
<td>Closed $15M registered direct offering</td>
<td>Manufacture 3xRegistration Batches for Nyxol Blow-Fill-Seal (BFS) Eye Drops</td>
<td>Submit Nyxol NDA filing for RM in late 2022</td>
<td></td>
</tr>
<tr>
<td>Journal Publications</td>
<td>Report Positive Phase 2 Data for Presbyopia</td>
<td>Complete 6-month Rabbit Tox Study</td>
<td>Manufacture Commercial Batches of Nyxol Eye Drop</td>
<td></td>
</tr>
</tbody>
</table>

Ongoing partnering discussions with leading ophthalmic companies (including European and Asian players)

*Additional Studies for NVD and DR based on Data Readouts*
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)*

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

<table>
<thead>
<tr>
<th>DRSS Score</th>
<th>Description</th>
<th>Retinal Image</th>
<th>Percent of patients with a ≥ 2 step improvement on the DRSS score at week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (10)</td>
<td>DR Absent</td>
<td>Healthy blood vessels with no bulges</td>
<td>13%</td>
</tr>
<tr>
<td>2 (20)</td>
<td>Micro-aneurysm only</td>
<td>Small bulges in blood vessel walls as well as other signs in the retina</td>
<td>20%</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>
<td>35%</td>
</tr>
<tr>
<td>4 (43)</td>
<td>Moderate NPDR</td>
<td>More blood vessels in larger areas of the retina show changes</td>
<td>43%</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>
<td>47%</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>
<td>90%</td>
</tr>
</tbody>
</table>

_A 13-point Scale Outlining the Various Stages of Diabetic Retinopathy_