Ocuphire Corporate Presentation

January 2021
Disclosures and Forward Looking Statements

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning Ocuphire Pharma, Inc.’s (“Ocuphire” or the “Company”) product candidates and potential. These forward-looking statements are based upon the Company’s current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) potential adverse reactions or changes to business relationships resulting from the announcement or completion of the merger; (ii) the success and timing of regulatory submissions and pre-clinical and clinical trials; (iii) regulatory requirements or developments; (iv) changes to clinical trial designs and regulatory pathways; (v) changes in capital resource requirements; (vi) risks related to the inability of the Company to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vii) legislative, regulatory, political and economic developments, and (viii) the effects of COVID-19 on clinical programs and business operations. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by the Company from time to time with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

The Company makes no representation or warranty, express or implied, as to the accuracy or completeness of the information contained in or incorporated by reference into this presentation. Nothing contained in or incorporated by reference into this presentation is, or shall be relied upon as, a promise or representation by the Company as to the past or future. The Company assumes no responsibility for the accuracy or completeness of any such information. This presentation may not be reproduced or provided to any other person (other than your advisor) without our prior written consent. By accepting delivery of this presentation, you agree to the foregoing and agree to return this presentation and any documents related thereto and any copies thereof to us or to destroy the same if you do not make an investment in any securities. The information contain within this presentation shall not, except as hereinafter provided, without the prior written consent of the Company, be disclosed by you or your representatives in any manner whatsoever, in whole or in part, and shall not be used by you or your representatives other than for the purpose of evaluating the transaction described herein. By accepting delivery of this presentation you further acknowledge and agree aware of the restrictions imposed by the United States securities laws on the purchase or sale of securities by any person who has received material, nonpublic information from the issuer of the securities or any affiliate thereof and on the communication of such information to any other person when it is reasonably foreseeable that such other person is likely to purchase or sell such securities in reliance on such information for so long as the information remains material and nonpublic. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market shares and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.
# Ocuphire Opportunity

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

### 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 and 2 trials
  - Nyxol with > 150 patients treated across 7 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 obtained for both assets
- Stable, small-molecule drugs
  - Nyxol = single-use, preservative-free eye drop
  - APX3330 = oral pill

### Multiple Near-Term Data Catalysts with Capital Efficient Plan
- 4 late-stage trial readouts (2 Phase 3, 2 Phase 2) expected in 1Q through 4Q 2021
- $20+M financing provides sufficient cash to run capital-efficient ophthalmic-focused operations in 2021
- Analyst research coverage initiated by Cantor Fitzgerald and Encode Ideas
- Nyxol NDA filing in one or more indications targeted for early 2023
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

Kostas Charizanis, PhD, MBA
Senior Director Market Strategy and R&D

Mitch Brigell, PhD
Head Clinical Development and Strategy

Daniela Oniciu, PhD
Head CMC and Global Clinical Supply

Drey Coleman
Director Clinical Operations and Vendor Management

Laura Gambino
Project Management

Charlie Hoffmann, MBA
Tuck School of Business at Dartmouth

Amy Rabourn, CPA
Prudential

Kostas Charizanis, PhD, MBA
NeuroBo Pharmaceuticals

Mina Sooch, MBA
Gompshire Therapeutics

Mitch Brigell, PhD
Gompshire Therapeutics

Daniela Oniciu, PhD
Prudential

Drey Coleman
Goldman Sachs

Laura Gambino
Pfizer

Mina Sooch, MBA
Monitor

Mitch Brigell, PhD
Pfizer

Daniela Oniciu, PhD
ProNAi

Drey Coleman
Pfizer

Laura Gambino
IQVIA
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

$4-10B US Markets

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

*Multiple Phase 3 & Phase 2 Clinical Data Catalysts Expected Throughout 2021*

<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, Phase 1, Phase 2, Phase 3</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 2, Phase 3</td>
<td>Enrollment Complete, Initiated Phase 3 MIRA-2 trial 4Q2020; Data expected in 1Q21 (n=168)</td>
</tr>
<tr>
<td>0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops</td>
<td>Presbyopia (P)</td>
<td>Phase 2, Phase 3</td>
<td>Initiate 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 2, Phase 3</td>
<td>Initiate Phase 2 ZETA-1 trial 1Q2021; Data expected in 4Q21 (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>Pre-clinical, Phase 1, Phase 2</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>Phase 2, Phase 3</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)
<table>
<thead>
<tr>
<th>Drug Candidate</th>
<th>Phase 1 &amp; Phase 2 Trials</th>
<th>Subjects Dosed</th>
<th>Exposure in Humans</th>
<th>Patents to</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nyxol</strong></td>
<td>7</td>
<td>&gt; 150</td>
<td>28 Days</td>
<td>2034+</td>
</tr>
<tr>
<td></td>
<td>Phase 1 &amp; Phase 2 Trials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exposure in Humans</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>28 Days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patents to</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2034+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Studied in ocular refractory diseases (NVD) &amp; elderly glaucoma patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>505(b)(2) Development Pathway</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>APX3330</strong></td>
<td>11</td>
<td>&gt;340</td>
<td>365 Days</td>
<td>2034+</td>
</tr>
<tr>
<td></td>
<td>Phase 1 &amp; Phase 2 Trials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exposure in Humans</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>365 Days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patents to</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2034+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Studied in inflammation/hepatitis &amp; cancer patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NCE Development Pathway</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Nyxol®

- **NVD**  Night Vision Disturbances
- **RM**  Reversal of Mydriasis
- **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
First-in-Class Alpha 1/2 Blocker Eye Drop for Refractory Indications

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
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


Source: GlobalData Market Research Report, 2020

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>

"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"
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

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

**LYNX-1**

15 US sites
~160 patients with NVD

0.75% Nyxol
daily evening dose (14 days)

Placebo
daily evening dose (14 days)

Endpoints

**Primary:** % of subjects with \( \geq 3 \) 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)

Eligibility Screening Randomization

**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***

<table>
<thead>
<tr>
<th>% of Eyes with Mesopic Low Contrast Visual Acuity Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Subject Eyes</td>
</tr>
<tr>
<td>≥ 1 line</td>
</tr>
<tr>
<td>≥ 2 lines</td>
</tr>
<tr>
<td>≥ 3 lines</td>
</tr>
<tr>
<td>Placebo n=16</td>
</tr>
<tr>
<td>Nyxol n=32</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)**

<table>
<thead>
<tr>
<th>Baseline Pupil Diameter: Placebo 4.6mm, Nyxol 4.7mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 8</td>
</tr>
<tr>
<td>Day 15</td>
</tr>
<tr>
<td>Day 16</td>
</tr>
</tbody>
</table>

Source: NYXG-201

*N* 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.
Reversal of Mydriasis (RM) – Acute Treatment

Annual Exams and Specialty Visits Involve Dilation to Monitor Eye Health

The Problem

• At every annual eye exam and many 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 Currently Approved Therapies

~100M eye exams / year in US
Reversal of Mydriasis (RM) – Acute Treatment

Single Use Indication Leveraging a Precedent Approval Pathway

Nyxol’s Potential Differentiated Solution

• **Regulatory Precedent** with RevEyes (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 reverse mydriasis by counteracting the drugs (alpha agonists and cholinergic blockers) used to dilate the pupil

• **Convenient** 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

<table>
<thead>
<tr>
<th>Patients likely to request reversal of dilation</th>
<th>45%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye care providers likely to use reversal drops</td>
<td>40%</td>
</tr>
</tbody>
</table>

Source: GlobalData Market Research Report, 2020
RM MIRA-2 Phase 3 Registration Design

Randomized, Double-Blinded, Placebo-Controlled, Parallel, One-Day Trial

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

- 1:1 Randomization

- **Endpoints**
  - Primary: % of subjects returning to baseline (within 0.2 mm) pupil diameter at 90 min
  - Secondary:
    - % of subjects returning to baseline at 30min, 1h, 2h, 3h, 4h, 6h, 24h
    - Mean change in pupil diameter from mydriatic max at all timepoints
    - Accommodation (tropicamide)
    - Safety and tolerability (redness)

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

- **Top Line Expected 1Q21**

- **Eligibility**
  - **Screening**
  - **Randomization**

- **Mydriatic Agents:** phenylephrine (alpha agonist), tropicamide (cholinergic blocker), Paremyd® (combination)
Nyxol Demonstrated Clinical Effect in RM

**Key Endpoints Observed from MIRA-1 Phase 2b Trial**

**MIRA-1 Phase 2 Trial**

**Nyxol Reduced More Subjects to Pupil Diameter (PD) Baseline**

Percent of Subjects Returning to ≤ 0.2 mm of Baseline after Treatment With either Phenylephrine or Tropicamide

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo n=31</th>
<th>1% Nyxol n=31</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>1 hour</td>
<td>16%</td>
<td>29%</td>
</tr>
<tr>
<td>2 hours</td>
<td>13%</td>
<td>23%</td>
</tr>
<tr>
<td>4 hours</td>
<td>68%</td>
<td>77%</td>
</tr>
<tr>
<td>6 hours</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Source: MIRA-1

**Nyxol Reduced PD Faster Across Phenylephrine & Tropicamide Mydriatic Agents**

Reduction in Pupil Diameter after Patients received either Phenylephrine 2.5% or Tropicamide 1.0% in Study Eye

*p<0.05; **p<0.01; ***p<0.001; ****p<0.0001

Source: MIRA-1

**MIRA-2 protocol enhancements:**
1. 2 drops of Nyxol in study eye AND dark irides
2. dark/light irides
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

No Currently Approved Drug Therapies

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 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

Planned Randomized, Double-Blinded, Placebo-Controlled One-Week Trial

VEGA-1

20 US sites
~152 presbyopic patients

Eligibility Screening
Randomization
Screening

Visit 1
Baseline Nyxol
Baseline Nyxol
Baseline Placebo
Baseline Placebo

Visit 2
(3 – 5 Days Later)
LDP Drop
No Treatment
LDP Drop
No Treatment

Treatment Arms
Nyxol + LDP
Nyxol Alone
LDP Alone
Placebo Alone

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 Targeted for 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

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)

Percent of Subjects with VA Line Improvements

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

*P = 0.026

Source: ORION-1

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

Nyxol Alone

LDP Alone

Average pupil size in photopic conditions is 3.5 to 4+ mm
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
APX3330

- **DR**: Diabetic Retinopathy
- **DME**: Diabetic Macular Edema
- **wAMD**: Wet Age-Related Macular Degeneration

APX3330
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)
  - Anti-VEGF

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

- Neovascularization
- Steroids


Lucentis®

EYLEA®
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
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

Hemorrhages
Aneurysm
Abnormal Blood Vessels
"Cotton Wool" Spots

Diabetic Eye Opportunity

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

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
**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)
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

Phase 1 Clinical Trials

Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels

Human Pharmacokinetics of APX3330 at 120 mg/day

Source: Unpublished Data Dec 2019
Boards and Milestones
Prestigious Ocular Medical Advisory Board
Fortunate for the Insights of Leading KOLs & Drug Candidate Co-Founders
Ocuphire Board of Directors

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

Cam Gallagher, MBA
Chair, Board Director

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

James Manuso, PhD/MBA
Board Director

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Richard Rodgers, MBA
Board Director

Alan R. Meyer, MBA
Board Director
MFR/IP Advisor

Susan Benton, MBA
Board Director

Talfinium Investments, Inc.
2020 to 2022 Cadence of Milestones

Multiple Data Catalysts for Value-Building

- NVD Podium Presentation at AAO 2018
- Initiate/Report Phase 2b Data for ORION-1
- Initiate/Report Phase 2b Data for MIRA-1
- Expand Patent Estate

- Completion of APX3330 License
- ARVO 2020 Presentation for MIRA-1
- ARVO 2020 Presentation for ORION-1
- FDA EOP2 Meeting May 2020

- Announced Ocuphire Reverse Merger and PIPE Financing (Co-Led by Cantor and Canaccord)
- 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
  - Initiate Phase 2 DR/DME Trial
  - Report Phase 3 Data for RM
  - Enrollment of Phase 2 DR/DME trial
  - Report Phase 2 Data for DR/DME
  - Report 6-month Rabbit Tox Study
  - Initiate 2nd Phase 3 Trials for RM & NVD
  - Initiate Acute and Chronic Phase 3 Safety Trial

- Enrollment of Phase 3 NVD trial
  - Report Phase 3 Data for NVD
  - Enrollment of Phase 2 DR/DME trial
  - Report Phase 2 Data for DR/DME
  - Report Phase 3 Data for Presbyopia
  - Report 2nd Phase 3 Data for Presbyopia
  - Initiate Phase 3 Safety Data
  - Initiate Phase 3 DR/DME Trial(s)
  - Industry/Journal Publications
  - Registration Batches for Nyxol Blow-Fill-Seal Eye Drops

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

Nyxol NDA filing for RM & NVD in early 2023
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 ≥ 2 step improvement on the DRSS score at week 24

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

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