United States Securities and Exchange Commission
Washington, D.C. 20549

Form 8-K

Current Report

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 5, 2022

Ocuphire Pharma, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation)

001-34079
(Commission File Number)

11-3516358
(IRS Employer Identification No.)

37000 Grand River Avenue, Suite 120
Farmington Hills, MI
(Address of principal executive offices)

48335
(Zip Code)

Registrant’s telephone number, including area code: (248) 681-9815

N/A
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

<table>
<thead>
<tr>
<th>Title of each class</th>
<th>Trading Symbol(s)</th>
<th>Name of each exchange on which registered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Stock, $0.0001 par value</td>
<td>OCUP</td>
<td>Nasdaq Capital Market</td>
</tr>
</tbody>
</table>

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐
Item 7.01 Regulation FD Disclosure.

On January 5, 2022, Ocuphire Pharma, Inc. (the “Company”) issued a press release regarding the Company’s fourth quarter 2021 activity, cash balance and upcoming events. The press release also notes the Company’s total common stock outstanding as of December 31, 2021, which stood at 18,845,828 shares. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K (this “Report”).

Also on January 5, 2022, the Company posted an updated corporate presentation to its website at https://ir.ocuphire.com/presentations, which the Company may use from time to time in communications or conferences. A copy of the corporate presentation is attached as Exhibit 99.2 to this Report.

The information in this Report, including Exhibits 99.1 and 99.2 hereto, is furnished pursuant to Item 7.01 and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing. The Company’s submission of this Report shall not be deemed an admission as to the materiality of any information required to be disclosed solely to satisfy the requirements of Regulation FD.

This Report and the exhibits hereto contain forward-looking statements within the meaning of the federal securities laws. These forward looking statements are based on current expectations and are not guarantees of future performance. Further, the forward-looking statements are subject to the limitations listed in the exhibits hereto and in the other reports of the Company filed with the Securities and Exchange Commission, including that actual events or results may differ materially from those in the forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Exhibit Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.1</td>
<td>Press Release, dated January 5, 2022</td>
</tr>
<tr>
<td>99.2</td>
<td>Corporate Presentation, dated January 5, 2022</td>
</tr>
</tbody>
</table>
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

OCUPHIRE PHARMA, INC.

By:  /s/ Mina Sooch

Mina Sooch
Chief Executive Officer

Date: January 5, 2022
Ocuphire Provides Corporate Update: Announcing Enrollment Completion of Phase 3 Nyxol Trial, Enrollment Initiation of Nyxol Pediatric Trial, and an Investor R&D Day in January

Completed Enrollment of Nyxol® LYNX-1 Phase 3 NVD Trial

Initiated Enrollment of Nyxol MIRA-4 Pediatric Study in RM per Agreed Initial Pediatric Study Plan with FDA

Nyxol MIRA-3 Phase 3 Results, MIRA-4 Pediatric Results, and LYNX-1 Phase 3 Results Expected in Early 2022

Strengthened Balance Sheet Extends Runway into Q2 2023

Company to Host Virtual Investor R&D Day on January 31st

FARMINGTON HILLS, MI, January 5, 2022 – Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of refractive and retinal eye disorders, today provided a corporate update available on the Company’s website. This update includes recent progress on Nyxol® trials, the Company’s cash position, and the announcement of an Investor R&D day in late January.

“We are looking forward to a catalyst-rich 2022 and the opportunity to build on the tremendous progress over the past year advancing our differentiated therapeutic candidates in front and back of the eye indications,” stated Mina Sooch, MBA, President and CEO. “Our development program for Nyxol in the Reversal of Mydriasis (RM) indication is now in its final stages. We have recently agreed on an Initial Pediatric Study Plan (iPSP) with the FDA and began enrolling pediatric subjects ages 3 to 11 in the MIRA-4 study in late December. We also continue to enroll adults and 12 to 17 year-old subjects in MIRA-3, which is the second pivotal trial for the RM indication expected to read-out around the end of the first quarter. A positive outcome in MIRA-3 will position us to submit an NDA for Nyxol for RM in late 2022. We are also happy to report that this week marks the completion of over 140 subjects enrolled in LYNX-1, a Phase 3 pivotal trial for Nyxol in Night Vision Disturbances (NVD). We look forward to providing clinical updates on Nyxol in presbyopia and RM as well as APX3330 in diabetic retinopathy at our upcoming Virtual Investor R&D Day.”
Initiated Enrollment in MIRA-4 Pediatric Trial in Reversal of Mydriasis: Ocuphire recently enrolled the first subjects in MIRA-4, which is a randomized, double-masked, placebo-controlled study of Nyxol eye drops to reverse pharmacologically-induced mydriasis in healthy pediatric subjects. Approximately 20 pediatric subjects ages 3 to 11 will be enrolled with safety as the primary objective and efficacy as secondary objectives. Nyxol has the potential to address an estimated $500 million reversal of dilation market across pediatrics and adults, which has no current commercially available therapies.

Completed Enrollment of LYNX-1 Study in Night Vision Disturbances: Enrollment has been completed in the LYNX-1 Phase 3 clinical trial investigating Nyxol for the treatment of NVD. LYNX-1 is a randomized, double-masked, placebo-controlled registration study designed to evaluate the safety and efficacy of Nyxol compared to placebo in patients with NVD. NVD, also known as dim light vision disturbances (DLD), is a condition in which peripheral imperfections (aberrations) of the cornea scatter light when the pupil naturally dilates in dim light conditions. Patients with NVD commonly experience visually impeding glare, halos, starbursts and decreased contrast sensitivity. Based on GlobalData market research, about 38 million individuals in the US are believed to suffer from NVD. An estimated 16 million individuals have moderate-to-severe NVD that may benefit from Nyxol’s ability to reduce the pupil diameter and provide better night vision by eliminating the peripheral aberrations.

Key Anticipated 2022 Milestones:

- **Reversal of Mydriasis (RM):** Report top-line results in early 2022 from the Nyxol Phase 3 MIRA-3 registration trial and the MIRA-4 pediatric trial; Planning to file an NDA with FDA for Nyxol in RM indication in late 2022
- **Presbyopia:** Initiate Phase 3 program (VEGA 2/VEGA 3) in 1H 2022 investigating Nyxol and low-dose pilocarpine (LDP)
- **Night Vision Disturbances (NVD):** Report top-line results in early 2022 from the Nyxol Phase 3 LYNX-1 trial
- **Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME):** Report top-line results in 2H 2022 from the APX3330 Phase 2 ZETA-1 trial

$24.5M Cash at Year End: As of December 31, 2021, Ocuphire had cash and cash equivalents of approximately $24.5 million. We expect that our strengthened balance sheet will support operations into the second quarter of 2023, as compared to previous guidance of late 2022. Ocuphire had 18.8 million shares of common stock outstanding as of year-end.
Panel Discussion at LifeSci Partners Corporate Access Event on January 6, 2022: Mina Sooch, MBA, President, CEO and Founder, will participate in a virtual panel discussion “The Role of Gender Equality in Changing the Landscape of Life Sciences Innovation & Investment” during the LifeSci Partners 11th Annual Corporate Access Event on Thursday, January 6th, 12:00 to 12:55pm ET. To access the panel, please register here.

Company to Host Investor R&D Day on Monday January 31, 2022: Ocuphire will host a Virtual Investor R&D Day for the investment community at which six ophthalmic Key Opinion Leaders (KOLs) from retina, optometry and refractive surgery practices will share their thoughts on three large unmet indications, RM, presbyopia, and DR/DME, addressed by Ocuphire’s two late-stage clinical drug assets and provide status updates on the development programs for Nyxol and APX3330. The event will take place from 10:00am to 12:00pm ET on Monday, January 31st and will feature insights from David Boyer, M.D., Peter Kaiser, M.D., Paul M. Karpecki, O.D., F.A.A.O., James Katz, M.D., Mitchell Jackson, M.D., and Jay S. Pepose, M.D., Ph.D. To access the event, please register here.

About Ocuphire Pharma

Ocuphire is a publicly-traded (NASDAQ: OCUP), clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of refractive and retinal eye disorders. Ocuphire’s pipeline currently includes two small-molecule product candidates targeting multiple front and back of the eye indications. The company’s lead product candidate, Nyxol® (0.75% phentolamine ophthalmic solution), is a once-daily preservative-free eye drop formulation of phentolamine mesylate, a non-selective alpha-1 and alpha-2 adrenergic antagonist designed to reduce pupil size, and is being developed for several indications, including reversal of pharmacologically-induced mydriasis (RM), presbyopia and dim light or night vision disturbances (NVD), and has been studied in 9 clinical trials. Ocuphire reported positive top-line data in March 2021 for MIRA-2, the first Phase 3 registration trial for treatment of RM, and recently initiated the second Phase 3 registration trial (MIRA-3) in RM. Ocuphire also reported positive top-line data in June 2021 for VEGA-1, a well-controlled Phase 2 trial for the treatment of presbyopia. The Phase 3 clinical trial for Nyxol in NVD patients (LYNX-1) also recently fully enrolled. Ocuphire’s second product candidate, APX3330, is an oral tablet designed to inhibit angiogenesis and inflammation pathways relevant to retinal and choroidal vascular diseases, such as diabetic retinopathy (DR) and diabetic macular edema (DME) and has been studied in 11 Phase 1 and 2 trials. APX3330 is currently enrolling subjects in a Phase 2 clinical trial in subjects with DR/DME. As part of its strategy, Ocuphire will continue to explore opportunities to acquire additional ophthalmic assets and to seek strategic partners for late-stage development, regulatory preparation, and commercialization of drugs in key global markets. Please visit www.clinicaltrials.gov to learn more about Ocuphire’s ongoing 2nd phase 3 registration trial in RM (NCT05134974) and Phase 2 trial in DR/DME (NCT04692688). For more information on the recently completed trials, see the links to the 1st Phase 3 registration trial in RM (NCT04620213), Phase 2 trial in presbyopia (NCT04675151), and Phase 3 registration trial in NVD (NCT04638660). For more information, visit www.ocuphire.com.
Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are “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 the future clinical trials in RM, presbyopia, NVD and DR/DME, and statements regarding cash runway. These forward-looking statements are based upon Ocuhire’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) the success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; (ii) regulatory requirements or developments; (iii) changes to clinical trial designs and regulatory pathways; (iv) changes in capital resource requirements; (v) risks related to the inability of Ocuhire to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vi) legislative, regulatory, political and economic developments, (vii) changes in market opportunities, (viii) the effects of COVID-19 on clinical programs and business operations, (ix) the success and timing of commercialization of any of Ocuhire’s product candidates and (x) the maintenance of Ocuhire’s intellectual property rights. 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 Ocuhire from time to time with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Ocuhire undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Ocuhire Contacts

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www.ocuhire.com

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LifeSci Advisors
cdavis@lifesciadvisors.com
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 future milestones, including the potential for Nyxol to be a “best in class” presbyopia drop. 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) timing or ability for the company to achieve its targeted milestones; (ii) the success and timing of regulatory submissions and preclinical and clinical trials; (iii) regulatory requirements or developments; (iv) changes in 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.

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Differentiated, Late-Stage Pipeline Targeting Large Unmet Ophthalmic Markets Of The Front And Back Of The Eye

- Nyxol with > 330 patients treated across 9 trials (505(b)(2) regulatory pathway)
- APX3330 with > 340 patients treated across 11 trials (NCE development pathway)
- Nyxol and APX3330 achieved promising clinical data and favorable safety profile across multiple Phase 1, 2, and 3 trials

Poised For Commercial Success

- Addressing 4 large markets with unmet needs: RM, Presbyopia, NVD and DR/DME
- Successful trial execution with 2 recent positive Phase 3 & Phase 2 data read-outs for Nyxol in RM and Nyxol + LDP Presbyopia, respectively
- Stable, small-molecule drugs with commercial scalability
- Robust and growing IP portfolio: US and global issued thru 2034 for both assets as well as new 2039 Nyxol patent issued for presbyopia

Multiple Value Creation Opportunities With A Capital-efficient Plan

- $24.5 million cash reported at 12-31-21 sufficient for operations into 2Q 2023
- Lower-cost, fast-enrolling, shorter-duration clinical trials
- Favorable, precedent regulatory environment for ophthalmic drug approval
- Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and HCW
## Large Unmet Opportunities For The Aging Eye

*Nyxol To Treat Front Of The Eye And APX3330 For The Back Of The Eye Diseases*

<table>
<thead>
<tr>
<th>Condition</th>
<th>US Market Opportunity</th>
<th>Patients</th>
<th>Market Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presbyopia</td>
<td><strong>$9B - $18B</strong></td>
<td>128 M</td>
<td>$325M - $1B</td>
</tr>
<tr>
<td>Night Vision Disturbances</td>
<td><strong>$2B - $4B</strong></td>
<td>16 M</td>
<td></td>
</tr>
<tr>
<td>Reversal of Mydriasis</td>
<td><strong>$3B - $7B</strong></td>
<td>10 M</td>
<td></td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td><strong>$1B - $3B</strong></td>
<td></td>
<td></td>
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</tbody>
</table>

Source: GlobalData Market Research Report, 2020; Company Estimates for Market Size
## Ocuphire Pipeline & Clinical 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>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Regulatory Approval</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Reversal of Mydriasis (RM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MIRA-3 Phase 3 data expected in early 2022 (n=330)</td>
</tr>
<tr>
<td>0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops</td>
<td>Presbyopia (P)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MIRA-4 Pediatric safety study data expected in early 2022 (n=20)</td>
</tr>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Dim Light or Night Vision Disturbances (NVD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VEGA Phase 3 program initiated in H122 (n=300x2)</td>
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<tr>
<td>APX3330 Oral Pill</td>
<td>Diabetic Retinopathy (DR)/ Macular Edema (DME)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LYNX-1 Phase 3 data expected in early 2022 (n=140)</td>
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<tr>
<td>APX2009 (Intravitreal or Local Delivery)</td>
<td>DME or Wet Age-Related Macular Degeneration (wAMD)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Seeking partner funding for IND enabling studies and further development</td>
</tr>
</tbody>
</table>

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*Note: 0.75% Nyxol (Phentolamine Ophthalmic Solution) is the same as 1% Nyxol (Phentolamine Mesylate Ophthalmic Solution)*
NYXOL® EYE DROPS

- RM: Reversal of Mydriasis
- P: Presbyopia
- NVD: Night Vision Disturbance
Nyxol MOA & History
Phentolamine Mesylate Reformulated As A Proprietary Topical Eye Drop ➔ Nyxol

Phentolamine Mesylate is Active Ingredient in Nyxol: α1 & α2 Antagonist

<table>
<thead>
<tr>
<th>Blocking α1</th>
<th>Blocking α1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduces Pupil Size</td>
<td>Dilates Blood Vessels</td>
</tr>
</tbody>
</table>

Nyxol blocks α1 receptors on the Iris Dilator Muscle

- Decreases Pupil Size (Moderate Miosis)

Phentolamine mesylate is currently approved for 2 indications:
- Regitine® (Pheochromocytoma) – intravenous injection approved in 1952
- OraVerse® (Reversal of oral anesthesia) – intramuscular injection approved in 2008

9 Phase 1, Phase 2, and Phase 3 Trials
> 330 Subjects Dosed
Exposure in Humans 28 Days
 Patent Coverage 2034+

505(b)(2) Regulatory Approval Pathway
### Nyxol Product Candidate Profile

**Novel, Differentiated Alpha 1/2 Blocker Eye Drop For Refractive Indications**

<table>
<thead>
<tr>
<th>Effective</th>
<th>Favorable Safety Profile</th>
<th>Durable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nyxol Improves Vision by Decreasing Pupil Size</strong></td>
<td><strong>No Systemic Effects</strong>&lt;br&gt;Near &amp; Distance Visual Acuity&lt;br&gt;Contrast Sensitivity (night)</td>
<td><strong>Effects Last ≥ 24 Hours</strong>&lt;br&gt;Nighttime Use of Nyxol reduced pupil size for up to 24 - 36 hours</td>
</tr>
<tr>
<td>No Changes in Blood Pressure&lt;br&gt;No Changes in Heart Rate</td>
<td><strong>Well-Tolerated Topical Effects</strong>&lt;br&gt;Mild, Transient, Reversible Eye Redness</td>
<td>With nighttime use, patients wake up without eye redness</td>
</tr>
<tr>
<td><strong>IOP Unchanged or Decreased</strong></td>
<td><strong>No Headaches</strong>&lt;br&gt;Favorable safety profile vs competitors</td>
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</table>

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

- Chronic daily dosing of Nyxol at bedtime reduced pupil size for up to 24 - 36 hours
- With nighttime use, patients wake up without eye redness

---

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

RM Patient, Age 51
Reversal Of Mydriasis (RM) Market Opportunity

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

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

100M+
General and specialty eye exams per year

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

80% of Patients
Likely to request a reversal of dilation drop

$10 - $20
Price range for cash pay per patient with room for physician markup

No Current Commercially Available Treatments

Nyxol's MOA has a minimal side effect profile (unlike cholinergic agonists such as pilocarpine)

95% of Dilating Drops
Used by Eye Care Providers were used in MIRA Clinical Trials

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

1. GlobalData Market Research Report
2. GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (4-7 on a scale of 1-7)
3. GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (6-10 on a scale of 0-10)
MIRA-2/3 Phase 3 Registration Trial Design
Randomized, Double-Masked, Placebo-Controlled, Parallel, One-Day Trial

12 to 16 US sites
185 to 330 target healthy subjects

Eligibility Screening
Randomization

0.75% Nyxol
Mydriatic Agent A, B, or C
Nyxol drop(s) (2 drops study eye, 1 drop fellow eye)

Mydriasis -1 Hour
Treatment (Max. Dilation) 0 min
Primary Endpoint
Follow Up Visit

30min 90min

Mydriatic Agent A, B, or C
Placebo drop(s) (2 drops study eye, 1 drop fellow eye)

1:1 2:1

Primary: % of subjects (study eye) returning to baseline (within 0.2 mm) photopic pupil diameter (PD) at 90 min
Secondary: % of subjects returning to baseline at 0 min, 30 min, 1 hr, 90 min 2 hr, 3 hr, 4 hr, 6 hr, 24 hr (overall, by mydriatic agent, by iris color)
- Mean change in pupil diameter at all timepoints
- Accommodation (Tropicamide/Paremyd)
- Visual Acuity with Glare (new)
- Pupillary Light Reflex (new)
- Safety and tolerability (redness)

Endpoints

Enrollment MIRA-3 Started in 4Q21
Topline Results Expected in Early 2022

Mydriatic Agents 3:1:1 – 2.5% phenylephrine (alpha-1 agonist), 1% tropicamide (cholinergic blocker), Paremyd® (combination)
MIRA-2 RM Phase 3 Trial Met Primary & Secondary Endpoints

49% Of Patients Returned To < 0.2mm Of Baseline At 90mins Vs. 7% Placebo

Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD)

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

MIRA-2 Phase 3 Trial

Mean Pupil Diameter

*p<0.0001

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
Rapid Efficacy With A Favorable Safety Profile In Reversing Mydriasis With Nyxol

- Met primary endpoint at 90 minutes with high statistical significance with 2 and 1 drop of Nyxol
- Met all key secondary endpoints with high statistical significance
  - Nyxol more rapidly reduced PD across all 3 mydriatic agents - phenylephrine, tropicamide, and Paremyd®
  - More subjects returned to PD baseline with Nyxol in both light and dark irides
  - Nyxol demonstrated a faster return to baseline accommodation
  - Nyxol reduced the dilation time by ~4 hrs

- No serious AEs, no drop-outs from AEs, no systemic AEs were observed in ≥ 5% of subjects
- Mild, transient conjunctival hyperemia reported in the first hour and declined steadily thereafter. Baseline mean of 0.7, the mean hyperemia score increased by approximately 1.0 unit on CCLRU scale
NDA Submission Targeted In Late 2022
Ongoing Activities Sets Ocuphire On Path To A Potential Regulatory Approval In 2023

**Target Label Indication**
The treatment of pharmacologically induced mydriasis produced by adrenergic (e.g. phenylephrine) or parasympatholytic (e.g. tropicamide) agents, or a combination thereof.

5 single unit dose vials pack

**Nyxol®**

**P3 Clinical Trial**
Complete a 2nd Phase 3 trial in RM with ~330 subjects which also meets 24-hour safety population exposure

**Pediatric Safety**
Complete RM trial with 20 subjects ages 3 to 11 per agreed FDA initial pediatric plan

**Manufacturing**
Complete 3 registration batches on 1-year CMC stability

**Regulatory Approval**
Submit NDA by Late 2022

**Nydol® Target Label Indication**
The treatment of pharmacologically induced mydriasis produced by adrenergic (e.g. phenylephrine) or parasympatholytic (e.g. tropicamide) agents, or a combination thereof.
Pre-Commercial & Go-To-Market Strategy
Activities Underway To Support Capital-Efficient Nyxol RM Commercial Launch

Engage leading Key Opinion Leaders and Professional Societies to establish OCUP as an emerging company to address unmet needs in the front and back of the eye disorders

Establish Ocuphire as a patient-centric company and leader in ocular health through education and patient access programs (also using digital and social media marketing)

Conduct HCP segmentation and targeting to drive early adoption and capture post-market data and patient experience

Initiate branded and unbranded education for ophthalmologists, optometrists and practice professionals

<table>
<thead>
<tr>
<th>Eye Care Practitioners in US</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Retina Specialists</td>
<td>3,000</td>
</tr>
<tr>
<td>Total Optometrists</td>
<td>46,000</td>
</tr>
<tr>
<td>Total Ophthalmologists</td>
<td>20,000</td>
</tr>
</tbody>
</table>
“By Age 45, 80% of Americans will struggle with Presbyopia, and by age 50, nearly everyone will.”

NY Times
2021: The Time For Presbyopia Drops

Headlines From Academia And Industry Articles Thru The Year With An Early First Approval

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

-OIS

Sources: Academic review articles, journals, and publications
Presbyopia Is A Burgeoning Opportunity

Large Market Being Developed, Pupil Modulation Eye Drops May Replace 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

Vuity™ is the only FDA approved Eye Drop, Launched in Dec 2021

Significant room for improvement for new entrants with better product attributes in a newly developed presbyopia eye drop market

~$9B - $18B Estimated US Presbyopia Market Opportunity

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

- Phentolamine (alpha1/2 antagonist)
- Novel MOA on iris dilator with 24+ hour durability
- Moderate 1+mm pupil reduction
- No daytime redness
- Well-tolerated with no systemic effects
- Stable, preservative-free, single-use vial

0.4% LDP

- Iris Sphincter Muscle Activation

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

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

Source: 1) Nyxol® data from 9 completed trials; Pilocarpine Product label and Literature
Presbyopia VEGA-1 Phase 2 Design

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

VEGA-1

17 US sites
150 presbyopic patients

0.75% Nyxol
4 arms

Placebo

Endpoints

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

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

No loss of distance vision
Pupil diameter at time points
Safety and tolerability (redness)

Eligibility Criteria

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

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

Clinical trial NCT#04675151. DCNVA = distance-corrected near visual acuity. BCDVA = best corrected distance visual acuity.
VEGA-1 Phase 2 Trial Met Primary & Secondary Endpoints
Nyxol + LDP Had Strong Response With ≥ 15 Letter Near Gain From 30 Minutes To 6 Hours

**VEGA-1 Phase 2 Trial**

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

![Bar chart showing percent of subjects with improvement from baseline in photopic DCNVA by time point.](chart)

- **Primary Endpoint**: Time (Hours)
- **Placebo (n=43)**
- **Nyxol+LDP (n=43)**

- **Durable benefit over 6 hours**
- **Rapid onset of efficacy**

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

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.
Secondary Endpoints: Improved DCNVA Without BCDVA Loss
Pre-Specified Endpoints Further Demonstrate Nyxol’s Component Efficacy & 10 Letter Effects

VEGA-1 Phase 2 Trial

≥ 15 Letter Gain In Near & < 5 Letter Loss In Distance at 30 Minutes

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

≥ 10 Letter Improvement in DCNVA at 30 Minutes*

Source: VEGA-1 TLR Table 14.2.2 Percent of Subjects with ≥ 15 Letters of Improvement in Photopic DCNVA and < 5 Letters of Loss in Photopic Binocular BCDVA by Time Point (PP Population); Table 14.2.1 Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point

* Trend seen at other assessed timepoints
Primary Endpoint: Mean Pupil Diameter Over Time
Achieved Pupil Size ~2mm in Nyxol+LDP Consistent With 3-line Improvement in Near Vision

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

**p<0.01***p<0.0001

Daily Evening Nyxol Dosing 12 hr minimum interval to Time 0

Nyxol+LDP arm statistically significant compared to all arms
Summary Of Positive VEGA-1 Phase 2 Results
Nyxol + LDP Had Strong Efficacy Response & Well Tolerated Safety Profile

- Met primary endpoint with statistical significance at 1 hour with Nyxol® plus Low-Dose Pilocarpine (LDP)
- Met key secondary endpoints with statistical significance
  - Gained 15 letters (3 lines) in near vision with less than 6 letters of distance vision loss at all timepoints vs. placebo and select timepoints for components
  - Rapid onset of efficacy within 30 mins
  - Durable near vision improvement through at least 6 hours
  - Sustained significant reduction in pupil diameter for at least 18 hours
  - Near vision efficacy seen both monocularly and binocularly
  - Efficacy in both light and dark irides

- No serious AEs, almost all AEs were mild
- No headaches, no brow aches, and no blurry vision AEs were reported
- No material change in distance vision under photopic and mesopic lighting
- No change in IOP
- Mild, transient conjunctival hyperemia (eye redness) observed in <5% of subjects
## Potential ‘Best in Class’ Presbyopia Drop

**Nyxol+LDP Combination Data Outperforms In Efficacy, Safety, Durability And Onset**

### Nyxol’s Potential Differentiated Solution

<table>
<thead>
<tr>
<th>Product Attributes*</th>
<th>Nyxol+LDP</th>
<th>VUITY™</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Efficacy (3 Line Gain in DCNVA - Primary Endpoint Responders)</td>
<td>61%</td>
<td>26-31%</td>
</tr>
<tr>
<td>2a) Safety: Loss of Distance in Mesopic</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2b) Safety: Tolerability</td>
<td>No Headaches</td>
<td>&gt;5% Headaches</td>
</tr>
<tr>
<td>2c) Safety: Conjunctival Hyperemia</td>
<td>&lt;5% redness</td>
<td>&gt;5% redness</td>
</tr>
<tr>
<td>3) Durability (responders at 6 hours)</td>
<td>37%</td>
<td>18%</td>
</tr>
<tr>
<td>4) Fast Onset (responders at 30 mins)</td>
<td>61%</td>
<td>35%</td>
</tr>
</tbody>
</table>

*Differences in cross trial comparisons are not necessarily statistically significant. Nyxol Data: ASCRS (July 2021) Abstract# 76645 (Phase 2) and 74336 (Phase 3). VUITY™ Data: FDA Label and AAO 2021 Presentation.*
Presbyopia Eye Drops Competitive Landscape

Validation of Pupil Modulating Drops Achieving Pin-Hole Effect & Efficacy, Many With Pilocarpine

Pupil modulation MOA
- Soften lens MOA
- Combination drugs

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

Cholinergic Agonist* (pilocarpine)

Visus (Brimonucle; brimonidine + carbachol)
Orasis (CSF-1; low dose pilo)
Alergen (VUTYTM; 1.25% pilo)
Eyenovia (MicroLine; 1 or 2% pilo)

NyxoL Next Steps
Advance into Phase 3 Presbyopia Registration Trials (1H22)
Potential NDA Submission (2023)

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

I’m no longer comfortable driving at night, especially with my son in the car. I have a hard time playing beach volleyball in the evenings due to the bright lights at the courts.

Post-LASIK, Age 42
Market Opportunity In Dim Light Or Night Vision Disturbances
No Approved Treatments With Ripe Opportunity For Growth

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.

No Approved Treatments
Pupil reduction with Nyxol may offer a potential solution to peripheral optical imperfections

$2B - $4B
Estimated US NVD Market Opportunity

Source: GlobalData Market Research Report, 2020
NVD LYNX-1 Phase 3 Registration Design

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

LYNX-1

20 US sites
140 - 160 patients with NVD

Eligibility Screening
Randomization

1:1

0.75% Nyxol
daily evening dose
(14 days)

Placebo
daily evening dose
(14 days)

Day 0
Day 8 Assessments
Day 16 Assessments

Primary Endpoint

Endpoints

Primary: % of subjects with ≥ 3 lines of improvement in mesopic low contrast best-corrected distance visual acuity (Day 8)

Secondary (Days 8 & 15):
- Pupil diameter
- Visual acuity measures (distance and near)
- Safety and tolerability (redness)

Phase 3 Initiated in Late 4Q20

Top Line Expected Early 2022
Nyrol 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>Percent of Subject Eyes</th>
<th>≥ 1 line</th>
<th>≥ 2 lines</th>
<th>≥ 3 lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo n=16</td>
<td>31%</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Nyxol n=32</td>
<td>69%</td>
<td>34%</td>
<td>13%</td>
</tr>
</tbody>
</table>

*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

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>Day</th>
<th>Pupil Diameter Change from Baseline (mm and %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 8</td>
<td>-0.99 (-20%)</td>
</tr>
<tr>
<td>Day 15</td>
<td>-1.00 (-21%)</td>
</tr>
<tr>
<td>Day 16</td>
<td>-0.88 (-19%)</td>
</tr>
</tbody>
</table>

Source: NYXG-201
APX3330 TABLETS

DR  Diabetic Retinopathy

DME  Diabetic Macular Edema
Diabetic Retinopathy & Macular Edema

Oral Alternatives To Injectable Therapies Are Needed For Earlier Stages Of Disease

The Problem

- Diabetic retinopathy (DR) and diabetic macular edema (DME) are a leading cause of vision loss worldwide.
- Diabetes damages small blood vessels within the eye causing leakage, oxygen starvation, and abnormal vessel growth.
- DR patients are not routinely treated with approved injectable anti-VEGF drugs.
  - DR progresses resulting in vision loss.
- Current treatment for DME are not satisfactory.
  - 25% non-responders
  - 50% partial responders to anti-VEGF drugs.

Limited Retinal Treatment Options for Diabetic Patients

Large, Unmet Need in Diabetic Eye Diseases (US)

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

$1B - $3B
Estimated US DME Market Opportunity

$3B - $7B
Estimated US DR Market Opportunity

APX3330: Drug Development History And Patents

**Significant Preclinical & Clinical Data Supporting Human Safety, MOA, and PK**

- **APX3330**  
  New Chemical Entity

- **11 Phase 1 & Phase 2 Trials**
- **>340 Subjects Dosed**
- **Exposure in Humans 365 Days**
- **Patent Coverage 2034+**

- **Preclinical Efficacy & Toxicology Package**
- **APX3330 IND**
- **6 Phase 1 Trials**
- **5 Phase 2 Trials**
- **Phase 2b Trials**
- **Phase 3 Registration**
- **NDA Filing**

- **Studied in inflammation/hepatitis & cancer patients**  
  *(Studied by Eisai & Apexian, respectively)*

- **Focus on Ophthalmology**

**Focus on Ophthalmology**
**APX3330 History And Ref-1 Inhibition Mechanism**

*Ref-1 Involved In Multiple Key Pathways That Contribute To Diabetic Retinopathy and DME*

**Mechanism of Action – Ref-1 Inhibition**

- Ref-1 (reduction-oxidation effector factor-1) is a novel target discovered by Dr. Mark R. Kelley at Indiana University School of Medicine
- APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of Ref-1
- APX3330 previously developed by Eisai for multiple hepatic inflammatory indications and later by Apexian for advanced solid tumors
  - Similar oncology origin as approved anti-VEGFs
- MOA uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1

APX3330 down-regulates VEGF protein and anti-inflammatory cytokines

In Vivo And In Vitro Evidence Of APX Dual Pathway Mechanism Of Action

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

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

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

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

Lesion Volume Decrease With Oral APX3330 In Murine Laser CNV Model Similar To EYLEA® Data


- Published data on EYLEA.
Phase 1/2 Clinical Trials: PK Data Supporting The ZETA-1 Trial

**APX3330 Is Bioavailable And Reaches The Retina Via Oral Administration**

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

- **Mouse**
  - 25 mg/kg APX3330 oral gavage measured in mouse retina

- **Rat**
  - 10 mg/kg APX3330 oral gavage measured in rat eye

- **Human**
  - 300 mg BID (600 mg/day total)
    - Established PBPK model predicts APX3330 reaches sufficient human retinal concentrations

---

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

*First-In-Class Ref-1 Inhibitor With Favorable Human Safety Data*

<table>
<thead>
<tr>
<th>Expected Efficacy Data</th>
<th>Favorable Safety Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improving Eye Health in Diabetics</strong></td>
<td><strong>Few Systemic Adverse Effects</strong></td>
</tr>
<tr>
<td>↓ Inflammation</td>
<td>• &lt; 5% Mild Gastrointestinal (diarrhea)</td>
</tr>
<tr>
<td>↓ Abnormal Angiogenesis</td>
<td>• &lt; 5% Mild Skin Rash (reversible)</td>
</tr>
<tr>
<td><strong>Enhance Compliance &amp; Exposure</strong></td>
<td>• Lack of Significant Acute Neurologic, Cardiovascular, Liver, or Pulmonary toxicity</td>
</tr>
<tr>
<td>Oral pill may reduce the burden of frequent anti-VEGF injections</td>
<td><strong>No Ocular Effects</strong></td>
</tr>
<tr>
<td></td>
<td>• No observed ocular AEs</td>
</tr>
</tbody>
</table>

*APX3330: Well-tolerated Oral Dose up to 600mg/day
Twice Daily Dosing*
DR/DME ZETA-1 Phase 2b Design

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

ZETA-1

24 US sites
~100 participants with moderate-to-severe NPDR or mild PDR
Noncentral DME is permitted

Eligibility Screening
Randomization

1:1

APX3330 600mg/day (BID)

Week 0
Week 4
Week 12
Week 24

Primary Endpoint

Placebo BID

Endpoints

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

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

Exploratory:
• Labs / PK

Phase 2b Start Initiated in April 2021
Top Line Expected in 2022

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)
Innovative Approach For Retinal Diseases With APX Platform

APX3330 May Treat Patients Across The Spectrum Of Retinal Diseases

Potential Differentiated Solution

- Potential First Oral Rx for Retina Diseases
  - First-line earlier intervention for the diabetic eye
  - Add-on therapy to current anti-VEGF treatments
- Proven Novel Mechanism
  - May decrease both inflammation and angiogenesis
- Convenient Daily Regimen
- Favorable Oral Safety Profile
  - As seen in 11 completed Phase 1 and Phase 2 clinical trials
- Improve Patient Compliance
  - Potentially alleviate the frequent burden of injections

DR
DME
Wet AMD
Dry AMD
RVO
GA

Current anti-VEGF treatments:
APX2009
APX2014
APX3330 (Local Delivery)
Team/Boards, Milestones, And Financial Data
Ocuphire's World-Class Medical Advisory Board

Fortunate For The Insights Of Leading KOLs & Drug Candidate Co-Founders

Jay Pepease, MD, PhD
UCLA

Mitch Jackson, MD
Chicago Medical School

James Katz, MD
University of Illinois

Thomas Samuelson, MD
University of Minnesota

Ed Holland, MD
Loyola University Chicago

Jack Holladay, MD
University of Texas

Marquette McDonald, MD
Columbia University

Y. Ralph Chu, MD
Northwestern University

Paul Karpecki, OD
Indiana University

Eliot Lazar, MD
Georgetown University

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

David Boyer, MD
Chicago Medical School

Peter Kaiser, MD
Harvard Medical School

Peter Kaiser Associates Medical Group

David Boyer, MD
Chicago Medical School

David Boyer, MD
Baylor University

Michael Allingham, MD, PhD
University of North Carolina

Marc Johnson, MD
University of Texas

Michael Allingham, MD, PhD
University of North Carolina

Douglas Davies, OD
University of Nevada
Ocuphire Board of Directors
Seasoned Directors With Decades Of Drug Development, M&A/Financings, And Ophthalmology
Oculifire Cadence Of Milestones

Multiple Data Catalysts On Path To NDA(s)

2021

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

2022

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

Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)
Ophthalmology – An Attractive Biotech Sector

Deal Activity And FDA Approvals In Ophthalmology In 2021

Deal Activity

<table>
<thead>
<tr>
<th>Date</th>
<th>Company/Event</th>
<th>Value ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2021</td>
<td>Alcon</td>
<td>$3.25B</td>
</tr>
<tr>
<td>October 2021</td>
<td>Théa</td>
<td>~$2B</td>
</tr>
<tr>
<td>December 2021</td>
<td>Rayner</td>
<td>~$1B</td>
</tr>
<tr>
<td>December 2021</td>
<td>Novartis</td>
<td>~$1.5B</td>
</tr>
<tr>
<td>September 2021</td>
<td>Allergan</td>
<td>$1.75B</td>
</tr>
</tbody>
</table>

New Product Approvals

7 of 60 Total FDA Drug Approvals in 2021 Were Ophthalmic Drugs

- Alcon Septrinza
- Allergan Avanir
- Théa Thea
- Genentech Sustiva
- Rayner Gyroscope
- Novartis              
- Allergan Ophthamolog
- Bausch Health Xipere
- Santen Bioepis
- Samsung Byooviz

Source: 1. Endpoint Dec 28, 2021 - Hitting a new record on drug approvals, the FDA offers a thumbs up to another atopic dermatitis contender; OIS Year in Review 2021; Company press releases
## OCUP – Market Snapshot

*Active Trading Volume And Sufficient Cash Runway Through 2Q 2023*

<table>
<thead>
<tr>
<th>Ticker</th>
<th>OCUP</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>$3.73</td>
<td>As of 12-31-21</td>
</tr>
<tr>
<td>Market Cap</td>
<td>$64.8 M</td>
<td>As of 12-31-21</td>
</tr>
<tr>
<td>Shares Outstanding</td>
<td>18.8 M</td>
<td>As of 12-31-21</td>
</tr>
<tr>
<td>Cash</td>
<td>$24.5 M</td>
<td>As of 12-31-21 (unaudited)</td>
</tr>
<tr>
<td>Cash Runway</td>
<td>Sufficient into 2Q 2023</td>
<td>Guidance as of 1-5-22</td>
</tr>
<tr>
<td>Average Daily Volume</td>
<td>390 K</td>
<td>As of 12-31-21 (Dec. Avg)</td>
</tr>
<tr>
<td>Short Interest</td>
<td>868 K; 5.1% of Float</td>
<td>As of 12-15-21</td>
</tr>
</tbody>
</table>

### Research Analyst Coverage on OCUP

<table>
<thead>
<tr>
<th>John Newman</th>
<th>Canaccord Genuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kristen Kluska</td>
<td>Cantor Fitzgerald</td>
</tr>
<tr>
<td>James Molloy</td>
<td>Alliance Global Partners</td>
</tr>
<tr>
<td>Prakhar Agrawal</td>
<td>Jones Trading</td>
</tr>
<tr>
<td>Matthew Caulfield</td>
<td>H. C. Wainwright</td>
</tr>
</tbody>
</table>

Source: FactSet
NVD Endpoint: 5% Low Contrast Visual Acuity (LCVA) Chart

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)**

<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>Micro-aneurysm only</td>
<td>Mild NPDR</td>
<td>Moderate NPDR</td>
<td>Moderately Severe NPDR</td>
<td>PDR – Mild, Moderate, and Severe</td>
</tr>
</tbody>
</table>

### Retinal Image
- **Healthy blood vessels with no bulges**
- **Small bulges in blood vessel walls as well as other signs in the retina**
- **More changes in the blood vessels in the retina and small spots of blood can become more visible**
- **More blood vessels in larger areas of the retina show changes**
- **Many of the blood vessels in the retina show visible changes**
- **Increased growth of new, damaged blood vessels**

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

---

Primary Endpoint of APX3330 ZETA-1 Trial

Percent of patients with a ≥ 2 step improvement on the DRSS score at week 24