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

37000 Grand River Avenue, Suite 120
Farmington Hills, MI

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

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 2.02 Results of Operations and Financial Condition.

On November 12, 2021, Ocuphire Pharma, Inc. (the “Company”) issued a press release announcing its financial results for the quarter ended September 30, 2021. A copy of this press release is furnished herewith as Exhibit 99.1 to this Current Report and is incorporated herein by reference.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 2.02, and Exhibit 99.1 hereto, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Company’s filings under the Securities Act of 1933, as amended (the “Securities Act”), or the Exchange Act, whether made before or after the date hereof, regardless of any incorporation language in such a filing, except as expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

On November 15, 2021, 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 99.1 to this Current Report on Form 8-K (this “Report”).

The information in this Report, including Exhibit 99.1 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 Exhibit 99.1 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 Exhibit 99.1 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.

(d) Exhibits

<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Exhibit Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.1</td>
<td>Press Release, dated November 12, 2021</td>
</tr>
<tr>
<td>99.2</td>
<td>Corporate Presentation, dated November 15, 2021</td>
</tr>
</tbody>
</table>
SIGNATURES

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: November 15, 2021
Ocuphire Announces Financial Results for the Third Quarter 2021   and Provides Corporate Update

On Track to Initiate Additional Phase 3 FDA Registration Trials for Nyxol® Eye Drops in Reversal of Mydriasis (RM) in 4Q21 and Presbyopia in 1H22

Three Clinical Trial Data Readouts Expected in Early 2022 for Nyxol in Night Vision Disturbance, RM, and RM for Pediatric Patients

Planned NDA Submission for Nyxol in Reversal of Mydriasis Indication in Late 2022

More Publications Supporting Novel Transcription Factor (Ref-1) Inhibitor, APX3330, Targeting Both Neovascularization and Inflammation in Retinal Diseases

Currently Recruiting for Phase 2 Trial Evaluating APX3330 for the Treatment of Diabetic Retinopathy with Data Expected in 2H22

FARMINGTON HILLS, Mich., November 12, 2021 - 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 announced financial results for the third quarter of 2021 and provided a corporate update.

“The third quarter marked continued progress across our late-stage clinical programs and opportunities for multiple data presentations at major medical meetings,” said Mina Sooch, MBA, President and CEO of Ocuphire Pharma. “We have already achieved two successful clinical trials for Nyxol. In reversal of mydriasis (RM), we reported positive results in a Phase 3 trial and are on track to initiate the second Phase 3 trial before year end. In presbyopia, we reported positive results in a Phase 2 clinical trial. We are also delighted to see the early US regulatory approval of Allergan’s VUITY™ eye drops, the first pharmaceutical therapy for the large presbyopia market.”

“We are also very pleased to see a growing body of supportive research for our Phase 2 oral drug candidate, APX3330, which inhibits known pro-angiogenic and pro-inflammatory pathways. As a highly differentiated, first-in-class and orally-delivered therapy, we believe APX3330 will be an important source of potential value creation with the opportunity to broadly address the unmet global clinical need in diabetic retinopathy and treatment burden in other retinal diseases.”
“This week marks Oc有用eर’’s one-year anniversary of public trading on the Nasdaq and we are proud to have achieved so many important clinical and business milestones in that time. We thank our clinical trial participants and investigators for their continued support. Looking ahead, we believe 2022 is shaping up to be an even more exciting and catalyst-rich year to build significant value for our company and our shareholders, with cash on hand that provides runway into late 2022 to achieve these milestones.”

Key Anticipated Future Milestones

• **Reversal of Mydriasis (RM):** Initiate second Phase 3 (MIRA-3) registration trial in subjects 12 and older and a small pediatric trial in subjects ages 3 to 11 (MIRA-4) in the fourth quarter of 2021 investigating Nyxol with results expected in early 2022; Planning to file NDA submission with FDA for Nyxol in RM indication in late 2022

• **Presbyopia:** Initiate Phase 3 program (VEGA-2) in first half of 2022 investigating Nyxol and Low-Dose Pilocarpine (LDP)

• **Night Vision Disturbances (NVD):** Top-line data expected in early 2022 from Phase 3 (LYNX-1) registration trial investigating Nyxol

• **Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME):** Top-line data expected in the second half of 2022 for the randomized, well-controlled Phase 2 (ZETA-1) trial investigating APX3330

Third Quarter and Recent Business Highlights

**Presentations and Publications**

• In November, clinical data on Nyxol® and APX3330 were accepted for presentation at poster sessions at the American Academy of Ophthalmology (AAO) 2021 annual meeting to take place in New Orleans, November 12 – 15. In addition, Ocphilе presented new data on improvement in intermediate vision and Snellen equivalent near vision at the Eyecelerator@AAO 2021 conference on November 11. Ocphilе was one of two companies presenting clinical data for presbyopia at this meeting.

• In October, the Company announced the publication of a review article within the Special Issue “Advances in Molecular Activity of Potential Drugs” of the International Journal of Molecular Sciences, focused on how novel inhibitors of APE1/Ref-1 such as APX3330 may have the potential to improve disease outcomes for retinal disease patients. The article underscores the role of the APE1/Ref-1 protein in pro-angiogenic pathways associated with neovascular eye disease including diabetic retinal diseases and age-related macular degeneration. It can be accessed online at the following link: Inhibition of APE1/Ref-1 for Neovascular Eye Disease: From Biology to Therapy.
• In October, the Company announced the publication of a review article in *Cells* titled “Potential Therapeutic Candidates for Age-Related Macular Degeneration” noting the potential of APX3330 (referred to as “E3330”) for the treatment of age-related macular degeneration (AMD). Because APE1/Ref-1 has been shown to contribute to retinal angiogenesis, the authors conclude that APE1/Ref-1 inhibitors such as APX3330 could inhibit the abnormal blood vessel formation seen in AMD by reducing retinal endothelial cell proliferation, migration, and tube formation. The article can be accessed online at the following link: Potential Therapeutic Candidates for Age-Related Macular Degeneration (AMD).

• In October, Michael J. Allingham, MD, PhD presented at the 39th Annual Scientific Meeting of the American Society of Retina Specialists (ASRS) (Diabetic Retinopathy 1 Symposium), highlighting the favorable safety and tolerability data for APX3330 in over 300 healthy volunteers and cancer/inflammation disease patients across 11 Phase 1 and Phase 2 studies. Also, Mina Sooch, CEO, presented APX3330 history and the design of the ongoing Phase 2 trial in DR at the OIS Retina Innovation Summit@ASRS.

• In July, the Company announced publication in the *Journal of Cellular Signaling* featuring Ocophire’s novel oral Ref-1 inhibitor APX3330 in Phase 2 trial for the treatment of retinal disease which highlighted the favorable safety profile of APX3330 and its unique anti-angiogenic and anti-inflammatory mechanism of action properties relevant to a broad range of retinal diseases.

• In July, at the 2021 American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting, Dr. Jay S. Pepose, Medical Advisor and Board Director, presented papers featuring positive results for Nyxol in two studies: Phase 2 Presbyopia (VEGA-1) and Phase 3 Reversal of Mydriasis (MIRA-2). The Phase 3 MIRA-2 data presentation at ASCRS won the Best Paper of the Session.

• In July, Mina Sooch, CEO, participated in the presbyopia drug therapy panel at the Eyeceelerator@ASCRS 2021 held on July 22nd and in the Eye on Innovation panel at the Virtual Salon Series held on July 28th.

**Intellectual Property**

• U.S. Patent and Trademark Office issued patent no. 11,160,770 “Compounds, compositions and methods for treating oxidative DNA damage disorders” which provides protection for APX2009 and other APX pipeline candidates.

**Third Quarter and Year-To-Date 2021 Financial Highlights**

As of September 30, 2021, the Company had cash and cash equivalents of approximately $22.2 million. Net cash used in operating activities for the nine months ended September 30, 2021 was $13.7 million.
Collaborations revenue was $0.5 million and $0.6 million for the three months and nine months ended September 30, 2021, respectively. Revenue during the periods was derived from the license agreements with Biosense Global, LLC and Processa Pharmaceuticals, Inc. related to certain technology transfers. There was no collaborations revenue recognized during the comparable prior year periods.

General and administrative expenses for the three months and nine months ended September 30, 2021 were $1.6 million and $6.7 million, respectively, compared to $0.6 million and $1.5 million for the comparable periods in 2020, respectively. The increases in the current periods were primarily attributable to administrative employee headcount, stock-based compensation, professional services, insurance, legal and settlement costs, and costs associated with operating as a public company subsequent to the reverse merger.

Research and development expenses for the three months and nine months ended September 30, 2021 were $3.1 million and $10.4 million, respectively, compared to $1.4 million and $2.3 million for the comparable periods in 2020, respectively. In the current periods, the increases were primarily attributable to new clinical trials and manufacturing activities for Nyxol and APX3330 as well as regulatory, preclinical and other development activities.

The loss from operations for the three and nine months ended September 30, 2021 was $4.2 million and $16.6 million, respectively, compared to $1.9 million and $5.9 million for the three and nine months ended September 30, 2020, respectively.

There was a non-cash expense of $33.8 million related to fair value change in warrant liabilities recorded for the nine months ended September 30, 2021 compared to a benefit of $0.2 million recorded for the nine months ended September 30, 2020 related to premium conversion derivatives. The reported losses also included non-cash stock-based compensation expense of $0.5 million and $1.4 million during the three and nine months ended September 30, 2021, respectively, and $0.6 million and $1.0 million during the three and nine months ended September 30, 2020, respectively.

For further details on Ocuvre’s financial results refer to the Company’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, as filed with the Securities and Exchange Commission.
Ocuphire is a publicly-traded (NASDAQ: OCUP), clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of several eye disorders. Ocuphire’s pipeline currently includes two small-molecule product candidates targeting front and back of the eye indications. The company’s lead product candidate, Nyxol® (0.75% phentolamine ophthalmic solution) Eye Drops, 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 including the recently completed Phase 3 trial in RM and Phase 2 trial in presbyopia. Ocuphire reported positive topline data in March 2021 for MIRA-2, a Phase 3 FDA registration study for treatment of RM. Ocuphire also reported positive top-line data in June 2021 for VEGA-1, a Phase 2 trial for the treatment of presbyopia. Nyxol is also currently in Phase 3 clinical development for NVD. 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 completed Phase 2 trials, recently completed Phase 3 registration trial in RM (NCT04620213), recently completed Phase 2 trial in presbyopia (NCT04675151), ongoing Phase 3 registration trial in NVD (NCT04638660), and Phase 2 trial in DR/DME (NCT04692688). For more information, please 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 expected timing of our future clinical trials in RM, NVD, presbyopia, and DR/DME; the extent of the Company’s cash runway. These forward-looking statements are based upon Ocuphire’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 Ocuphire 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 Ocuphire’s product candidates and (x) the maintenance of Ocuphire’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 Ocuphire 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. Ocuphire undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Ocuphire Contacts

Mina Sooch, President & CEO
Ocuphire Pharma, Inc.
ir@ocuphire.com
www.ocuphire.com

Corey Davis, Ph.D.
LifeSci Advisors
cdavis@lifesciadvisors.com
Ocuphire Pharma, Inc.
Condensed Consolidated Balance Sheets
(in thousands, except share amounts and par value)

<table>
<thead>
<tr>
<th></th>
<th>As of September 30, 2021</th>
<th>As of December 31, 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$22,250</td>
<td>$16,399</td>
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<tr>
<td>Short-term investments</td>
<td>383</td>
<td>—</td>
</tr>
<tr>
<td>Prepaid and other assets</td>
<td>560</td>
<td>1,269</td>
</tr>
<tr>
<td>Total current assets</td>
<td>23,193</td>
<td>17,668</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$23,204</td>
<td>$17,682</td>
</tr>
<tr>
<td><strong>Liabilities and stockholders’ equity (deficit)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current liabilities:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounts payable</td>
<td>$1,434</td>
<td>$1,214</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>1,204</td>
<td>1,971</td>
</tr>
<tr>
<td>Total current liabilities</td>
<td>2,638</td>
<td>3,185</td>
</tr>
<tr>
<td>Warrant liabilities</td>
<td>—</td>
<td>27,964</td>
</tr>
<tr>
<td><strong>Total liabilities</strong></td>
<td>2,638</td>
<td>31,149</td>
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<tr>
<td><strong>Commitments and contingencies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preferred stock, par value $0.0001; 10,000,000 shares authorized as of September 30, 2021 and December 31, 2020; no shares issued and outstanding at September 30, 2021 and December 31, 2020.</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Common stock, par value $0.0001; 75,000,000 shares authorized as of September 30, 2021 and December 31, 2020; 17,295,434 and 10,882,495 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively.</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Additional paid-in-capital</td>
<td>103,619</td>
<td>19,207</td>
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<tr>
<td>Accumulated deficit</td>
<td>(83,055)</td>
<td>(32,675)</td>
</tr>
<tr>
<td><strong>Total stockholders’ equity (deficit)</strong></td>
<td>20,566</td>
<td>(13,467)</td>
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<tr>
<td><strong>Total liabilities and stockholders’ equity (deficit)</strong></td>
<td>$23,204</td>
<td>$17,682</td>
</tr>
</tbody>
</table>
Ocuphire Pharma, Inc.
Condensed Consolidated Statements of Comprehensive Loss
(in thousands, except share and per share amounts)
(unfinished)

<table>
<thead>
<tr>
<th></th>
<th>For the Three Months Ended September 30,</th>
<th>For the Nine Months Ended September 30,</th>
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<tbody>
<tr>
<td></td>
<td>2021</td>
<td>2020</td>
</tr>
<tr>
<td>Collaborations revenue</td>
<td>$ 489</td>
<td>$ —</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General and administrative</td>
<td>1,595</td>
<td>565</td>
</tr>
<tr>
<td>Research and development</td>
<td>3,126</td>
<td>1,383</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>4,721</td>
<td>1,948</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(4,232)</td>
<td>(1,948)</td>
</tr>
<tr>
<td>Interest expense</td>
<td>—</td>
<td>(179)</td>
</tr>
<tr>
<td>Fair value change of warrant liability and premium conversion derivatives</td>
<td>—</td>
<td>879</td>
</tr>
<tr>
<td>Gain on note extinguishment</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Other income, net</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Loss before income taxes</td>
<td>(4,230)</td>
<td>(1,248)</td>
</tr>
<tr>
<td>Benefit (provision) for income taxes</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Net loss</td>
<td>(4,230)</td>
<td>(1,248)</td>
</tr>
<tr>
<td>Other comprehensive loss, net of tax</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Comprehensive loss</td>
<td>$ (4,230)</td>
<td>$ (1,248)</td>
</tr>
<tr>
<td>Net loss per share:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic and diluted</td>
<td>$ (0.25)</td>
<td>$ (0.33)</td>
</tr>
<tr>
<td>Number of shares used in per share calculations:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic and diluted</td>
<td>16,925,006</td>
<td>3,743,907</td>
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</tbody>
</table>
Ocuphire Corporate Presentation

Mina Sooch CEO

November 15, 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 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) the success and timing of regulatory submissions and pre-clinical and clinical trials; (ii) regulatory requirements or developments; (iii) changes in capital resource requirements; (iv) changes to clinical trial designs and regulatory pathways; (v) changes in capital resource requirements; (vi) risks related to the instability of the Company to obtain sufficient additional capital; (vii) risks and uncertainties related to future milestones; (viii) changes in the regulatory, political, and economic developments; and (ix) 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 contained within this presentation shall not, except as hereinafter provided, be disclosed by you or your representatives to any other person, for any purpose, 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 to be bound by 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 share 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.
### 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: Reversal of Mydriasis (RM), Presbyopia (P) & Dim Light / Night Vision Disturbances (NVD)
- APX3330 tablets target chronic back of the eye indications: Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME), a leading cause of blindness in diabetic patients

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

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

### Multiple Near-Term Data Catalysts with Capital Efficient Plan
- Initiated 4 late-stage trials (2 Phase 3, 2 Phase 2) with readouts expected in 2021-2022
  - Reported positive P3 data in RM in 1Q21 with Nyxol NDA submission targeted late 2022
  - Reported positive P2 data in Presbyopia in 2Q21 with plans to advance to P3 in 2022
- $22 million cash reported at the end of 3Q 2021 sufficient for operations through late 2022
- Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, Spartan, and Encode Ideas
Ocuphire Management Team

Decades of Biotech and Drug Development Experience

Mina Sooch, MBA
President & CEO and Founder

Drey Coleman
VP, Clinical Operations

Amy Rabourn, CPA
VP, Finance

Charlie Hoffmann, MBA
VP Corporate Development and Operations

Mitch Briggell, PhD
Head, Clinical Development and Strategy

Daniela Oniciu, PhD
Global Head, R&D, Chemistry and Product Development

Ronil Patel, MSS
Senior Director BD and Market Strategy

Chris Ernst
Global Head, QA and Manufacturing

Barbara Withers, PhD
VP, Clinical and Regulatory Strategy

Drey Coleman
VP, Clinical Operations
Large Unmet Opportunities for the Aging Eye

Developing Drugs to Treat Front & Back of the Eye Diseases

Source: GlobalData Market Research Report, 2020; Company Estimates for Market Size

- **Reversal of Mydriasis**
  - U.S. Market Opportunity:
    - Front: $325M - $1B
  - U.S. Prevalence: ~100M pupil dilations per year

- **Presbyopia**
  - U.S. Prevalence: ~120M
  - U.S. Markets: ~$10+ to ~$20+B
  - US Market Opportunity: $9B - $18B

- **Night Vision Disturbances**
  - U.S. Prevalence: ~16M adults
  - US Market Opportunity: $2B - $4B

- **Diabetic Retinopathy**
  - U.S. Prevalence: ~7M
  - US Market Opportunity: $3B - $7B

- **Diabetic Macular Edema**
  - U.S. Prevalence: ~750K
  - US Market Opportunity: $1B - $3B

$4 to $10B US Markets

---

Source: GlobalData Market Research Report, 2020; Company Estimates for Market Size
### 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>0.75% Nyxol®, Eye Drop</td>
<td>Reversal of Mydriasis (RM)</td>
<td>Pre-clinical</td>
<td>Initiated Phase 3 MIRA-2 trial 4Q20; Topline data reported in 1Q21 (n=185)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase 1</td>
<td>Initiate Phase 3 MIRA-3 trial 2H21; Data expected in early 2022 (n=330)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase 2</td>
<td>Initiate Pediatric trial 2H21; Data expected in early 2022 (n=20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase 3</td>
<td>Initiated Phase 2 VEGA-1 trial 1Q21; Topline data reported in 2H21 (n=150)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 3 program in 1H22</td>
</tr>
<tr>
<td>0.75% Nyxol®, + Low-Dose 0.4% Pilocarpine Eye Drops</td>
<td>Presbyopia (P)</td>
<td>Positive Data Readout</td>
<td>Initiated Phase 3 LYNX-1 trial 4Q20; Data expected in early 2022 (n=160)</td>
</tr>
<tr>
<td>0.75% Nyxol®, Eye Drop</td>
<td>Dim Light or Night Vision Disturbances (NVD)</td>
<td>Recruiting</td>
<td>Initiated Phase 2 ZETA-1 trial Apr21; Data expected in 2H22 (n=100)</td>
</tr>
<tr>
<td>APX3330 Oral Pill</td>
<td>Diabetic Retinopathy (DR) Macular Edema (DME)</td>
<td>Recruiting</td>
<td>Initiated Phase 3 LYNX-1 trial 4Q20; Data expected in early 2022 (n=160)</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>
</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, 2, and 3 Clinical Programs with MIRA-2 Data Leading the NDA Path**

<table>
<thead>
<tr>
<th></th>
<th><strong>Nyxol</strong></th>
<th></th>
<th><strong>APX3330</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects Dosed</td>
<td>&gt;330</td>
<td>Subjects Dosed</td>
<td>&gt;340</td>
</tr>
<tr>
<td>Phase Trials</td>
<td>Phase 1, Phase 2, and Phase 3</td>
<td>Phase 1 &amp; Phase 2 Trials</td>
<td></td>
</tr>
<tr>
<td>Exposure in Humans</td>
<td>28 Days</td>
<td>Exposure in Humans</td>
<td>365 Days</td>
</tr>
<tr>
<td>Patents to</td>
<td>2034+</td>
<td>Patents to</td>
<td>2034+</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Studied in multiple ocular refractive indications</td>
<td>Studied in inflammation/hepatitis &amp; cancer patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>505(b)(2) Development Pathway</td>
<td>NCE Development Pathway</td>
<td></td>
</tr>
</tbody>
</table>

*Ocuphire*
Nyxol®

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

Phentolamine Mesylate
Nyxol History & MOA
Rationale for Differentiated Product Profile & 505(b)(2) Path

- Nyxol’s active ingredient, phentolamine mesylate (PM), is currently approved for 2 indications
  - Pheochromocytoma (60+ years ago, Regitine®) – intravenous injection
  - Reversal of oral anesthesia (10+ years ago, OraVerse®) – intramuscular injection
- PM has been reformulated as a topical eye drop (Nyxol)
- Nyxol is a first-in-class non-selective α1 and α2 blocker product candidate
  - MOA of relaxing the iris dilator muscle (α1)
  - Redness is an on-target α1 effect on sclera vessels (transient, mild)

Phentolamine Mesylate

- Reduces Pupil Size
  - α1: Iris Dilator Blockade
- Dilates Blood Vessels (Vasodilation)
  - α1: Smooth Muscle Blockade
# Nyxol Product Candidate Profile

**Novel Alpha 1/2 Blocker Eye Drop for Refractive Indications (505(b)(2) Pathway)**

<table>
<thead>
<tr>
<th><strong>Nyxol: 0.75% Phentolamine Ophthalmic Solution</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Preservative Free, EDTA Free, and Stable</td>
</tr>
</tbody>
</table>

## Efficacy Data

**Improving Vision**

- ↓ Pupil Size (moderate miotic)
- ↑ Contrast Sensitivity (night)
- ↑ Near Visual Acuity (light/dark)
- ↑ Distance Visual Acuity

## Safety Data

**No Systemic Effects**

- No Changes in Blood Pressure
- No Changes in Heart Rate

**Tolerated Topical Effects**

- Mild / Transient / Reversible Eye Redness

**IOP Unchanged or Decreased**

- ↓ Intraocular Pressure (IOP) at Normal Baseline

---

*Chronic daily dosing of Nyxol at bedtime demonstrated no significant daytime redness and durability of effects for more than 24 hours*
Nyxol®

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

Phentolamine Mesylate
Reversal of Mydriasis (RM) – Acute Treatment
Annual Exams and Specialty Visits Involve Dilation to Monitor Eye Health

The Problem

• At many annual eye exams and specialty visits, pupils are pharmacologically dilated, impairing vision for 6-24 hours

• Dilated eyes:
  – heightened sensitivity to light
  – inability to focus
  – reading, working, and driving are difficult
  – halos and glare

“...I have to stay indoors. They say it only lasts a few hours, but it lasts all day, and it is very annoying.”
RM Patient, Age 51

No Current Commercially Available Treatments

~100M eye exams / year in US

Source: GlobalData Market Research Report, 2020
Reversal of Mydriasis (RM) – Acute Treatment
Single Use Indication Leveraging a Precedent Approval Pathway

Nyxol’s Potential Differentiated Solution

- **Regulatory Precedent** with Rev-Eyes (an alpha 1 blocker), approved by the FDA in 1990 but shortly thereafter discontinued (not for safety or efficacy reasons)

- **Clinical Effect** to potentially reduce pupil size and counteract the effect of mydriatic drugs (alpha agonists and cholinergic blockers) used to dilate the pupil

- **Convenient and Stable** eye drop given at the office that may allow vision to return to normal sooner

- **Tolerable** with a minimal side effect profile (unlike cholinergic agonists such as pilocarpine)

Seeking Treatment Findings

<table>
<thead>
<tr>
<th></th>
<th>Patients likely to request reversal of dilation¹</th>
<th>80%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye care providers likely to use reversal drops²</td>
<td>76%</td>
<td></td>
</tr>
</tbody>
</table>

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

MIRA-2
12 US sites
168 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 Time -1 Hour
Treatment Time 0 (Max Dilation)

Placebo

Placebo drop(s) (2 drops study eye, 1 drop fellow eye)

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)

Endpoints

Started and Completed Enrollment in 4Q20 – 185 Subjects
Topline Results Expected in 1Q21 → Reported in March 2021

Mydriatic Agents 3:1:1 – 2.5% phenylephrine (alpha 1 agonist), 1% tropicamide (cholinergic blocker), Paremyd® (combination)
Primary Endpoint: % of Subjects Study Eye Returning to Baseline PD at 90 Min

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

Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD)

Nyxol Reduced PD Faster Across All Mydriatic Agents*
Secondary Endpoint: Mean Pupil Diameter Over Time by Mydriatic Agent

Nyxol Reduced Pupil Diameter With All Mydriatic Agents; More Rapidly with Phenylephrine as Expected

**MIRA-2 Phase 3 Trial**

**Nyxol More Rapidly Reduced PD in Subjects Across All 3 Mydriatic Agents**

**Mean Pupil Diameter**

- Phenylephrine
- Tropicamide and Paremyd

Source: mITT Population, MIRA-2 Trial. Standard Error bars are shown.
Secondary Endpoint: % of Subjects Returning to Baseline PD by Iris Color

Evidence of Efficacy in Subjects with Either Light or Dark Irides, with a More Vigorous Response in Light Irides

MIRA-2 Phase 3 Trial

More Subjects Returned to PD Baseline with Nyxol in Both Light and Dark Irides

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

Source: MIRA-2 Trial mITT Population, Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)
Secondary Endpoint: Accommodation And Time Savings

Nyxol Demonstrates a Faster Return to Baseline Accommodation and Shorter Dilation Time by 4-5 Hours

Source: MIRA-2 CSR table #14.2.3.2.1. PP population is the per protocol population.

Note: Worsening of accommodation was defined as an amplitude decrease of greater than 1 diopter.

Average Time to Return to ≤ 0.2 mm of Baseline PD

<table>
<thead>
<tr>
<th>Overall</th>
<th>Placebo</th>
<th>Nyxol</th>
<th>Δt = 3.5 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Eye</td>
<td>2.3</td>
<td>1.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Non-Study Eye</td>
<td>2.9</td>
<td>2.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>1.4</td>
<td>1.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Tropicamide</td>
<td>3.4</td>
<td>2.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Paremyd</td>
<td>3.6</td>
<td>2.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Mydriatic Agent</td>
<td>7.5</td>
<td>6.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Dark Irides</td>
<td>5.1</td>
<td>4.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Light Irides</td>
<td>8.3</td>
<td>6.1</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Source: MIRA-2 CSR table #14.2.3.2.1. PP population is the per protocol population.
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
  - 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.

Path to Registration
1. Complete a second RM Phase 3 trial with increased subjects ~330 to also meet 24-hour safety population exposure
2. Complete RM trial with 20 subjects ages 3 to 11 per pediatric plan
3. Complete registration batches with 1-year CMC stability and make commercial batches

Submit NDA by Late 2022

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

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

GlobalData market research report


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

$5 - $20 Price range surveyed for cash pay per patient with room for physician markup

> 100M+ General and specialty eye exams per year

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

> $6B Eye Exam Market Exams, the third-largest category, grew faster than both prescription lenses and frames

Physician's Use of Mydriatic Agents

- Tropicamide Alone: 52%
- Tropicamide and Phenylephrine: 18%
- Phenylephrine Alone: 16%
- Paremyd®: 9%
- Cyclopentolate: 5%
- Others: 9%

Use of phenylephrine, tropicamide, Paremyd®, or combinations of such comprise nearly 95% of dilating eye drops used by eyecare professionals.

OptoMap: Retinal screening for those wanting to avoid dilations but not a replacement for full dilated eye exam → $40-65 paid by patients

1. GlobalData market research report
Nyxol®

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

Phentolamine Mesylate
2021: The Time for Presbyopia Drops

Headlines From Academia and Industry Articles Thru the Year with an Early First Approval

FDA APPROVAL OF ABBVIE EYE DROP A NEW MOMENT IN PRESBYOPIA

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

-OIS

Presbyopia treatment options now and on the horizon

Presbyopia — A Review of Current Treatment Options and Emerging Therapies

Presbyopia-Correcting drops: The next frontier

Presbyopia Treatment Market Size Projected to Rise Lucratively by 2026 end

Sources: Academic review articles, journals, and publications
Presbyopia – Chronic Opportunity

Aging Population Drives Demand for Alternatives to Reading Glasses & Very Large Market

The Problem

- Lens loses ability to change shape when viewing objects up close as we age
- Dependence on reading glasses for intermittent and prolonged use
- Growing need for therapies that improve, rather than hinder, quality of life

"Effectively everyone over 40 will have the problems with reading."

Physician KOL

Seeking Treatment Findings

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

No Currently Approved Drug Therapies

120 M Patients

~$9-$18B Market Opportunity

Market Assumptions:
Total patients - 120 million patients
Price per month - $50+
Patients considering eyedrops - ~50%
Refills (Months) - 3 to 6

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

Pupil Modulation Eye Drops May Replace Reading Glasses

Nyxol’s Potential Differentiated Solution

- “Pin-hole” effect of Nyxol and low dose pilocarpine may improve near vision by enhancing depth of field as validated by other devices/therapies
- More durable combination of two miotics affecting different muscles (iris dilator and sphincter) involved in pupil size modulation
- Tolerable use with minimal side effects expected with chronic evening use of Nyxol and daytime use of fractional concentration of pilocarpine

“This would just become part of my daily routine for my eyes to be able to see things up close. How convenient is that?”

Presbyopic Patient, Age 49
Product Profile: Nyxol® + Low-Dose Pilocarpine (LDP) Combo

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

0.75% Nyxol

- Iris Dilator Muscle Inhibition

0.4% LDP

- Iris Sphincter Muscle Activation

• Phentolamine (alpha1/2 antagonist) approved non-ocular injectable indications decade(s) ago 505(b)(2)
• Novel MOA on iris dilator with 24+ hour durability
• Moderate 1+mm pupil reduction
• No daytime redness w/ chronic evening dosing Nyxol
• Well-tolerated with no systemic effects
• Stable, preservative-free, single use vial

Source: 1) Nyxol® data from 8 completed trials; Pilocarpine Product label and Literature

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

505(b)(2) Novel MOA on iris dilator with 24+ hour durability

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

Daytime drop

Evening drop
Presbyopia VEGA-1 Phase 2 Design
Randomized, Double-Masked, Placebo-Controlled, Multi-Center One-Week Trial

VEGA-1

Visits 1 and 2:
- Visit 1: Baseline, Evening Dosing (3-4 doses), LDP Drop
- Visit 2: Baseline, No Treatment, LDP Drop

Treatment Arms:
- Nyxol + LDP
- Nyxol Alone
- LDP Alone
- Placebo Alone

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

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)

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.
Primary Endpoint: % of Subjects ≥ 15 Letter Gain in Photopic DCNVA at 1 Hour

Primary Endpoint Was Significantly Met for Nyxol + LDP Gaining ≥ 15 Letters Near Vision

VEGA-1 Phase 2 Trial

Primary Endpoint: Percent of Subjects with ≥ 15 Letters DCNVA Improvement from Baseline Binocular (PP Population)

Time (Hours) Placebo (n=43) Nyxol+LDP (n=43)

p=0.003 61%

Secondary Endpoint: Percent of Subjects with ≥ 10 Letters DCNVA Improvement from Baseline Binocular (PP Population)

Time (Hours) Placebo (n=43) Nyxol+LDP (n=43)

p=0.006 79%

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

Source: VEGA-1 Table 14.2.1.2 % of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters is 3 lines and 10 letters is 2 lines.
Efficacy Endpoints: % of Subjects ≥ 15 Letter DCNVA Gain Across Timepoints

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

Source: VEGA-1 TLR Table 14.2.1.2 Percent of Subjects with Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters is 3 lines.
2nd Endpoint: % of Subjects ≥ 15 Letter Gain In Near & < 5 Letter Loss In Distance

Phase 3 Approval Endpoint Confirmed Greater Efficacy of Combo over Components at Multiple Timepoints

VEGA-1 Phase 2 Trial

Statistics Compared to Nyxol+LDP arm

Percent of Subjects with 15 Letter Improvement in DCNVA and < 5 Letter Loss in BCDVA Binocular

![Bar chart showing percent of subjects with 15 letter improvement in DCNVA and less than 5 letter loss in BCDVA at different time points.]

- Placebo (n=43): 14% at 0.5 hours, 26% at 1 hour, 28% at 2 hours
- Nyxol+LDP (n=43): 61% at 0.5 hours, 61% at 1 hour, 63% at 2 hours
- Nyxol (n=30): 33% at 0.5 hours, 28% at 1 hour, 14% at 2 hours
- LDP (n=31): 0% at 0.5 hours, 42% at 1 hour, 39% at 2 hours

Source: VEGA-1 TLR Table 14.2.2.2 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)

Even with a small sample size, combination arm provided statistically meaningful results at 30 min and 2 hours vs. LDP and Nyxol alone arms.
Secondary Endpoint: Mean Pupil Diameter Over Time

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

VEGA-1 Phase 2 Trial

Best Eye
Mean Pupil Diameter

**p<0.01
***p<0.0001

Daily Evening Nyxol Dosing 12hr minimum interval to Time 0

Baseline

Placebo (n=43) Nyxol+LDP (n=43) Nyxol (n=30) LDP (n=31)

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

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

- No serious AEs, almost all AEs were mild
- 0% headaches or brow aches reported for Nyxol+LDP arm
- ≤ 5% mild, transient conjunctival hyperemia AEs in Nyxol+LDP arm
- No change in distance vision for Nyxol + LDP arm
  - 0% had ≤ 5 letter distance loss in photopic lighting
  - Only 5% distance loss in mesopic lighting
- No change in IOP

Source: VEGA-1 Study Results (Safety Population, n=150); Only a single subject difference between mITT (n=148) and PP population (n=147)
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 compared to VUITY™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy (all time-points)</td>
<td>✓ +</td>
</tr>
<tr>
<td>Safety: Maintain Distance Vision (especially at night)</td>
<td>✓ +</td>
</tr>
<tr>
<td>Safety: Tolerability (no headaches)</td>
<td>✓ +</td>
</tr>
<tr>
<td>Durability (at least 6 hours)</td>
<td>✓ +</td>
</tr>
<tr>
<td>Fast Onset (within 30 mins)</td>
<td>✓ +</td>
</tr>
<tr>
<td>Convenience (daily drops)</td>
<td>✓</td>
</tr>
<tr>
<td>Tunable Pupil Modulation</td>
<td>✓ +</td>
</tr>
</tbody>
</table>

ASCRS (July 2021) Abstract# 76645 (Phase 2) and 74336 (Phase 3) and VUITY™ Label

✓ +: Indicates better compared to Vuity
✓ : Indicates comparable to Allergan/AbbVie based on Phase 3 BID dosing (NCT04983589)
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)

Other Cholinergic Agonists*

Visus
(Brimonol®; brimonidine + carbachol)

Lenz
(PRX-100, aceclidine)

Orasis
(CSF-1; Low dose pilo)

Ocuphire
(1.25% pilo)

Eyenovia
(MicroLine, 1 or 2% pilo)

Allergan
(Vuity®; 1.25% pilo)

Ocuphire
(0.75% hyzol + 0.4% pilo)

Alpha Antagonist & pilocarpine*

Next Steps: Advance into Phase 3
Presbyopia Registration Trials in 1H 2022
Towards a Potential NDA Filing in 2023

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

Phase 3
- Novartis
(EV-06)

Phase 2
- Allergan
(Vuity®; 1.25% pilo)

Phase 1
- Orasis
(CSF-1; Low dose pilo)
- Ocuphire
(0.75% hyzol + 0.4% pilo)

33 Corporate Websites, Grzybowski, A, Markelwicte A, Zemaitiene R; A Review of Pharmacological Presbyopia Treatment. 2020
Nyxol®

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

Phentolamine Mesylate
Im 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

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

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>
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>
</tr>
</thead>
<tbody>
<tr>
<td>Patients willing to try a new eye drop treatment</td>
</tr>
<tr>
<td>Patients avoiding driving at night</td>
</tr>
</tbody>
</table>
NVD LYNX-1 Phase 3 Registration Design
Ongoing Randomized, Double-Masked, Placebo-Controlled Two-Week Trial

LYNX-1
- 20 US sites
- ~160 patients with NVD

Randomization

Eligibility Screening

0.75% NyxoL daily evening dose (14 days)

Placebo daily evening dose (14 days)

Phase 3 Initiated in Late 4Q20
Top Line Expected Early 2022

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)
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

- Placebo n=16
- Nyxol n=32

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

Source: NYX-021

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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR</td>
<td>Diabetic Retinopathy</td>
</tr>
<tr>
<td>DME</td>
<td>Diabetic Macular Edema</td>
</tr>
<tr>
<td>wAMD</td>
<td>Wet Age-Related Macular Degeneration</td>
</tr>
</tbody>
</table>
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
- 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 Retina Treatment Options for Diabetics

Large, Unmet Need in Diabetic Eye Diseases (US)

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

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

- 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.

- 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)

Tao Yan et al. APX3330 Promotes Neurorestorative Effects after Stroke in Type One Diabetic Rats. Aging and Disease. Vol 9, Oct 2018

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 for Retinal Indications

**APX3330: Well-tolerated Oral Dose up to 600mg/day**

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

*Twice a day dosing of APX3330 being developed to provide steady state effectiveness with a tolerable chronic safety profile*
**DR/DME ZETA-1 Phase 2b Design**

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

### ZETA-1

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

#### Eligibility Screening

#### Randomization

1:1

#### APX3330 600mg

- **Twice daily oral dose (24 weeks)**

#### Placebo

- **Twice daily oral dose (24 weeks)**

### Endpoints

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

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

**Exploratory:**
- Labs / PK

### Phase 2b Start Initiated in April 2021

### Top Line Expected in 2H22
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
Boards and Milestones
Ocuphire's World-Class Medical Advisory Board
Fortunate for the Insights of Leading KOLs & Drug Candidate Co-Founders
Ocuphire Board of Directors
Seasoned Directors with Decades of Drug Development, M&A/Financings, and Ophthalmology
<table>
<thead>
<tr>
<th>2021</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔️ Report Positive Phase 3 Data for RM (MIRA-2)</td>
<td>✔️ Report Phase 3 Data for NVD</td>
</tr>
<tr>
<td>✔️ Report Positive Phase 2 Data for Presbyopia (VEGA-1)</td>
<td>✔️ Report 2nd Phase 3 Data for RM</td>
</tr>
<tr>
<td>✔️ New Patent Claims for Presbyopia</td>
<td>✔️ Report Pediatric Data in RM</td>
</tr>
<tr>
<td>✔️ ASCRS 2021 Presentation for MIRA-2 &amp; VEGA-1</td>
<td>✔️ Submit Nyxol NDA for RM</td>
</tr>
<tr>
<td>✔️ Manufacture 3xRegistration Batches for Nyxol Blow-Fill-Seal (BFS) Eye Drops</td>
<td>✔️ Report Phase 2 Data for DR/DME</td>
</tr>
<tr>
<td>✔️ Initiate 2nd Phase 3 RM and Pediatric RM trial</td>
<td>✔️ Initiate Two Phase 3 Presbyopia Trials</td>
</tr>
<tr>
<td></td>
<td>✔️ Initiate Phase 3 Chronic Safety Trial</td>
</tr>
</tbody>
</table>

Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)
### Recent FDA Ophthalmology Drug Approvals

**FDA Record Number of Drugs Approved for Front and Back of the Eye in 2021**

<table>
<thead>
<tr>
<th>Company</th>
<th>Drug</th>
<th>Indication</th>
<th>Date</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santen</td>
<td>Cyclosporine Topical Ophthalmic Emulsion</td>
<td>Severe Vernal Keratoconjunctivitis</td>
<td>June 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td>Oyster Point</td>
<td>OC-01 Nasal Spray</td>
<td>Dry Eye Disease</td>
<td>October 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td>Ocular</td>
<td>Dextenz™</td>
<td>Ocular Itching Associated with Allergic Conjunctivitis</td>
<td>October 2021</td>
<td>sNDA Approved</td>
</tr>
<tr>
<td>BAUSCH + Health</td>
<td>Xipere™</td>
<td>Macular Edema associated with Uveitis</td>
<td>October 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td></td>
<td>MydCombi™</td>
<td>Fixed combination mydriatic microdose system</td>
<td>October 2021</td>
<td>CRL, now drug/device classification</td>
</tr>
<tr>
<td></td>
<td>Susvimo™</td>
<td>Wet-AMD</td>
<td>October 2021</td>
<td>New Product Approval</td>
</tr>
<tr>
<td></td>
<td>Vuity ™</td>
<td>Presbyopia</td>
<td>October 2021</td>
<td>Approved Two months in advance</td>
</tr>
</tbody>
</table>

Source: Company websites, 2020 10K annual reports, Q2 2021 quarterly reports
## OCUP – Market Snapshot

### Sufficient Cash Runway Through 2022

<table>
<thead>
<tr>
<th>Ticker</th>
<th>OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>$4.02</td>
</tr>
<tr>
<td>Market Cap</td>
<td>~$70 M</td>
</tr>
<tr>
<td>Common Shares Outstanding</td>
<td>17.3 M</td>
</tr>
<tr>
<td>Cash</td>
<td>$22.2 M</td>
</tr>
<tr>
<td>Cash Runway</td>
<td>Sufficient through 2022</td>
</tr>
<tr>
<td>Average Daily Volume</td>
<td>~200 K</td>
</tr>
<tr>
<td>Short Interest</td>
<td>~445K; &lt;3% of Float</td>
</tr>
</tbody>
</table>

**Source:** FactSet

**Research Analyst - Institutional Coverage on OCUP**

<table>
<thead>
<tr>
<th>Name</th>
<th>Firm</th>
</tr>
</thead>
<tbody>
<tr>
<td>James Molloy</td>
<td>Alliance Global Partners</td>
</tr>
<tr>
<td>John Newman</td>
<td>Canaccord Genuity</td>
</tr>
<tr>
<td>Kristen Kluska</td>
<td>Cantor Fitzgerald</td>
</tr>
<tr>
<td>Prakhar Agrawal</td>
<td>Jones Trading</td>
</tr>
</tbody>
</table>

**Close on 11-1-21**

**As of 11-1-21**

**As of 11-1-21**

**As of 9-30-21**

**Guidance as of 9-30-21**

Source: FactSet
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
**Primary Endpoint of APX3330 ZETA-1 Trial**

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

---

### 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>Microaneurysm only</td>
<td>Mild NPDR</td>
<td>Moderate NPDR</td>
<td>Moderately Severe NPDR</td>
<td>P Mod – DR 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**