Ocuphire Corporate Presentation

Mina Sooch CEO

March 30, 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>
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<tbody>
<tr>
<td>• 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), &amp; Presbyopia (P)</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>
</tbody>
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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 and 2 trials</td>
</tr>
<tr>
<td>✓ Nyxol with &gt; 240 patients treated across 8 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>

<table>
<thead>
<tr>
<th>Significant IP Portfolio and Small Molecule CMC Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• US and global issued patents thru 2034 obtained for both assets</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>

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<thead>
<tr>
<th>Multiple Near-Term Data Catalysts with Capital Efficient Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 4 late-stage trial readouts (2 Phase 3, 2 Phase 2) expected in 1Q21 through early 2022</td>
</tr>
<tr>
<td>• Positive Phase 3 data in RM in 1Q, with Nyxol NDA filing targeted for early 2023</td>
</tr>
<tr>
<td>• 20+M financing provides sufficient cash to run capital-efficient ophthalmic-focused operations in 2021</td>
</tr>
<tr>
<td>• Analyst research coverage initiated by Cantor Fitzgerald, Canaccord, JonesTrading, and Encode Ideas</td>
</tr>
</tbody>
</table>
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

Drey Coleman
Head Clinical Operations

Laura Gambino
Director Project Management

Charlie Hoffmann, MBA
Tuck School of Business at Dartmouth

Amy Rabourn, CPA
Michigan Ross

Ronil Patel, MS
Florida Tech

Mitch Brigell, PhD
Kansas State University

Daniela Oniciu, PhD
University of Florida

Drey Coleman
UCF

Laura Gambino
Eastern Michigan University
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

Diabetic Retinopathy
U.S. Prevalence: ~7M

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

$4-10B US Markets

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>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>Dim Light or Night Vision Disturbances (NVD)</td>
<td>Pre-clinical</td>
<td>Initiated Phase 3 LYNX-1 trial 4Q2020; Data expected in 3Q21 (n=160)</td>
</tr>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Reversal of Mydriasis (RM)</td>
<td>Phase 1</td>
<td>Recent Positive Data Readout</td>
</tr>
<tr>
<td>0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops</td>
<td>Presbyopia (P)</td>
<td>Phase 2</td>
<td>Initiated Phase 2 VEGA-1 trial 1Q2021; Data expected in 2Q21 (n=152)</td>
</tr>
<tr>
<td>APX3330 Oral Pill</td>
<td>Diabetic Retinopathy (DR)/ Macular Edema (DME)</td>
<td>Phase 3</td>
<td>Initiate Phase 2 ZETA-1 trial 1Q2021; Data expected by early 2022 (n=100)</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></td>
<td>Next steps: IND enabling studies (with partner funding)</td>
</tr>
<tr>
<td>Combo (0.75% Nyxol® + Latanoprost) Eye Drops</td>
<td>Glaucoma (16 to 24 mmHg)</td>
<td></td>
<td>Next steps: 2nd line add-on Phase 2 trial (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 & Phase 2 Clinical Programs with MIRA-2 Data Leading the NDA Path

### Nyxol
- **8** Phase 1 & Phase 2 Trials
- **> 240** Subjects Dosed
- **28** Days Exposure in Humans
- **2034+** Patents to

  *Studied in ocular refractory diseases (NVD) & elderly glaucoma patients*

### APX3330
- **11** Phase 1 & Phase 2 Trials
- **> 340** Subjects Dosed
- **365** Days Exposure in Humans
- **2034+** Patents to

  *Studied in inflammation/hepatitis & cancer patients*

505(b)(2) Development Pathway
NCE Development Pathway
Nyxol®

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

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

Nyxol: Phentolamine 0.75% 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
- **NVD**: Night Vision Disturbances
- **P**: Presbyopia

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)

Source: GlobalData Market Research Report, 2020
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

Mydriasis

Time -1 Hour

Mydriatic Agent A, B, or C

Placebo

0.75% Nyxol

Nyxol drop(s)

(2 drops study eye, 1 drop fellow eye)

Treatment

Time 0 (Max Dilation)

Mydriatic Agent A, B, or C

Placebo drop(s)

(2 drops study eye, 1 drop fellow eye)

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)

Started and Completed Enrollment in 4Q20 – 185 Subjects

Topline Results Expected in 1Q21 – Reported on 3/15/21

Mydriatic Agents 3:1:1 – 2.5% phenylephrine (alpha 1 agonist), 1% tropicamide (cholinergic blocker), Paremyd® (combination)
Nyxol Met the Primary and Secondary Endpoints at 90 Min; Additionally at 60 Min and All Subsequent Timepoints

Nyxol Reduced More Subjects to Pupil Diameter (PD) Baseline

Percent of Subjects Returning to ≤ 0.2 mm of Baseline

Nyxol Reduced PD Faster Across All Mydriatic Agents*

Mean Pupil Diameter

Source: MIRA-2 TLR table #14.2.1.1 (mITT)

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

Nyxol Reduced More Subjects to Pupil Diameter (PD) Baseline in Subjects with Either Light or Dark Irides

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

Source: MIRA-2 TLR table #14.2.1.6 (mITT). 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 Reduced Irises PD Faster in Subjects Receiving Either One of the Three Mydriatic Agents

Phenylephrine

- Nyxol n=56
- Placebo n=55

Tropicamide or Paremyd

- Nyxol n=38
- Placebo n=36

Source: MIRA-2 TLR table #14.2.2.3 (mITT). Standard Error bars are shown.
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 20-30 RM trial with ages 3 through 17 per pediatric plan
3. Complete commercial registration batches and one year CMC Stability

File for NDA by Early 2023

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

A Substantial Revenue Opportunity for Nyxol in Reversal of Mydriasis

• ~100M comprehensive and specialty eye exams in US per year
• No current commercially available treatment for reversing dilation
  – Optomap ultra-wide field camera used for a retinal evaluation without the need for dilation; ~$40 – $65 cost to patient\(^1\)
• Findings from recent US market research\(^2\):
  – Over 65% patients report moderate to severe negative impact of dilated exams
  – Cash pay price range surveyed $5-$20 per patient treatment
  – 45% patients said they would likely request a dilation reversal drop

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

• Eye exam market posted a 3.3% growth to $6.39B\(^3\)
• Given the efficacy of Nyxol to reverse dilation regardless of eye color, there are additional markets outside of the US for potential commercialization

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1. Corcoran Consulting Group FAQ for Optomap imaging 01/2021
2. GlobalData market research report
Nyxol®

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

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>
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<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**

- 15 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 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

- ≥ 1 line: 31%, p=0.029
- ≥ 2 lines: 69%, p=0.04
- ≥ 3 lines: 6%

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

- Placebo n=20
- 1% Nyxol n=19

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.
Nyxol®

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

Phentolamine Mesylate
Presbyopia – Chronic Opportunity

Aging Population Drives Demand for Alternatives to Reading Glasses

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

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% |
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 increasing depth of focus 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

“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*
Presbyopia VEGA-1 Phase 2 Proposed Design

Ongoing Randomized, Double-Masked, Placebo-Controlled One-Week Trial

VEGA-1

20 US sites
~152 presbyopic patients

Eligibility Screening
Randomization
Screening

Visit 1
Baseline
Nyxol
No Treatment
Placebo

Visit 2 (3 – 5 Days Later)
LDP Drop
Nyxol + LDP
Nyxol Alone
LDP Alone
Placebo Alone

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)

Phase 2 Start Initiated in 1Q21

Top Line Expected 2Q21

LDP = low-dose pilocarpine (0.4%)
Nyxol Demonstrated Clinical Effect in Presbyopia

Key Endpoints Observed from Multiple Phase 2 Trials

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**ORION-1 Phase 2 Trial**

**Improvements in DCNVA with Nyxol Alone**

With No Change in Distance Vision

Near VA Line Improvement at Day 15
(Full Analysis Set, Study Eye, Photopic)

- Placebo (n = 20)
- Nyxol (n = 19)

- ≥ 1 line: 63% (Nyxol), 20% (Placebo)
- ≥ 2 lines: 11% (Nyxol), 0% (Placebo)
- ≥ 3 lines: 5% (Nyxol), 0% (Placebo)

*p = 0.026

Source: ORION-1

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**Pinhole PD Size Illustrated with Addition of LDP to Nyxol**

1.5 to 2+ mm PD reduction

*Achieve the pin-hole (1.6 to 2 mm) effect*

- ~0.7 to 1+ mm
- ~0.7 to 1+ mm

- Nyxol Alone
- LDP Alone

Average pupil size in photopic conditions is 3.5 to 4+ mm

---

*Note: This is an excerpt from a slide. The full context and data are not provided in the image.*
An ideal formulation for presbyopia treatment would meet the following criteria:

- Comfort and tolerability
- Fast onset
- Long duration
- Efficient pupil size modulation
- Strong safety profile
- Maintain good distance visual acuity

### Cholinergic Agonists

<table>
<thead>
<tr>
<th>Company</th>
<th>Product</th>
<th>MOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergan</td>
<td>PRX-100; aceclidine</td>
<td>Soften lens MOA</td>
</tr>
<tr>
<td>Orasis</td>
<td>CSF-1; Low dose pilo</td>
<td>Combination drugs</td>
</tr>
<tr>
<td>Novartis</td>
<td>EV-06</td>
<td></td>
</tr>
<tr>
<td>Ocuphire</td>
<td>(0.75% Nyxol + 0.4% pilo)</td>
<td>Pupil modulation MOA, Combination drugs</td>
</tr>
<tr>
<td>Visus</td>
<td>Brimochole; brimonidine + carbachol</td>
<td>Other Cholinergic Agonists*</td>
</tr>
<tr>
<td>EyeNovia</td>
<td>MicroLine; 1 or 2% pilo</td>
<td></td>
</tr>
<tr>
<td>Ocuphire</td>
<td>MicroDilate; pilo</td>
<td>Other Cholinergic Agonists*</td>
</tr>
<tr>
<td>Alpha Antagonist &amp; pilocarpine*</td>
<td>NDA</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>AGN-190584; 1.25% pilo</td>
<td></td>
</tr>
<tr>
<td>Ocuphire</td>
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<td>Other Cholinergic Agonists*</td>
</tr>
</tbody>
</table>

*act on sphincter and ciliary muscles in dose-dependent manner
## APX3330

<table>
<thead>
<tr>
<th>DR</th>
<th>Diabetic Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>DME</td>
<td>Diabetic Macular Edema</td>
</tr>
<tr>
<td>wAMD</td>
<td>Wet Age-Related Macular Degeneration</td>
</tr>
</tbody>
</table>

APX3330
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.

Injectable Anti-VEGF Approved Therapies Not Commonly Used for NPDR

Diabetic Eye

<table>
<thead>
<tr>
<th>Diabetic Eye Opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR</td>
</tr>
<tr>
<td>DME</td>
</tr>
</tbody>
</table>

APX3330 is a Ref-1 Inhibitor

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

Mechanism of Action – Ref-1 Inhibition

- Hypoxia
  - Ref-1
  - HIF-1α
  - VEGF (Signaling Cascade)
- Inflammation
  - Ref-1
  - NF-κB
  - TNF-α
  - Chemokines
  - Other Growth Factors (Signaling Cascade)
- Neovascularization
- Steroids


Lucentis®
EYLEA®
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

Source: Unpublished Data Dec 2019

Phase 1 Clinical Trials

Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels

Human Pharmacokinetics of APX3330 at 120 mg/day

Human 120 mg/day

Mice 25 mg/kg

-55%
APX3330 Product Candidate Profile
First-in-Class Ref-1 Inhibitor Phase 2 Ready for Retina Diabetic Indications

APX3330: 600mg Oral Dose
(120mg or 300mg tablets)

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
ZETA-1

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

APX3330 600mg

Twice daily oral dose (24 weeks)

Placebo

Twice daily oral dose (24 weeks)

Endpoints

Primary: % of subjects with ≥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 Targeted for 1Q21

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

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Lead Independent Director, Board Director

James Manuso, PhD/MBA
Board Director

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2021 to 2022 Ocuphire Cadence of Milestones

Multiple Data Catalysts on Path to NDA(s)

- ✓ Completion of APX3330 License
- ✓ ARVO 2020 Presentation for MIRA-1 & ORION-1
- ✓ FDA EOP2 Meeting May 2020
- ✓ Completion of Transaction (Nasdaq: OCUP)
- ✓ Initiate Phase 3 RM Trial
- ✓ Initiate Phase 3 NVD Trial
- ✓ Complete Nyxol Market Research
- ✓ Journal Publications

- ✓ Enrollment of Phase 3 RM Trial
- ✓ Initiate Phase 2 Presbyopia Trial
- ✓ Report Positive Phase 3 Data for RM
- ✓ Initiate Phase 2 DR/DME Trial
- ✓ Enrollment of Phase 2 Presbyopia Trial
- ✓ Report Phase 2 Data for Presbyopia
- ✓ New Patent Claims

- ❑ Report 2nd Ph3 RM
- ❑ Report Phase 3 Data for NVD
- ❑ Enrollment of Phase 2 DR/DME Trial
- ❑ Industry Conferences & Publications
- ❑ Complete 6-month Rabbit Tox Study
- ❑ Registration Batches for Nyxol Blow-Fill-Seal Eye Drops
- ❑ Initiate 2nd P3 RM & Ped RM trial for NDA

- 2020
- 1H 2021
- 2H 2021
- 2022*
- 2023

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

*Additional Studies for NVD, P, DR based on Data Readouts
NVD Endpoint: 5% Low Contrast Visual Acuity (LCVA) Chart

* * * 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 ≥2 step improvement on the DRSS score at week 24

<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**

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