

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:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.0001 par value	OCUP	Nasdaq Capital Market

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.**(d) Exhibits**

Exhibit Number	Exhibit Description
<u>99.1</u>	Press Release, dated January 5, 2022
<u>99.2</u>	Corporate Presentation, dated January 5, 2022

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: 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 (DLVD), 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 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

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Exhibit 99.2



Ocuphire Corporate Presentation

Mina Sooch CEO

January 5, 2022

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 pre-clinical and clinical trials; (iii) regulatory requirements or developments; (iv) changes to clinical trial designs and regulatory pathways; (v) changes in capital resource requirements; (vi) risks related to the inability of the Company to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vii) legislative, regulatory, political and economic developments, and (viii) the effects of COVID-19 on clinical programs and business operations. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by the Company from time to time with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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OCUPHIRE PHARMA

NASDAQ: OCUP

A Look Ahead Into 2022:

- Nyxol MIRA-3 trial for RM **EARLY 2022**
- Nyxol Pediatric trial for RM **EARLY 2022**
- Nyxol LYNX-1 trial for NVD **EARLY 2022**
- APX3330 ZETA-1 trial for DR/DME **2H22**

RM = Reversal of Mydriasis
NVD = Night Vision Disturbances
DR/DME = Diabetic Retinopathy/Diabetic Macular Edema

■ 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

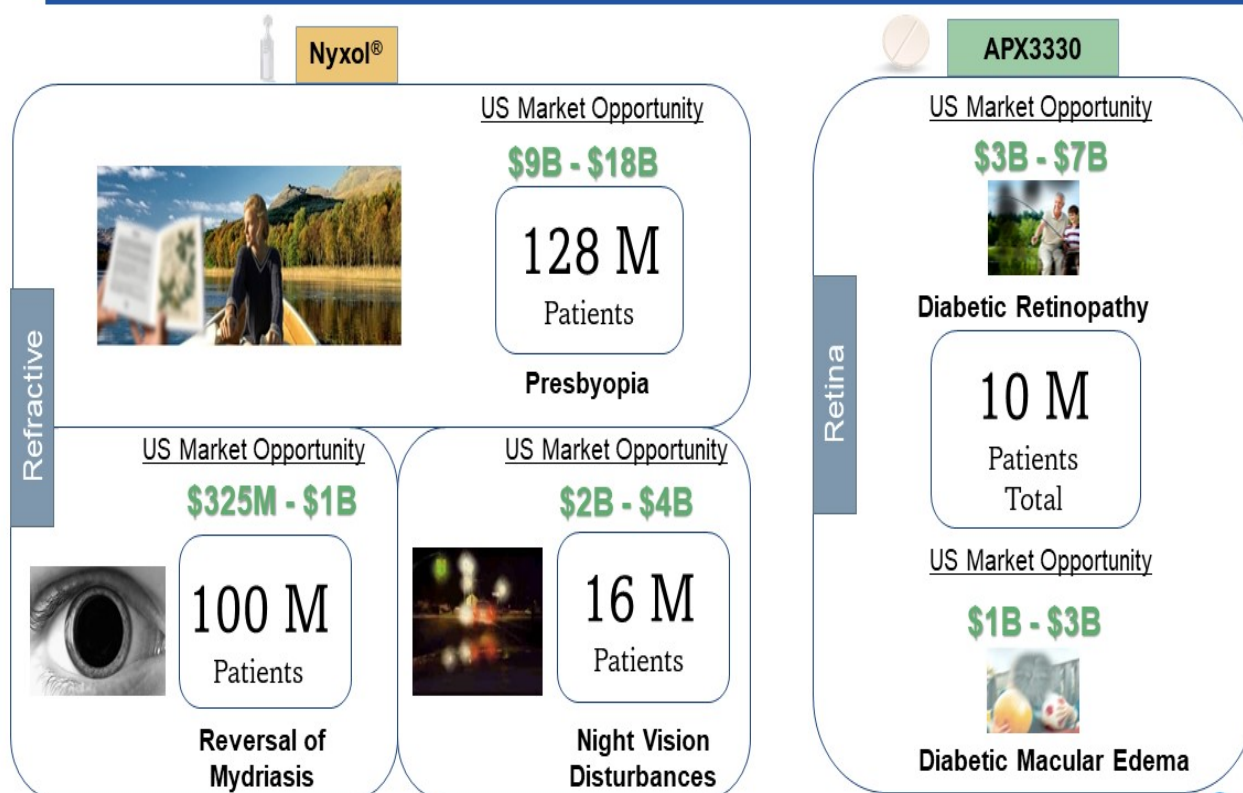
- ✓ Addressing 4 large markets with unmet needs: RM, Presbyopia, NVD and DR/DME
- ✓ Successful trial execution with 2 recent positive Phase 3 & Phase 2 data read-outs for Nyxol in RM and Nyxol + LDP Presbyopia, respectively
- ✓ Stable, small-molecule drugs with commercial scalability
- ✓ Robust and growing 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



Ocuphire Pipeline & Clinical Milestones

Multiple Phase 3 & Phase 2 Clinical Data Readouts Anticipated Over The Next Year

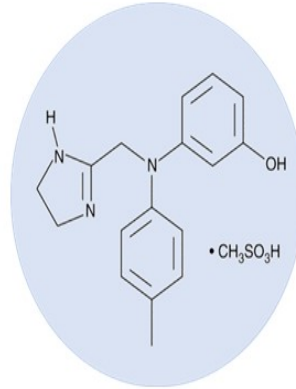
Product Candidate	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Regulatory Approval	Anticipated Milestones
0.75% Nyxol® Eye Drop	Reversal of Mydriasis (RM)						<input type="checkbox"/> MIRA-3 Phase 3 data expected in early 2022 (n=330) <input type="checkbox"/> MIRA-4 Pediatric safety study data expected in early 2022 (n=20)
0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops	Presbyopia (P)						<input type="checkbox"/> VEGA Phase 3 program initiated in 1H22 (n=300x2)
0.75% Nyxol® Eye Drop	Dim Light or Night Vision Disturbances (NVD)						<input type="checkbox"/> LYNX-1 Phase 3 data expected in early 2022 (n=140)
APX3330 Oral Pill	Diabetic Retinopathy (DR)/ Macular Edema (DME)						<input type="checkbox"/> ZETA-1 Phase 2 data expected in 2H22 (n=90)
APX2009 (Intravitreal or Local Delivery)	DME or Wet Age-Related Macular Degeneration (wAMD)						<input type="checkbox"/> Seeking partner funding for IND enabling studies and further development

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

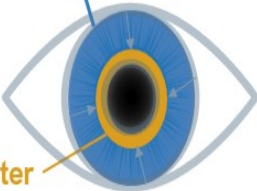



NVD

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	
Blocking α1 Reduces Pupil Size	Blocking α1 Dilates Blood Vessels
<div><p>Iris Dilator Muscle</p><p>Iris Sphincter Muscle</p></div> <div><p>Nyxol blocks α1 receptors on the Iris Dilator Muscle</p><p>↓</p><p>Decreases Pupil Size (Moderate Miosis)</p></div>	<div><p>Phentolamine mesylate is currently approved for 2 indications:</p><ul style="list-style-type: none">• Regitine® (Pheochromocytoma) – intravenous injection approved in 1952• OraVerse® (Reversal of oral anesthesia) – intramuscular injection approved in 2008</div>
<div><div>9</div><div>Phase 1, Phase 2, and Phase 3 Trials</div></div> <div><div>> 330</div><div>Subjects Dosed</div></div> <div><div>Exposure in Humans</div><div>28</div><div>Days</div></div> <div><div>Patent Coverage</div><div>2034+</div></div>	<div>505(b)(2) Regulatory Approval Pathway</div>

Nyxol Product Candidate Profile

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

Nyxol: 0.75% Phentolamine Ophthalmic Solution Preservative Free, EDTA Free, and Stable		
Effective	Favorable Safety Profile	Durable
Nyxol Improves Vision by Decreasing Pupil Size ↑ Near & Distance Visual Acuity ↑ Contrast Sensitivity (night) 	No Systemic Effects No Changes in Blood Pressure No Changes in Heart Rate Well-Tolerated Topical Effects Mild, Transient, Reversible Eye Redness IOP Unchanged or Decreased No Headaches Favorable safety profile vs competitors	Effects Last ≥ 24 Hours 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 

NYXOL[®]
for
REVERSAL OF
MYDRIASIS
(RM)

RM



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 year¹



> 65% of Patients

Report moderate to severe negative impact of dilated exams¹



80% of Patients

Likely to request a reversal of dilation drop²



\$10 - \$20

Price range for cash pay per patient with room for physician markup¹



95% of Dilating Drops

Used by Eye Care Providers were used in MIRA Clinical Trials¹

No Current Commercially Available Treatments

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

\$325M - \$1B

Estimated US RM
Market Opportunity

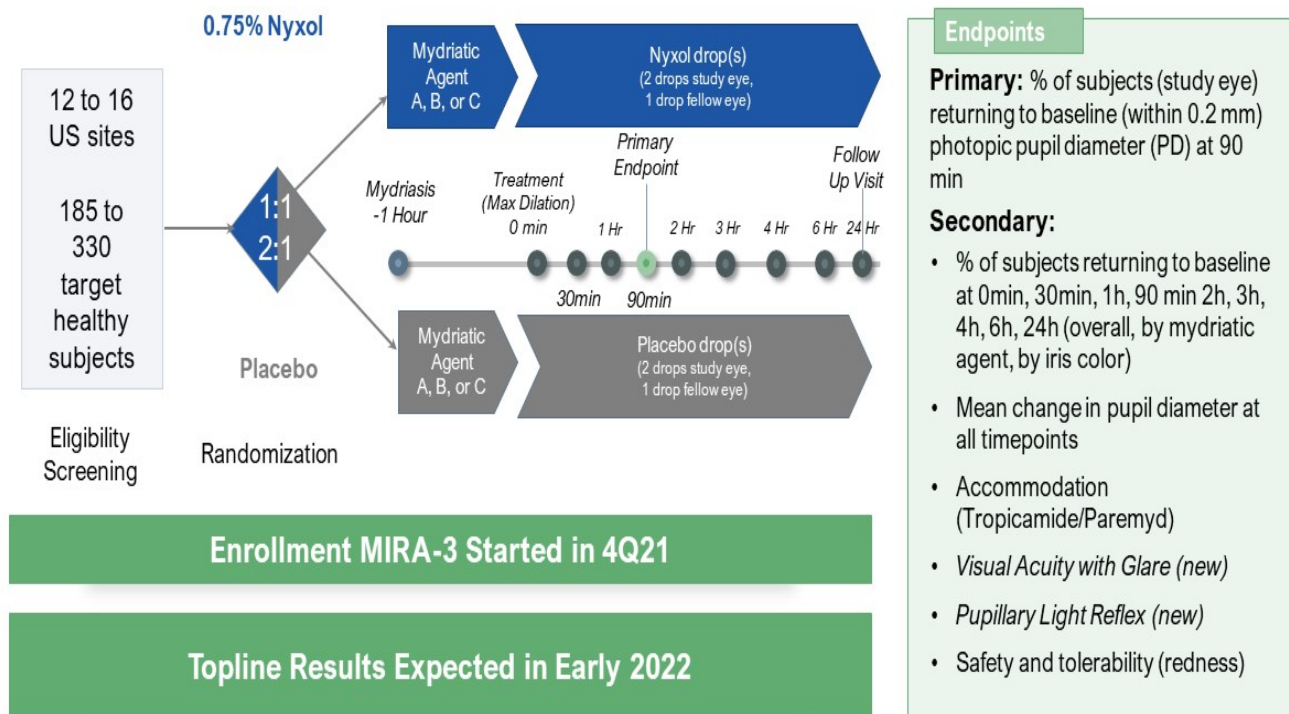
1. GlobalData Market Research Report

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)

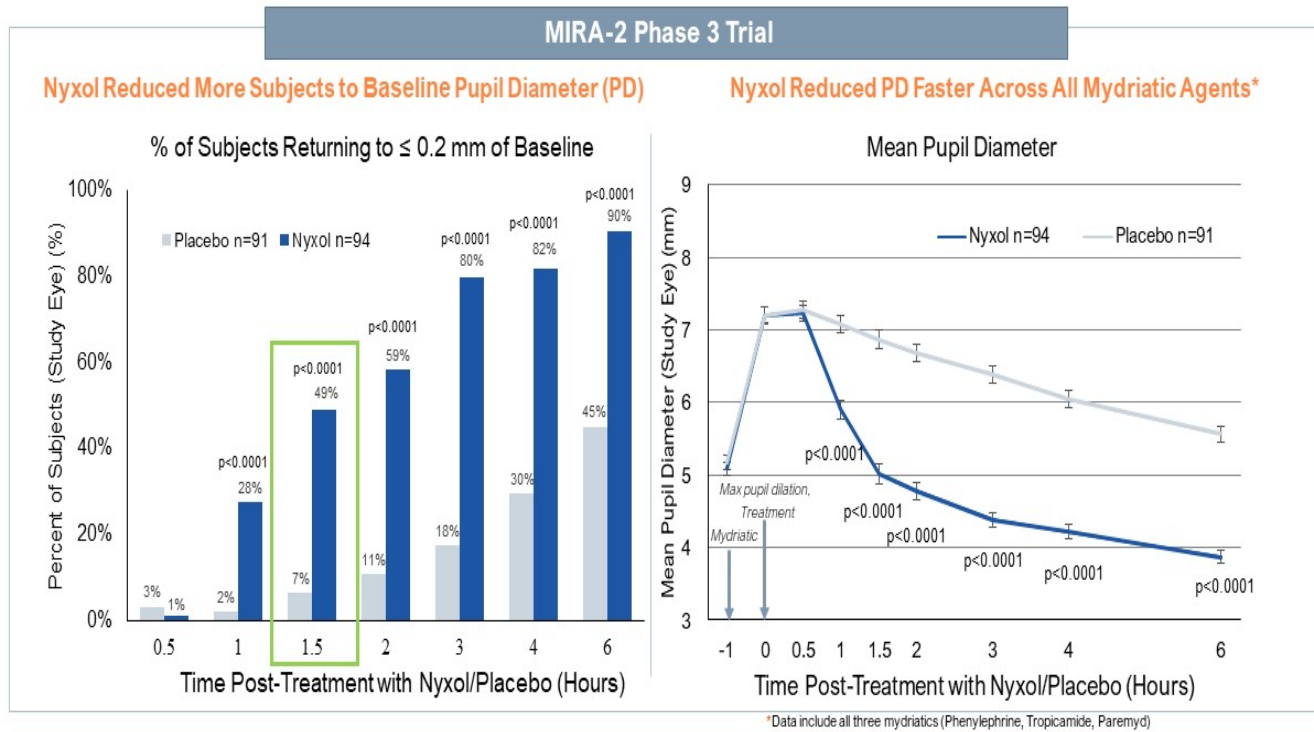
MIRA-2/3 Phase 3 Registration Trial Design

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



MIRA-2 RM Phase 3 Trial Met Primary & Secondary Endpoints

49% Of Patients Returned To $\leq 0.2\text{mm}$ Of Baseline At 90mins Vs. 7% Placebo



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

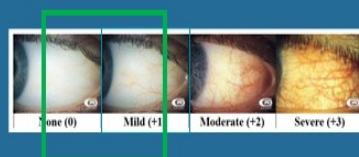
- Met all key secondary endpoints with high statistical significance

- 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 $\geq 5\%$ 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

Pre-Commercial & Go-To-Market Strategy

Activities Underway To Support Capital-Efficient Nyxol RM Commercial Launch



Market Development

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



Physician Targeting

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

Eye Care Practitioners in U.S.	
Total Retina Specialists	3,000
Total Optometrists	46,000
Total Ophthalmologists	20,000



Patient Journey

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)



Brand Awareness Across Eye Care Professionals

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



P

NYXOL[®] for PRESBYOPIA



*"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

September 22, 2021 | 11 min read

SAVE

Treatment landscape for presbyopia evolving toward noninvasive options

New options are on the horizon for presbyopia-correcting drops

August 30, 2021

Dr Marguerite B. McDonald

Ophthalmology Times Europe Journal, Ophthalmology Times Europe September 2021, Volume 17, Issue 07

Presbyopia treatment options now and on the horizon

Refractive
September 2021

Clinical Ophthalmology

Open Access Full Text Article

Presbyopia – A Review of Current Treatment Options and Emerging Therapies

Dovepress

Open access to scientific and medical research

REVIEW

Presbyopia PHYSICIAN

November 2021

Pharmaceuticals



Presbyopia PHYSICIAN

May 2021



FDA APPROVAL OF ABBVIE EYE DROP A NEW MOMENT IN PRESBYOPIA 10/29/2021

Article

Presbyopia-correcting drops: The next frontier

Pharmaceuticals are poised to enhance near vision for millions of presbyopes.

By Corinn Bergmann Koury July 1, 2021

CBS News

New FDA-approved eye drops could replace reading glasses for millions: "It's definitely a life changer"

CLINICAL UPDATE

Presbyopia-Correcting Eyedrops Move Ahead

How Presbyopia Correction Drops Will Change My Treatment Regimen

CRST Cataract & Refractive Surgery Today

"The correction of presbyopia remains ophthalmology's 'Holy Grail'..."

-OIS

Presbyopia Treatment Market Size Projected to Rise Lucratively by 2026 end

BioSpace

Ocuphire PHARMA

Presbyopia Is A Burgeoning Opportunity

Large Market Being Developed, Pupil Modulation Eye Drops May Replace Reading Glasses

The Problem

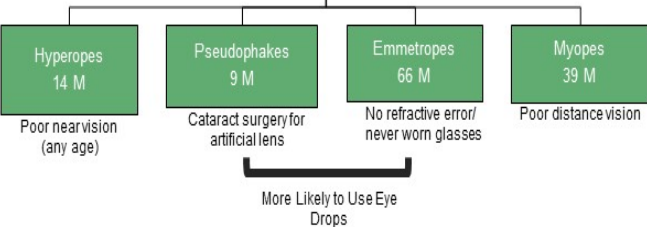
- Lens loses ability to change shape when viewing objects up close as we age
- Dependence on reading glasses for intermittent and prolonged use
- Growing need for therapies that improve, rather than hinder, quality of life

Global Reading Glasses Market (USD Billion), 2019 & 2027



>\$35B

Presbyopes (US)
~128 M



More Likely to Use Eye Drops

50% would use eye drop (37 M)



3-6 refills per year



Private Cash Pay
(Vuity \$79/refill List Price)

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

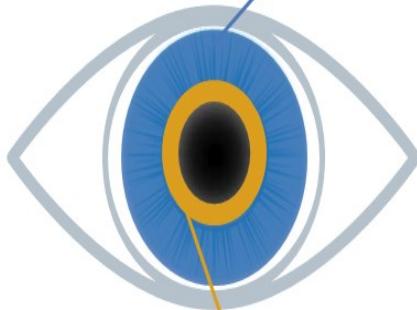


Iris Dilator
Muscle
Inhibition



Evening drop

- 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



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



Iris Sphincter
Muscle
Activation



Daytime drop

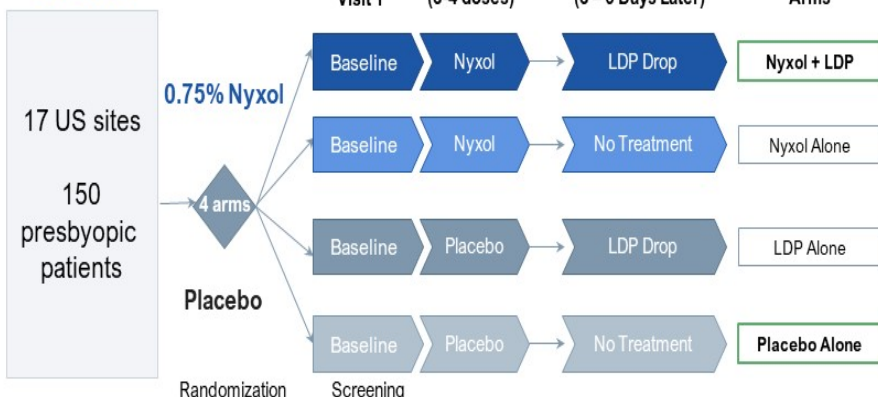
- Pilocarpine (cholinergic agonist)
- Known MOA on sphincter muscle with potent miotic effects at approved doses (1%, 2%, 4%)
- Low concentration avoids known tolerability issues:
 - headache and browache
 - redness
 - accommodative spasm causing loss of distance vision especially at night

0.4% LDP

Presbyopia VEGA-1 Phase 2 Design

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

VEGA-1



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

Endpoints

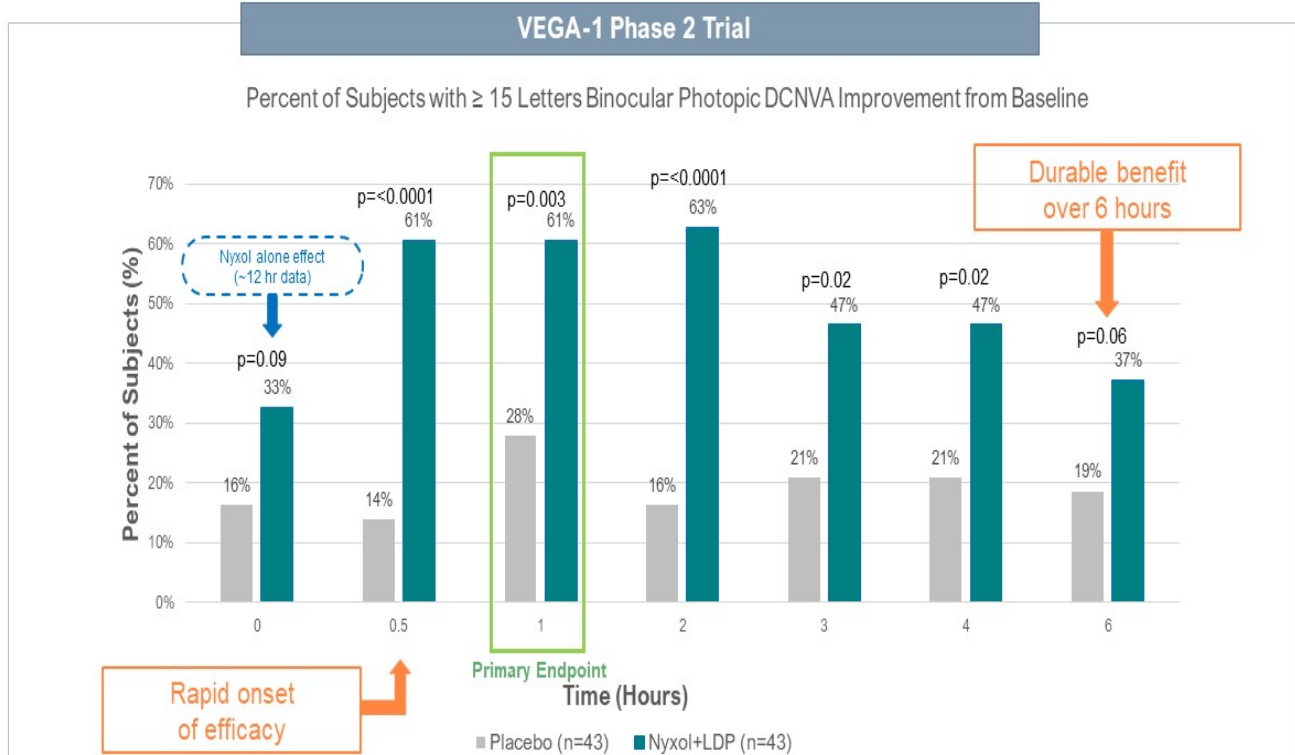
Primary: % of subjects with ≥ 3 lines of improvement in distance-corrected near visual acuity comparing Nyxol + LDP vs placebo alone at 1 hour

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)

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

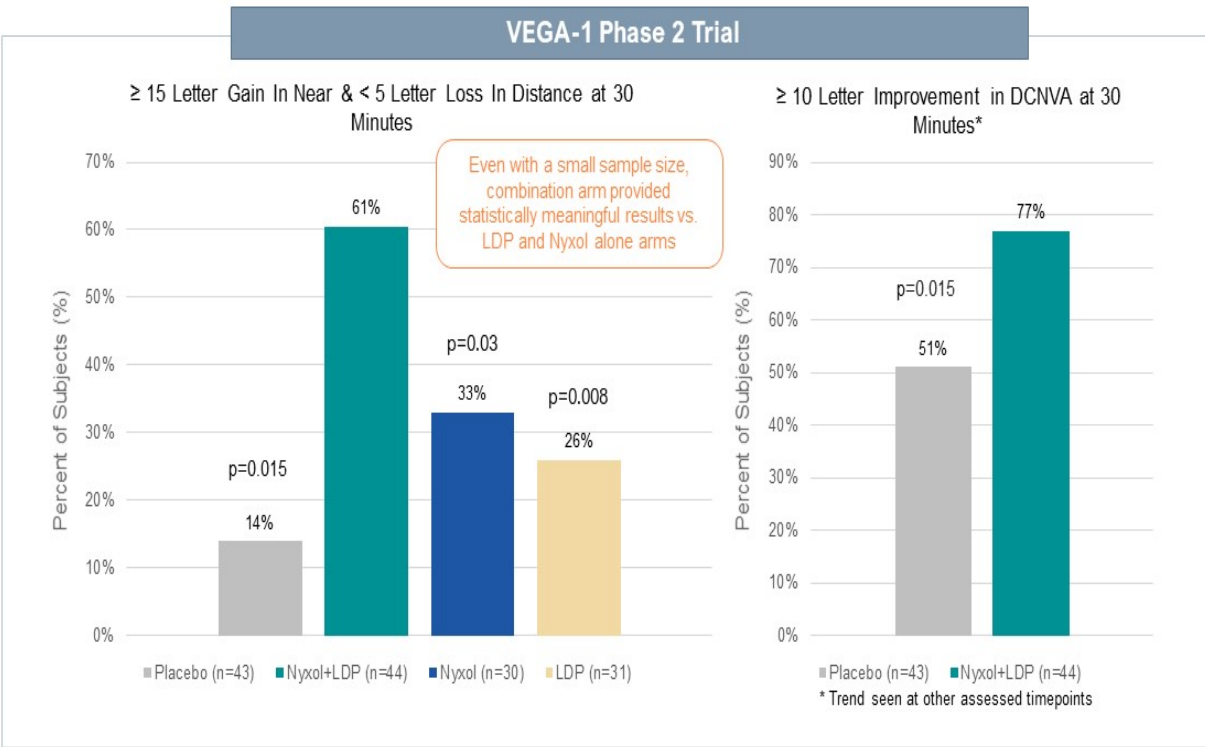


Note: PP population differs from mITT by only one subject; results were essentially identical.

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

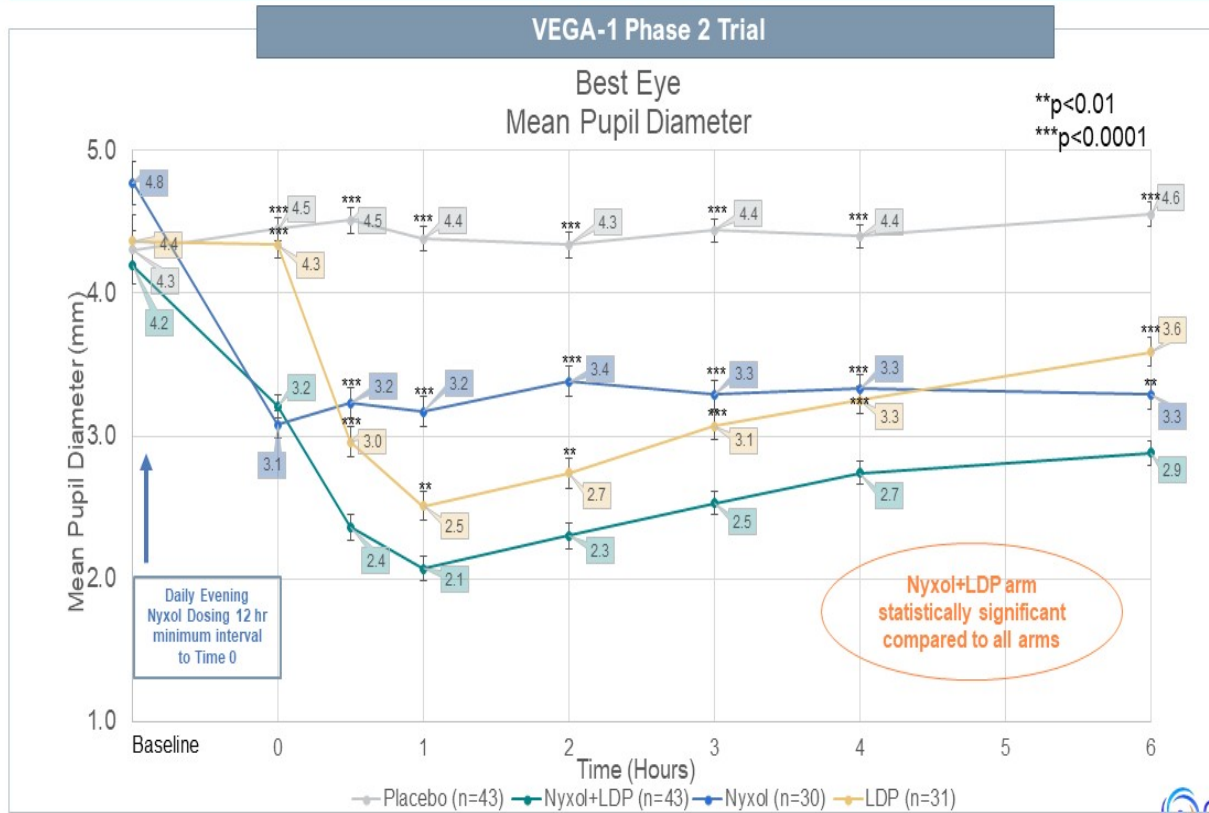
Pre-Specified Endpoints Further Demonstrate Nyxol's Component Efficacy & 10 Letter Effects



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); Table 14.2.1.2 Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point

Secondary Endpoint: Mean Pupil Diameter Over Time

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



Summary Of Positive VEGA-1 Phase 2 Results

Nyxol + LDP Had Strong Efficacy Response & Well Tolerated Safety Profile

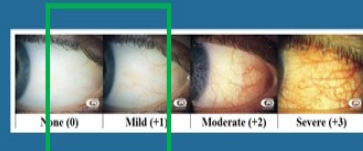
- Met primary endpoint with statistical significance at 1 hour with Nyxol® plus Low-Dose Pilocarpine (LDP)

- Met key secondary endpoints with statistical significance

- Gained 15 letters (3 lines) in near vision with less than 5 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

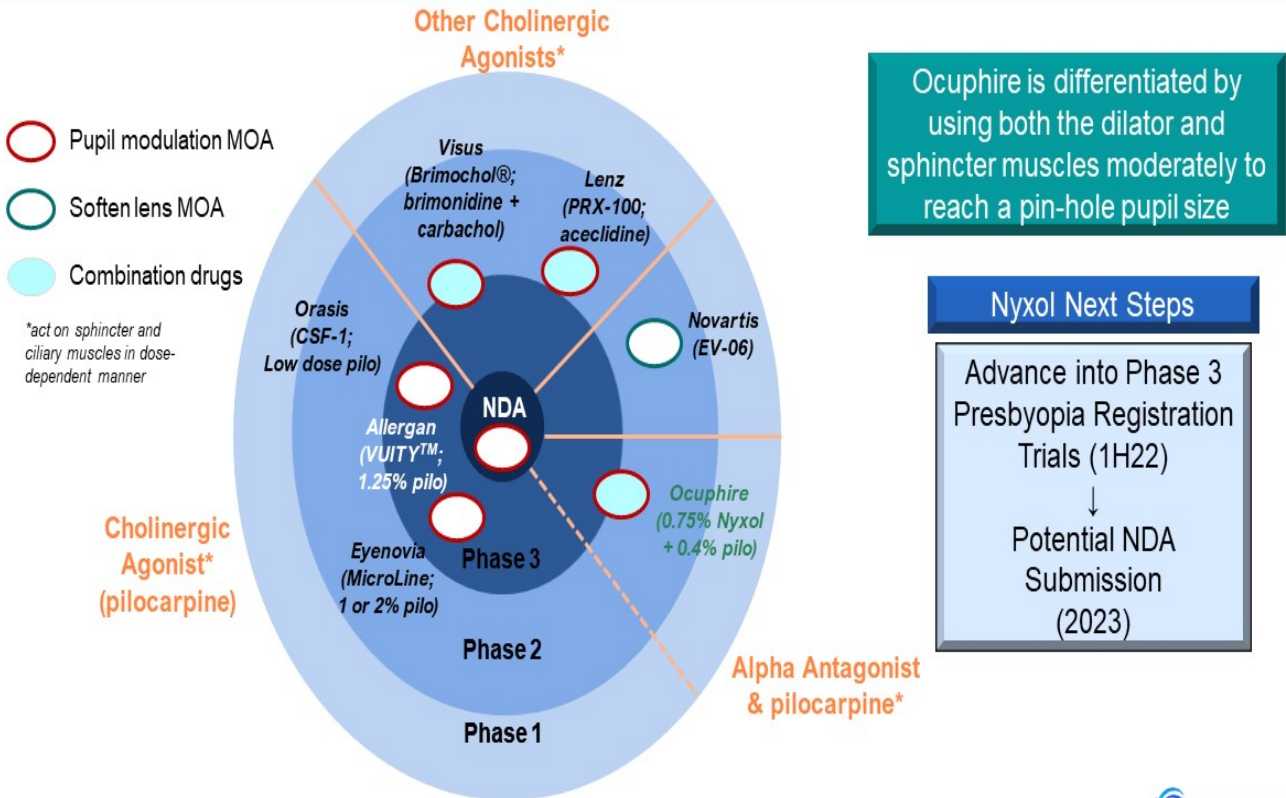
Nyxol+LDP Combination Data Outperforms In Efficacy, Safety, Durability And Onset

Nyxol's Potential Differentiated Solution

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

Presbyopia Eye Drops Competitive Landscape

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



NYXOL®

for

DIM LIGHT OR
NIGHT VISION
DISTURBANCES

NVD



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.

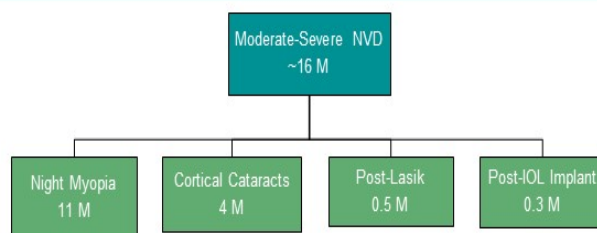
Post-LASIK, Age 42

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

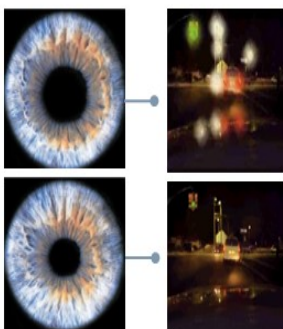


Seeking Treatment Findings

Patients willing to try a new eye drop treatment 67%

No Approved Treatments

Pupil reduction with Nyxol may offer a potential solution to peripheral optical imperfections



Before

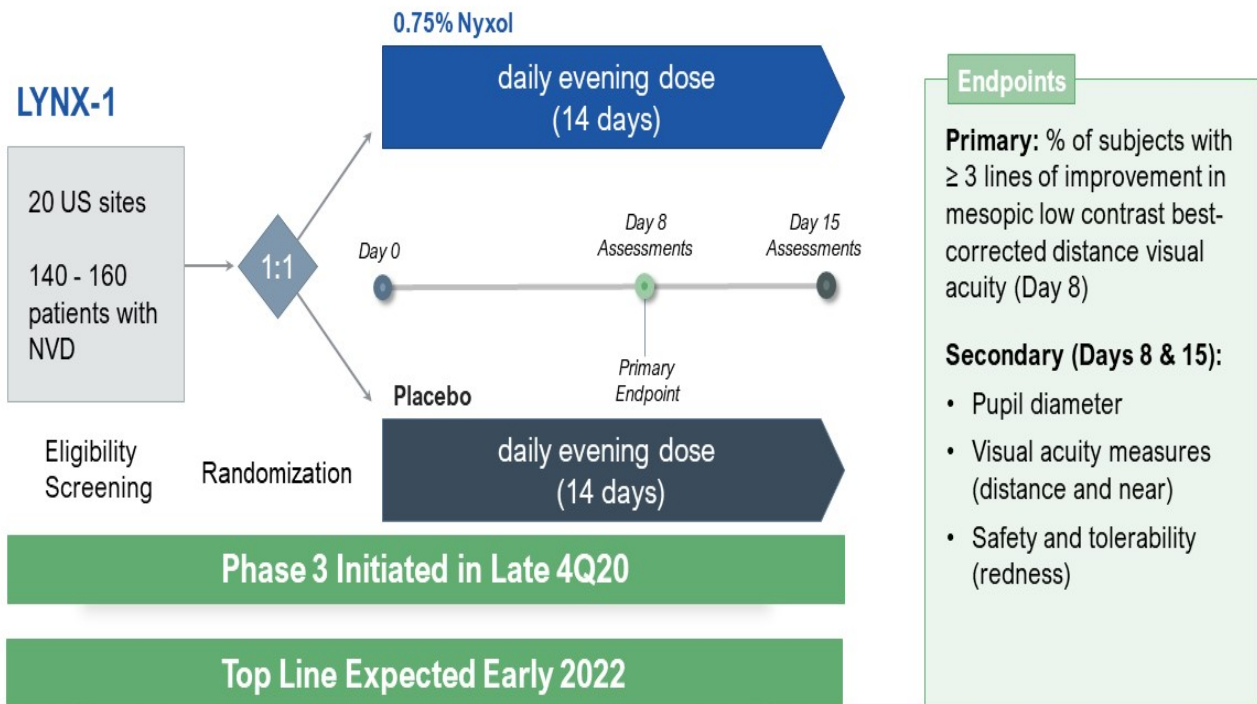
After

\$2B - \$4B

Estimated US NVD
Market Opportunity

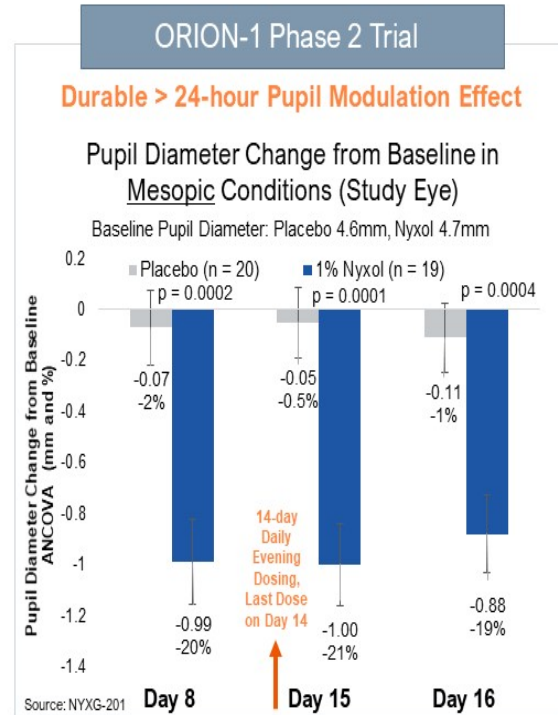
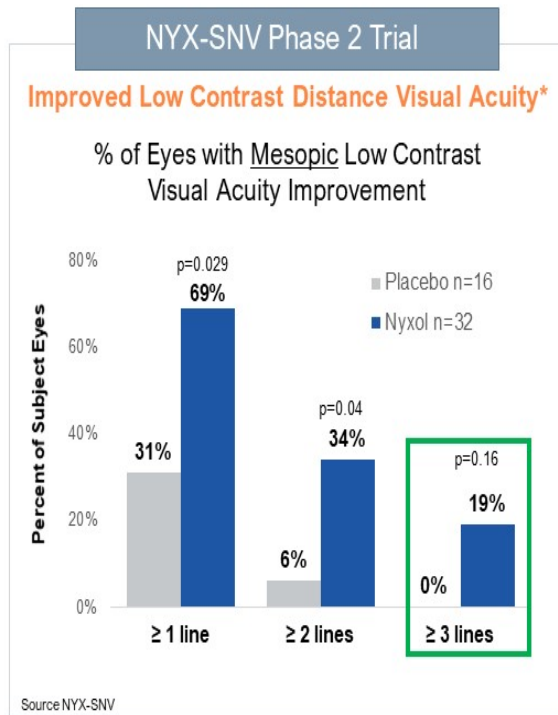
NVD LYNX-1 Phase 3 Registration Design

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



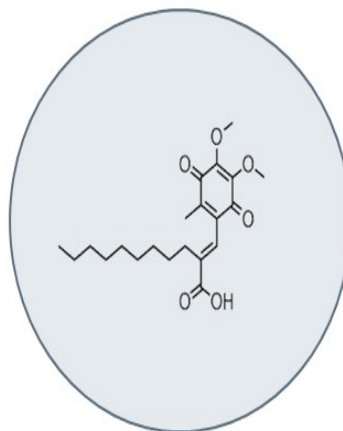
Nyxol Demonstrated Clinical Effect In NVD

Key Endpoints Observed In Multiple Phase 2 Trials



APX3330

TABLETS



DR

Diabetic Retinopathy



DME

Diabetic Macular Edema

The Problem

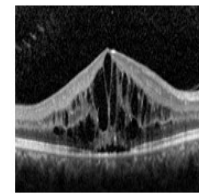
- Diabetic retinopathy (DR) and diabetic macular edema (DME) are a leading cause of vision loss worldwide
- Diabetes damages small blood vessels within the eye causing leakage, oxygen starvation, and abnormal vessel growth
- **DR patients are not routinely treated with approved injectable anti-VEGF drugs**
 - 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

DR



DME



Large, Unmet Need in
Diabetic Eye Diseases (US)

DR	~7.7M Patients
DME	~750K Patients

\$1B - \$3B

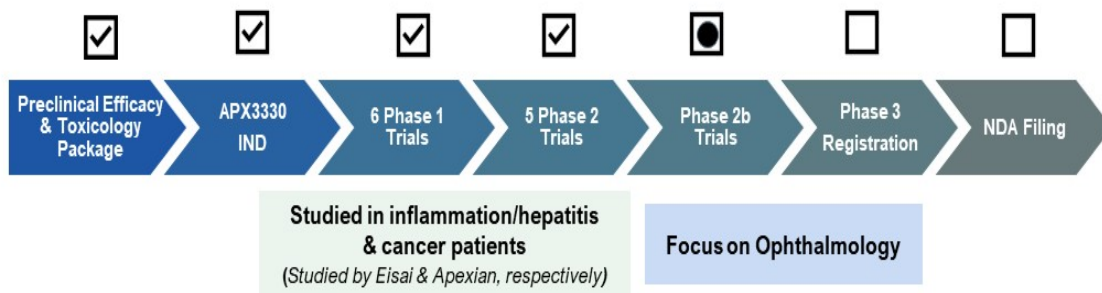
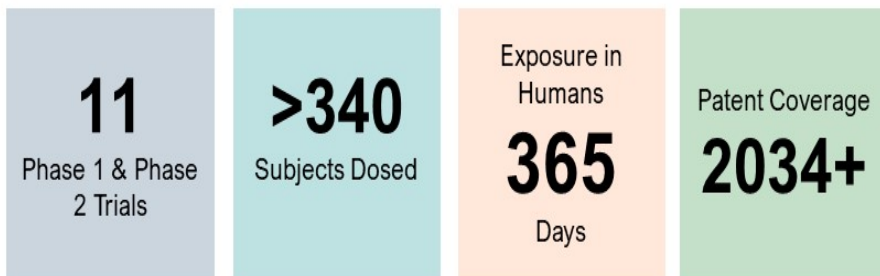
Estimated US DME
Market Opportunity

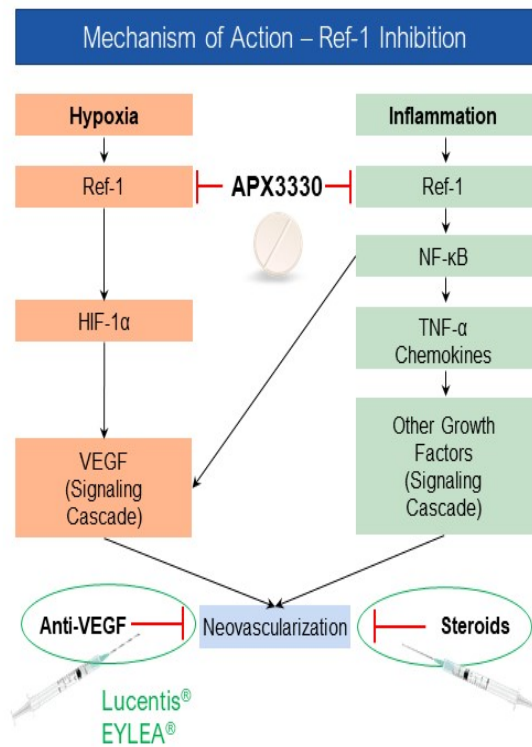
\$3B - \$7B

Estimated US DR
Market Opportunity

APX3330: Drug Development History And Patents

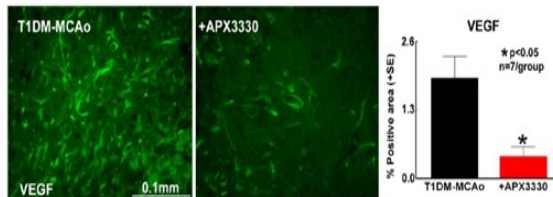
Significant Preclinical & Clinical Data Supporting Human Safety, MOA, and PK





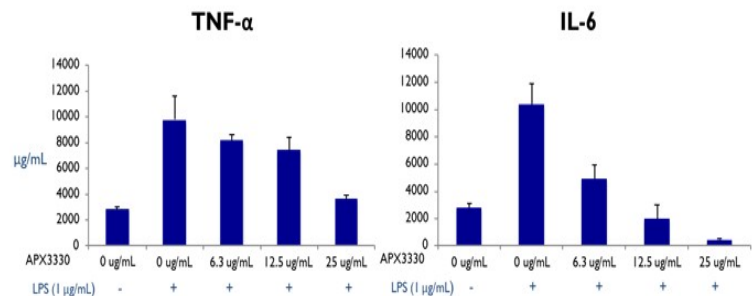
- Ref-1 (reduction-oxidation effector factor-1) is a novel target discovered by Dr. Mark R. Kelley at Indiana University School of Medicine
- APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of Ref-1
- APX3330 previously developed by Eisai for multiple hepatic inflammatory 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 Reduces VEGF Protein in the Brain of Preclinical Models

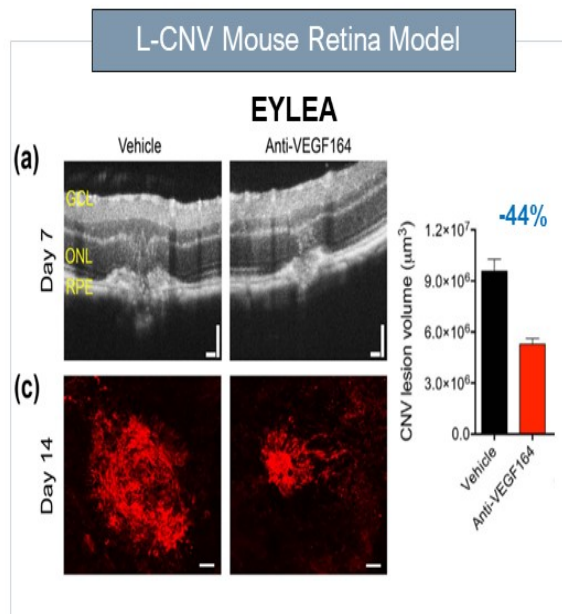
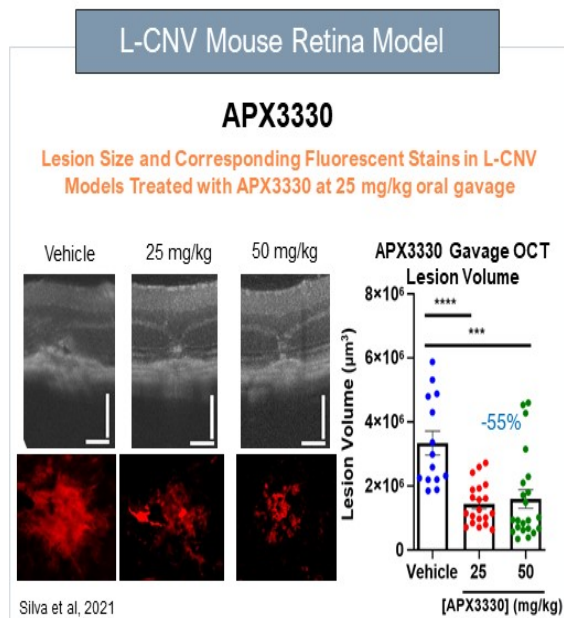


- Treatment of APX3330 (10mg/kg, oral gavage) in rats with type 1 diabetes and induced stroke shows a **significant decrease of VEGF signaling**.
- Increased VEGF is a hallmark of uncontrolled neovascularization and inflammation in diabetic retinopathies; current approved treatments successfully decrease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



- Silva et al. Oral APX3330 treatment reduces L-CNV lesions in preclinical mouse model and confirms Phase 2 DR/DME clinical dose with sufficient distribution to human retina using PBPK modeling. Presented at the ARVO 2021 Annual Meeting

- Published data on EYLEA

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



Mouse

25 mg/kg APX3330 oral gavage measured in mouse retina¹



Rat

10 mg/kg APX3330 oral gavage measured in rat eye²



Human

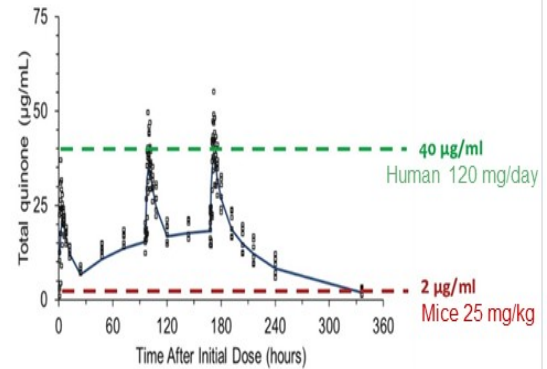
300 mg BID (600 mg/day total)

Established PBPK model predicts APX3330 reaches sufficient human retinal concentrations³



Phase 1 PK Clinical Data

Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels

Human Pharmacokinetics of APX3330 at 120 mg/day

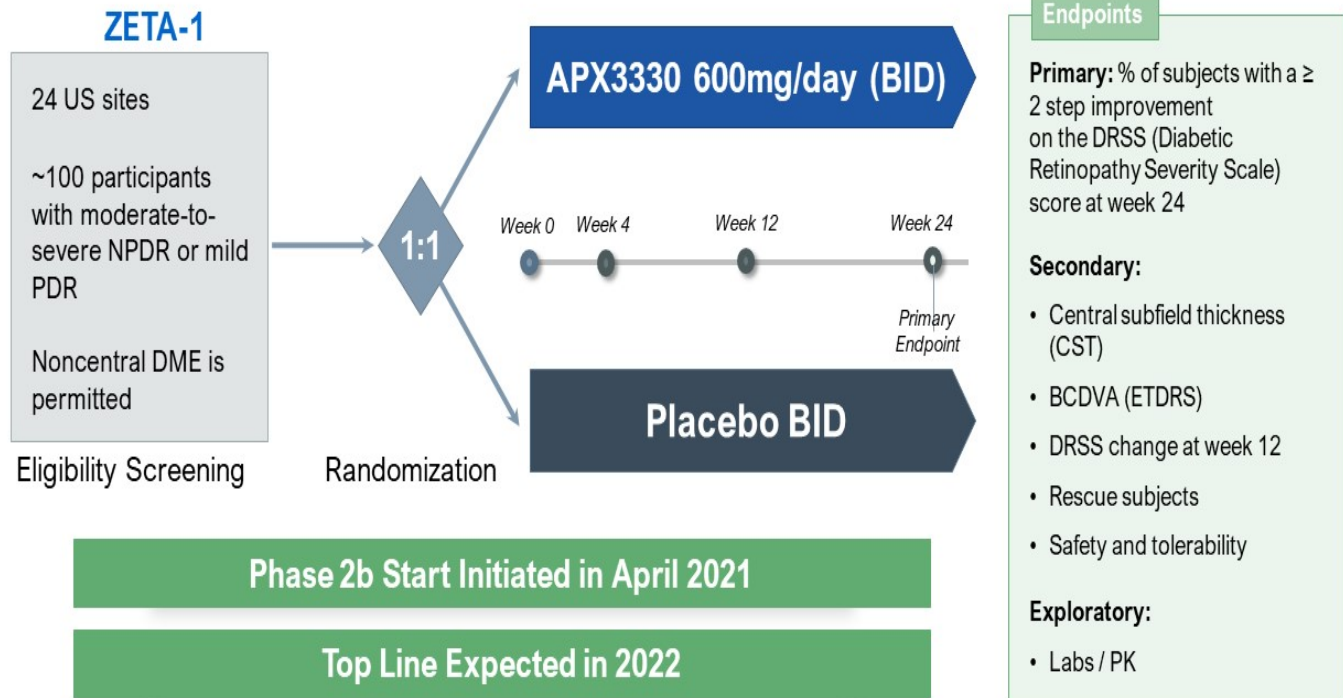


Source: Eisai/Apexian Human PK data

APX3330: Well-tolerated Oral Dose up to 600mg/day Twice Daily Dosing	
Expected Efficacy Data	Favorable Safety Profile
<p>Improving Eye Health in Diabetics</p> <ul style="list-style-type: none">↓ Inflammation↓ Abnormal Angiogenesis <p>Enhance Compliance & Exposure</p> <p>Oral pill may reduce the burden of frequent anti-VEGF injections</p> 	<p>Few Systemic Adverse Effects</p> <ul style="list-style-type: none">• < 5% Mild Gastrointestinal (diarrhea)• < 5% Mild Skin Rash (reversible)• Lack of Significant Acute Neurologic, Cardiovascular, Liver, or Pulmonary toxicity <p>No Ocular Effects</p> <ul style="list-style-type: none">• No observed ocular AEs 

DR/DME ZETA-1 Phase 2b Design

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



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

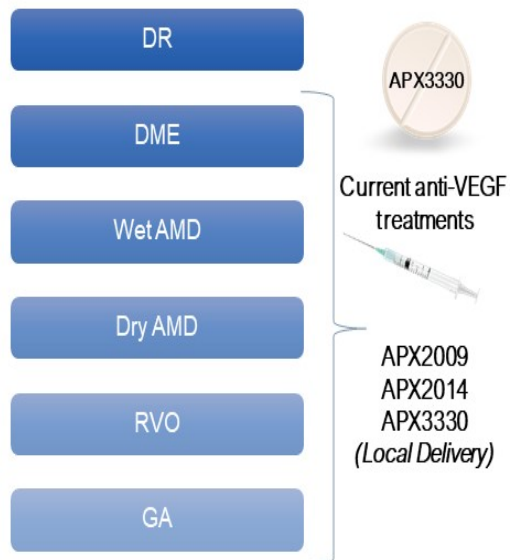
- **Convenient Daily Regimen**

- **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



Team/Boards, Milestones, And Financial Data

Ocuphire Management Team

Decades Of Biotech And Drug Development Experience



Charlie Hoffmann, MBA
VP Corporate Development and Operations

Tuck School of Business at Dartmouth

Ocularis Pharma Prudential
SynDev Rx Goldman Sachs



Mina Sooch, MBA
President & CEO and Founder

HARVARD BUSINESS SCHOOL

Gemphire Therapeutics Apjohn Ventures
MONITOR ProNAi



Barbara Withers, PhD
VP, Clinical and Regulatory Strategy

WAYNE STATE UNIVERSITY SCHOOL OF MEDICINE

aerpio GE UBC Pfizer



Amy Rabourn, CPA
VP, Finance

MICHIGAN ROSS

Gemphire Therapeutics Pfizer
NeuroBo PHARMACEUTICALS pwc



Mitch Brigell, PhD
Head, Clinical Development and Strategy

KANSAS STATE UNIVERSITY

aerpio Pfizer
NOVARTIS



Ronil Patel, MS
Senior Director BD and Market Strategy

FLORIDA TECH

BETALIQ Revitalid
POINT GUARD THERAPEUTICS OCULOS Integrated Insight



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

UF UNIVERSITY of FLORIDA

Gemphire Therapeutics ESPERION
Cerenis THERAPEUTICS Pfizer



Chris Ernst
Global Head, QA and Manufacturing

NORTHERN KENTUCKY UNIVERSITY

aerpio Akebia THERAPEUTICS
MED PACE



Drey Coleman
VP, Clinical Operations

OCULOS Integrated Insight

SIRION Therapeutics UCF



Ocuphire's World-Class Medical Advisory Board

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



Jay Pepose, MD, PhD
UCLA



Ed Holland, MD
Loyola University Chicago



eICON Medical

Eliot Lazar, MD
Georgetown University



Peter Kaiser, MD
Harvard Medical School



Mitch Jackson, MD
Chicago Medical School



Jack Holladay, MD
University of Texas



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



David Boyer, MD
Chicago Medical School



James Katz, MD
University of Illinois



Marguerite McDonald, MD
Columbia University



David Lally, MD
Vanderbilt University



David Brown, MD
Baylor University



Thomas Samuelson, MD
University of Minnesota



Y. Ralph Chu, MD
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Michael Allingham, MD, PhD
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Jeffrey Heier, MD
Boston University



Paul Karpecki, OD
Indiana University



Douglas Devries, OD
University of Nevada



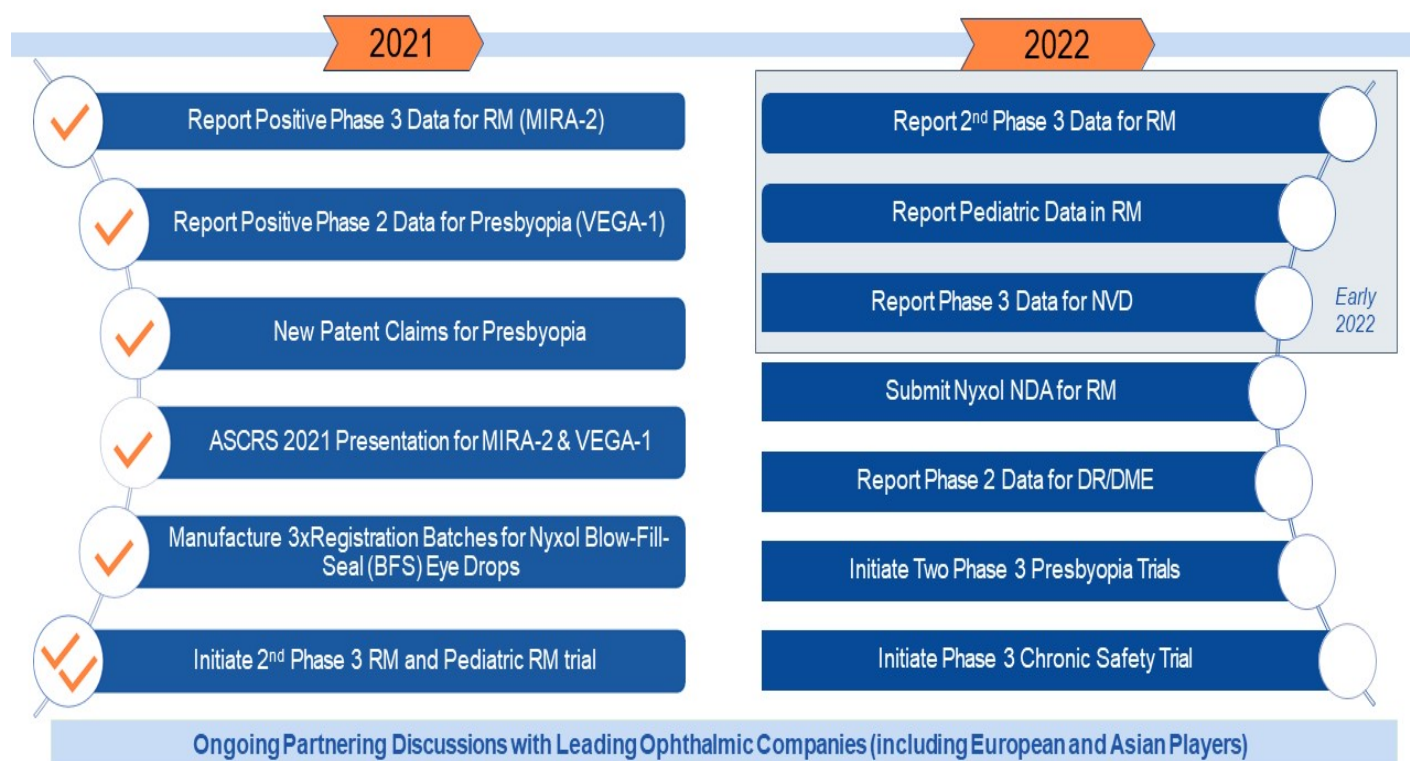
Ocuphire Board of Directors

Seasoned Directors With Decades Of Drug Development, M&A/Financings, And Ophthalmology

 <p>Cam Gallagher, MBA Chair, Board Director</p> <p>University of San Diego VELOSBIO ONCTERNAL therapeutics zentalis RetroSense THERAPEUTICS</p>	 <p>Mina Sooch, MBA Vice-Chair, Board Director President & CEO</p> <p>HARVARD BUSINESS SCHOOL Genphire Therapeutics Apjohn Ventures MONITOR ProNAi</p>	 <p>Sean Ainsworth, MBA Lead Independent Director, Board Director</p> <p>Washington University in St. Louis OLIN BUSINESS SCHOOL Allergan RetroSense THERAPEUTICS IMMUSOFT Programming Center</p>	 <p>Jay Pepose, MD, PhD Board Director</p> <p>UCLA David Geffen School of Medicine PeposeVision INSTITUTE Wilmer Eye Institute Washington University in St. Louis</p>
	 <p>James Manuso, PhD/MBA Board Director</p> <p>Columbia Business School astex[®] pharmaceuticals Talinium Investments, Inc. GALENICA ADVANCED TRANSDUCER TECHNOLOGIES</p>	 <p>Richard Rodgers, MBA Board Director</p> <p>CARLSON SCHOOL OF MANAGEMENT UNIVERSITY OF MINNESOTA TESARO[™] MGI Abraxis Bioscience P H R M A</p>	 <p>Susan Benton, MBA Board Director</p> <p>USF MUMA COLLEGE OF BUSINESS UNIVERSITY OF SOUTH FLORIDA Théa let's open our eyes Shire BAUSCH + LOMB</p>

Ocuphire Cadence Of Milestones

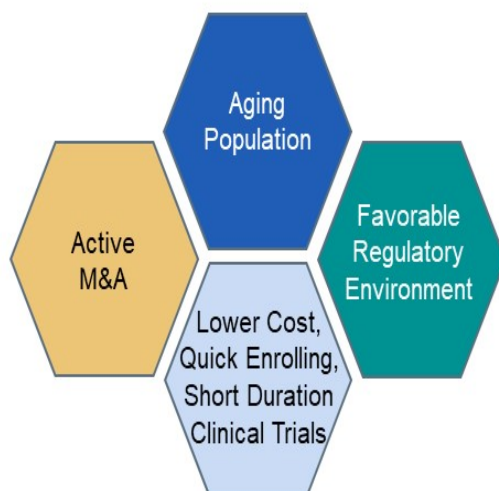
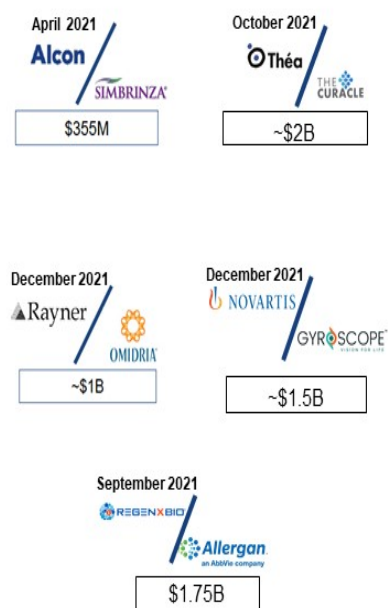
Multiple Data Catalysts On Path To NDA(s)



Ophthalmology – An Attractive Biotech Sector

Deal Activity And FDA Approvals In Ophthalmology In 2021

Deal Activity



New Product Approvals

7 of 60 Total FDA Drug Approvals in 2021 Were Ophthalmic Drugs¹



OCUP – Market Snapshot

Active Trading Volume And Sufficient Cash Runway Through 2Q 2023

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

Research Analyst Coverage on OCUP

John Newman	Canaccord Genuity
Kristen Kluska	Cantor Fitzgerald
James Molloy	Alliance Global Partners
Prakhar Agrawal	Jones Trading
Matthew Caulfield	H. C. Wainwright



www.ocuphire.com
ir@ocuphire.com

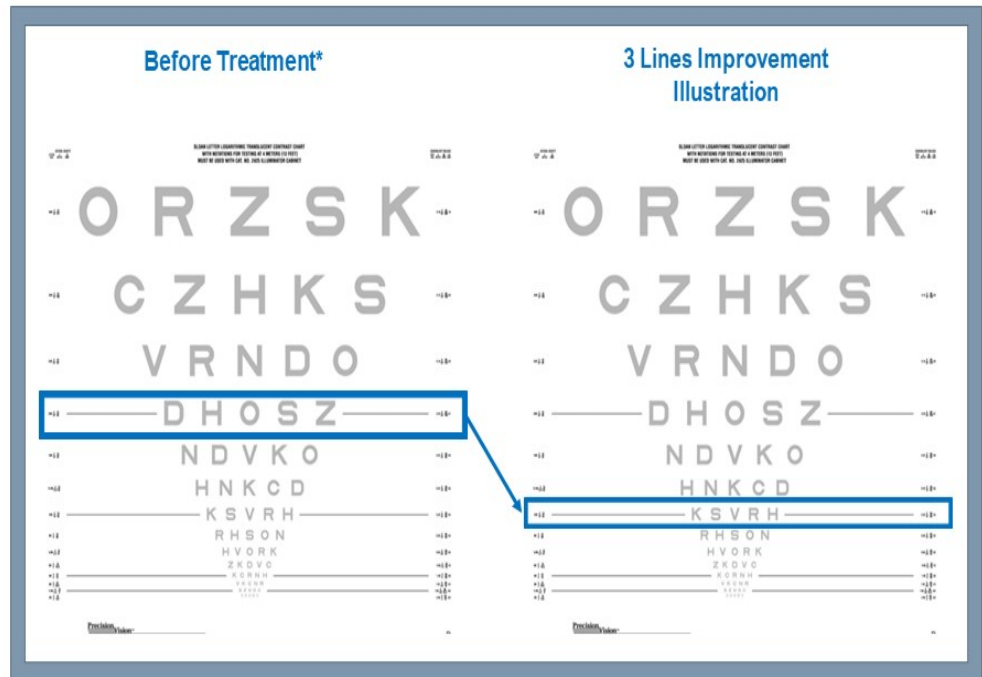


NVD Endpoint: 5% Low Contrast Visual Acuity (LCVA) Chart

FDA Accepted Endpoint For Contrast Sensitivity Assessment

Primary Endpoint of Nyxol LYNX-1 Trial

Percent of subjects
with ≥ 3 lines of
improvement in
mesopic low contrast
best-corrected
distance visual acuity
(7 days)









* Inclusion Criteria includes subjects with baseline mesopic LCVA of 20/100 or worse

DR/DME Endpoint: Diabetic Retinopathy Severity Scale (DRSS)

FDA Accepted Endpoint For DR (EYLEA® in PANORAMA Pivotal Trial)

Primary Endpoint
of APX3330
ZETA-1 Trial

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

						Patients included in the ZETA-1 Trial
DRSS Score	1 (10)	2 (20)	3 (35)	4 (43)	5, 6 (47, 53)	7 – 13 (60, 61, 65, 71, 75, 85, 90)
Description	DR Absent	Micro-aneurysm only	Mild NPDR	Moderate NPDR	Moderately Severe NPDR	PDR – Mild, Moderate, and Severe
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