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): May 19, 2022

Ocuphire Pharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-34079**	**11-3516358**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)
37000 Grand River Avenue, Suite 120 Farmington Hills, MI		**48335**
(Address of principal executive offices)		(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 May 19, 2022, Ocuphire Pharma, Inc. (the "Company") posted on its website an updated corporate presentation including the results of its LYNX-1 Phase 3 trial in night vision disturbances. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

The information in this Item 7.01, including Exhibit 99.1 attached hereto, is being furnished, shall not be deemed "filed" for any purpose, and shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On May 19, 2022, the Company issued a press release regarding the results of its LYNX-1 Phase 3 trial in night vision disturbances. A copy of the press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Information contained on or accessible through any website reference in the press release is not part of, or incorporated by reference in, this Current Report on Form 8-K, and the inclusion of such website addresses in this Current Report on Form 8-K by incorporation by reference of the press release is as inactive textual references only.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Investor Presentation Materials, dated May 19, 2022
99.2	Press Release, dated May 19, 2022
104	Cover Page Interactive Data File (embedded within Inline XBRL document).

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: May 19, 2022

Exhibit 99.1

Ocuphire PHARMA

Restore Vision & Clarity

Ocuphire Corporate Presentation

May 19, 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 the regulatory timelines, commercial timelines, product labels, cash runway, scalability, and future clinical trials in reversal of mydriasis (RM), presbyopia (P), dim light/night vision disturbance (NVD) and diabetic retinopathy (DR)/diabetic macular edema (DME), including the potential for Nyxol to be a "best in class" presbyopia drop and the potential market opportunity in RM/NVD/P/DR/DME. 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, costs, 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, including the scalability 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 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 also contains estimates and other statistical data made by independent parties and by us relating to market shares and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

Ocuphire

OCUPHIRE PHARMA

NASDAQ: OCUP

Multiple Catalysts in 2022:

- ✓ **Nyxol alone VEGA-1 P2 trial for P *JAN 2022***
- ✓ **Nyxol MIRA-3 P3 trial for RM *MAR 2022***
- ✓ **Nyxol MIRA-4 Pediatric trial for RM *APR 2022***
- ✓ **Nyxol LYNX-1 P3 trial for NVD *MAY 2022***
- APX3330 ZETA-1 P2b trial for DR/DME ***2H22***
- NDA Filing for Nyxol for RM ***LATE 2022***

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

Differentiated, Late-Stage Pipeline for Front and Back of the Eye

- ✓ Nyxol with > 650 patients treated across 12 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

Near-term Commercialization Opportunities in Multiple Large Unmet Markets

- ✓ Addressing 4 large markets with unmet needs: RM, Presbyopia, NVD, and DR/DME
- ✓ **Successful trial execution with 6 positive Phase 3 & Phase 2 data read-outs for Nyxol in RM, Presbyopia, and NVD**
- ✓ Stable, small-molecule drugs with commercial scalability
- ✓ Robust and growing IP portfolio: US and global patents issued thru 2034 for both assets as well as new 2039 Nyxol patent issued for presbyopia

Multiple data readouts in 2022 with Track Record of Execution

- ✓ $19.2 million cash reported at 3-31-22 sufficient for operations into 2Q 2023
- ✓ Highly experienced management, Board and KOLs with broad ophthalmic and biotech drug development and commercialization success
- ✓ Low-cost, fast-enrolling, short-duration clinical trials
- ✓ Favorable precedent regulatory environment for ophthalmic drug approval
- ✓ Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and HCW

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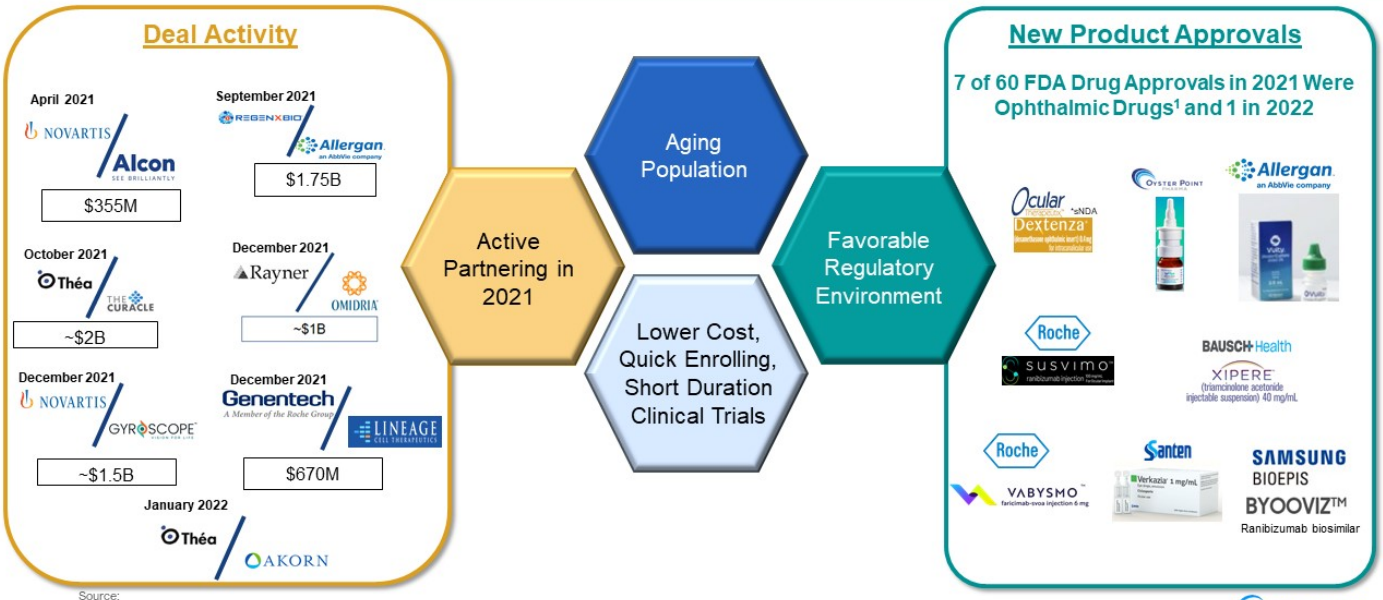
Ophthalmology – An Attractive Biotech Sector

Demographics, M&A, Regulatory Approvals and Efficient Trials Favor Ophthalmic Drugs



Source:
1. Endpoint Dec 29, 2021- Hitting a new record on drug approvals, the FDA offers a thumbs-up to another atopic dermatitis contender;
2. OIS Year in Review 2021;
3. Company press releases

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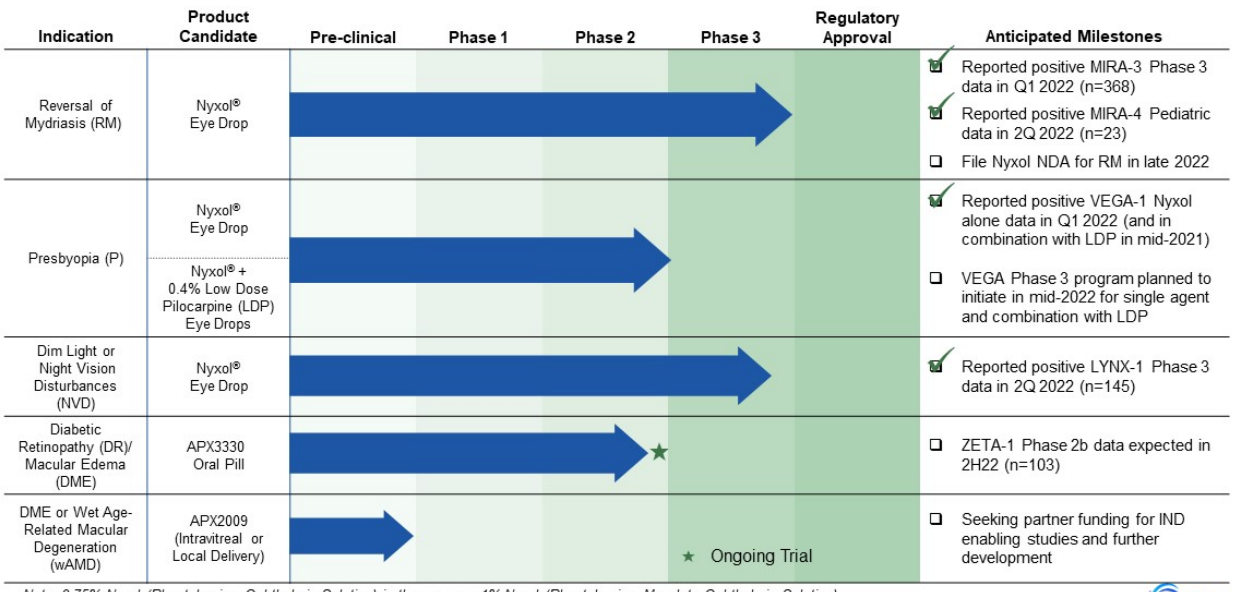
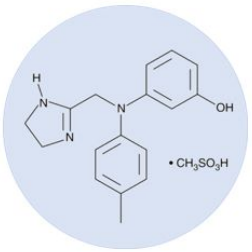
Looking Ahead: Ocuphire Pipeline & Clinical Milestones

Multiple Phase 3 & Phase 2 Clinical Data Readouts Anticipated this Year



Note: 0.75% Nyxol (Phentolamine Ophthalmic Solution) is the same as 1% Nyxol (Phentolamine Mesylate Ophthalmic Solution)



RM Reversal of Mydriasis

P Presbyopia

1 **Nyxol as a Single Drop for Presbyopia**

2  **Nyxol with LDP Adjunctive Therapy**

NVD Night Vision Disturbance

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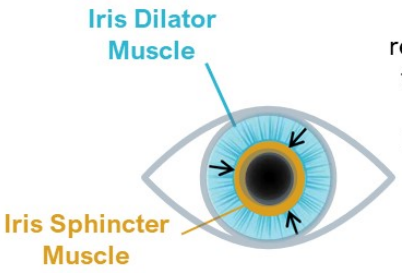
Nyxol's Differentiated MOA as an Alpha-1 Blocker

Phentolamine Mesylate Reformulated as a Proprietary Topical Eye Drop ➔ Nyxol®

Phentolamine Mesylate is the Active Ingredient in Nyxol: a Non-selective α1 & α2 Antagonist

Blocking α1 Reduces Pupil Size	**Blocking α1** Dilates Blood Vessels
 Nyxol blocks α1 receptors only found on the Iris Dilator Muscle ↓ Decreases Pupil Size (Moderate Miosis) without Affecting the Ciliary Muscle	 Phentolamine mesylate is approved for 2 indications: • Regitine® (Pheochromocytoma) – intravenous injection approved in 1952 • OraVerse® (Reversal of oral anesthesia) – intramuscular injection approved in 2008 *505(b)(2) Regulatory Approval Pathway*

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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

Efficacy Data	Favorable Safety Profile	Durable
Nyxol Improves Vision by Decreasing Pupil (~1-1.5mm) ↑ Near Vision ↑ Distance Vision ↑ 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** **Minimal to No Headaches**	**Effects Last ≥ 24 Hours** Chronic daily dosing of Nyxol at bedtime reduces pupil size for up to 24 to 36 hours 

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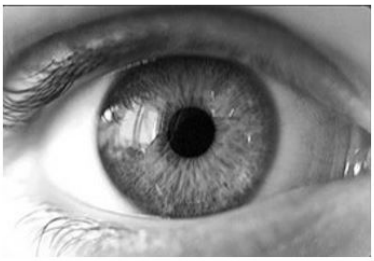
NYXOL® for REVERSAL OF MYDRIASIS (RM)

RM



"I had a premium cataract procedure by my MD, and I was unable to see clearly for two days. My doctor said it was due to my dilation. I did not expect my dilation to last that long."

"I have to visit my retina MD for my monthly injections, where I am dilated. Being dilated every month is a huge burden on my day."

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

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RM

Problem: Dilated Eyes for Exams and Procedures

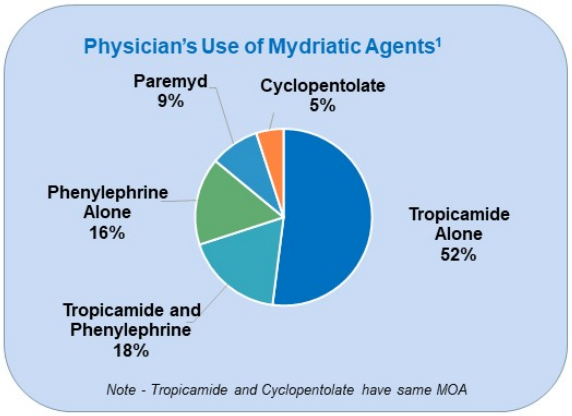
Patients Report Significant Side Effects after Dilated Eye Exam

The Problem

Pharmacologically-induced pupil dilation is part of standard care for annual and specialty eye exams…

…but there is 6 to 24 hours of impaired vision including:

- Inability to Focus
- Photophobia (sensitivity to light)
- Cycloplegia (loss of accommodation)
- Difficulty Reading and Driving
- Halos and Glare



NO REVERSAL DROPS COMMERCIALLY AVAILABLE

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1. GlobalData Market Research Survey; Oraverse and Regitine Label

RM

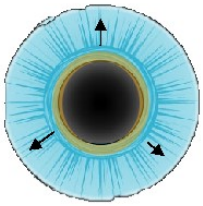
Nyxol Has Potential To Be The Only Option For RM

Physicians AVOID Use of Cholinergic Agonists (Pilocarpine) Due to Safety Risk on Ciliary Muscle

2 Classes of Mydriatic Agents

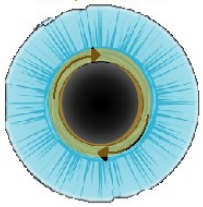
Phenylephrine (α1 agonist)

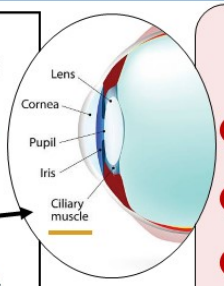
Sympathetic (primarily α1) innervation stimulates the iris dilator muscles



Tropicamide (anti-cholinergic)

Parasympathetic innervation stimulates the iris sphincter **and** ciliary muscle





Reversal via the Ciliary Muscle by Cholinergic Agonists* is Not a 'Safe' Option

- Retinal tear has been reported in some patients, especially high myopes[1]
- Induces accommodation spasm and reduction in distance vision[2]
- Induced anterior shift of the lens can increase the risk of acute angle-closure glaucoma[2]
- High incidence of brow ache and headache following installation[3]

Cholinergic Agonists include pilocarpine, carbachol, and aceclidine. Note, pilocarpine is rarely used off-label for RM given these safety concerns.

Nyxol® is the only eye drop in clinical development for multiple indications with a MOA that does not affect the ciliary muscle

1 Pilocarpine FDA Label (2017)
2. Optician (2012)- Mydriatic Drugs: Practical Considerations
3. Lee DA, Higginbotham EJ, 2005. Glaucoma and its treatment: a review. Am J Health Syst Pharm 62, 691–699.

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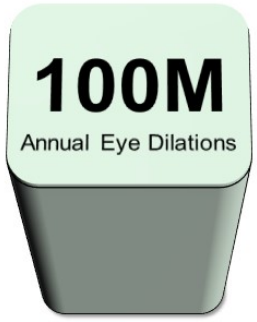
Reversal of Mydriasis Unmet Need & Landscape

With No Commercially Available Treatment, Nyxol is Uniquely Positioned as a New Reversal Drop

The Problem

- At many annual eye exams and specialty visits, pupils are pharmacologically dilated, impairing vision for **6-24 hours**
- Dilated eyes experience:
  - Heightened sensitivity to light
  - Inability to focus, headaches
  - Difficulty reading, working & driving
  - Halos and glare
  - Cycloplegia (loss of accommodation)

No Currently Available Treatments



Current Landscape:

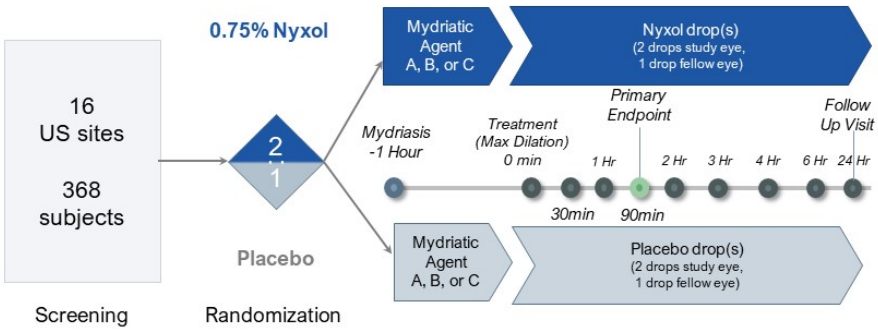
- Rare off-label use of cholinergic agonists (e.g., pilocarpine) given ciliary muscle safety issues
- Optomap® is offered by optometrists to avoid dilations for ~$50 cash-pay, however images may provide limited view of retina and disease pathology

Nyxol's MOA Uniquely Suited As A Reversal Drop For Dilations

Source – Optos plc Pricing

MIRA-3 Phase 3 Registration Trial Design

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



Key Eligibility Criteria

Inclusion: Healthy ≥ 12 years of age

Exclusion: Clinically significant ocular trauma, surgery, or non-refractive laser treatment within the 6 months prior to screening; and recent or current evidence of ocular disease, infection or inflammation in either eye

MIRA-3 Started in Nov 2021 ➔ Enrolled 368 in Feb 2022
Phase 3 Results Reported March 2022

Endpoints

Primary: % of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min

Key Secondary:

- % of subjects returning to baseline at 0min, 30min, 1h, 90 min 2h, 3h, 4h, 6h, 24h (overall, by mydriatic agent, by iris color)
- Mean time to return to baseline PD
- Mean change in pupil diameter at all timepoints
- Distance-Corrected Near Vision
- Accommodation (Tropicamide/Paremyd)
- Safety and tolerability

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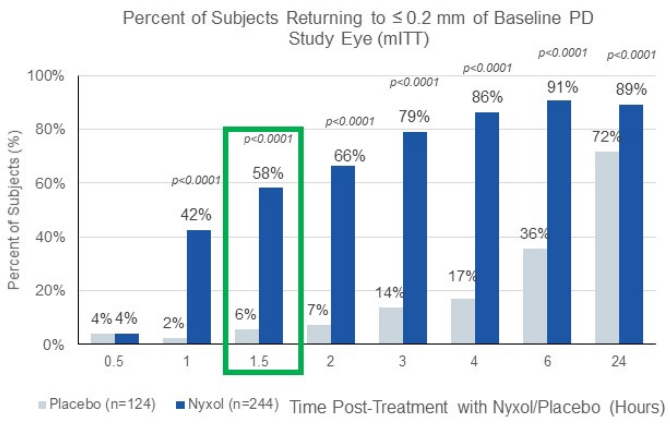
13 Mydriatic Agents 3:1:1 – A: 2.5% phenylephrine (alpha-1 agonist), B: 1% tropicamide (cholinergic blocker), C: Paremyd® (combination)

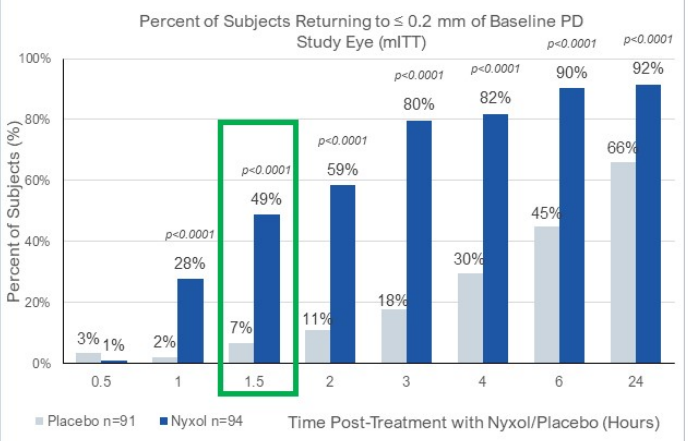
Primary Endpoint Achieved in Two FDA Registration Phase 3 Trials

Rapid, Consistent and Sustained Reversal of Pupil Dilation with Nyxol

MIRA-3 Phase 3 Trial



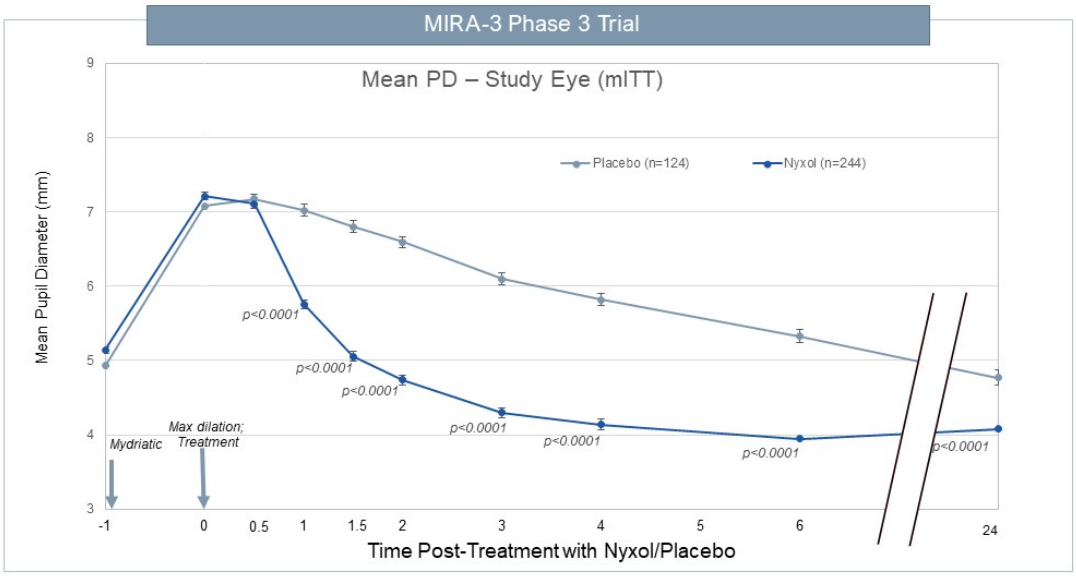
MIRA-2 Phase 3 Trial



Source: (Left panel) MIRA-3 Table 14.2.1.1 (mITT); (Right panel) MIRA-2 Table 14.2.1.1 (mITT). Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd).

MIRA-3: Mean Pupil Diameter Over Time

Nyxol Treatment Significantly Reduced PD Starting at 1 Hour Post-Dose Through 6 Hours



Source: MIRA-3 Table 14.2.2.1 (mITT). The p-values are change from max pupil dilation treatment compared to placebo.
Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd). Standard Error bars are shown.

RM

Summary of MIRA Registration Trial Designs

Randomized, Double-Masked, Placebo-Controlled, Parallel, Multi-Center, One-Day Trials

	MIRA-2 Phase 3	MIRA-3 2nd Phase 3
Number of US Sites	12	16
Subjects Enrolled	185	368
Eligibility	Healthy ≥ 12 years of age	Healthy ≥ 12 years of age
Randomization	1:1	2:1
Positive Data Readout	1Q 2021	1Q 2022
Primary Endpoint	% of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min	% of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min

In addition, 32 subjects were enrolled in positive MIRA-1 Phase 2 trial, a randomized, double-masked, placebo-controlled, crossover, multi-center trial as well as MIRA-4 pediatric safety trial of 23 children.

Total Subjects Enrolled

>550

Total Exposure To Nyxol

>330

Over 300 subjects have been treated with Nyxol and evaluated at 24-hours in the MIRA trials → satisfying regulatory requirements for drug safety exposure for the acute RM indication

Source: In order from left to right
MIRA-2 Trial NCT# 04620213
MIRA-3 Trial NCT# 05134974

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Summary of Three Positive Late-Stage MIRA Clinical Trials

Confirms Phase 3 Trials with Favorable Safety and Tolerability Profile and Rapid Mydriasis Reversal

Efficacy

- Pivotal trials met primary endpoint of return to baseline PD at 90 minutes after dilation
  - MIRA-3 Phase 3 (58% Nyxol vs. 6% placebo, p<0.0001)
  - MIRA-2 Phase 3 (49% Nyxol vs 7% placebo; p<0.0001)
- MIRA-4 pediatric trial achieved 64% Nyxol vs. 25% Placebo (p<0.0001)
- Met key secondary endpoints with high statistical significance
  - Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Efficacy with 1 or 2 drops
  - Accelerated return to normal distance-corrected near visual acuity
- Saving of ~4 hours in time to return to normal pupil diameter

Safety

- No deaths, serious AEs, or withdrawals due to AEs
- All treatment related AEs were mild in severity
- The only AE occurring in ≥ 5% of subjects treated with Nyxol was mild and transient conjunctival hyperemia and instillation site discomfort (11% Nyxol vs. 0% placebo)
- No distance visual acuity loss
- No change in vital signs
- Completion of MIRA-4 study satisfies Pediatric Research Equity Act (PREA) requirement

Source: mITT Population, MIRA-2, MIRA-3 and MIRA-4 Trial

RM

NDA Submission Targeted in Late 2022

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.

Preservative-Free Single Unit Vial (5-pack)

Nyxol®

P3 Clinical Trial
Completed 2nd Phase 3 trial in RM (enrolled 368 subjects), which also meets 24-hour safety population exposure requirement

Pediatric Safety
Completed trial with 23 subjects ages 3 to 11 per agreed FDA initial pediatric study plan

Ongoing

Manufacturing
Completed 3 registration batches; 1-year CMC stability will be available for NDA

Regulatory Approval
Submit NDA by late 2022, with expected approval review of 10 months

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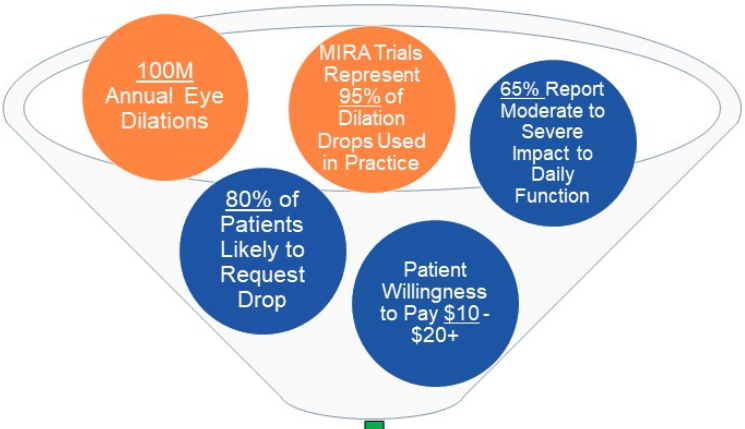
RM

Reversal of Mydriasis (RM) Market Opportunity

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

GlobalData Market Research Findings



~$500+M
Estimated US RM Market Opportunity

58%
physicians would start prescribing Nyxol within 1st year

0
Current Commercially Available Treatments

81%
patients would be more likely to schedule yearly eye exams with a reversal drop

68%
physicians would be willing to use Nyxol even if patients had to still wear sunglasses within 1st hour

Source: GlobalData Market Research Survey
Calculation: 100M Annual Eye Dilations X 65% X 80% X $10 per patient = $500+M Opportunity

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RM

More Efficient Launch Opportunity for Nyxol in RM

Launch is Poised to be Disruptive, Cost-Effective and Not Payor-Driven

Traditional Ophthalmic Launch	Ocuphire's Nyxol RM Launch
✗ Highly competitive markets (e.g., dry eye, glaucoma, allergy); little differentiation	✓ No competition or approved reversal drop → potential for Nyxol to be the only safe option
✗ Launch success takes time given payor (reimbursement) dependence	✓ Cash pay (no reimbursement barriers) allowing for quicker adoption
✗ Significant prior authorization & step-edits hurdles with burden to the practices	✓ Offering a significant value proposition to patients and practices
✗ Lengthy sales cycles and touchpoints due to chronic use and market access upkeep	✓ Shortened sales-cycle with acute use product
✗ Significant product education requirement	✓ No training given dilations routine in practices
✗ Complex distribution channel including specialty and retail pharmacies	✓ No specialty/retail pharmacy → direct to physician
✗ "**One product, one indication**" commercial model is inefficient with fixed cost infrastructure	✓ **"One product, several indications"** offers efficiencies in commercial operations

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Pre-Commercial 2022 & Go-To-Market Strategy 2023

Activities Underway to Support Capital-Efficient Nyxol RM Commercial Launch

Pre-Commercial Activity

- Market Development (KOLs)
- Physician Targeting
- Patient Journey
- Brand Awareness

Go-To-Market Strategy

Potential Options for Commercialization

Work with strategic or channel partner with existing commercial ophthalmic products

Hire contract commercial organization

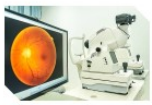
Build own salesforce

Components of an Efficient Launch

Landscape
No approved drug/competition; data-mining for high volume practices

Easy Adoption
Dilations are a routine part of practice; adoption requires no staff or patient training

Direct to Physicians
No need for pharmacy; no reimbursement, private pay



Retina
3,000 Retinal Specialists

Ophthalmology
20,000 Ophthalmologists

Optometry
46,000 Optometrists

Sources: ASRS; AMA; AAO; Women in Optometry (WO); AOA Excel and Jobson Medical Information; Physician Interviews Conducted by Ocuphire; GlobalData market research

NYXOL® for PRESBYOPIA

P

"By age 45, 80% of Americans will struggle with Presbyopia, and by age 50, nearly everyone will."
NY Times

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

Ocuphire PHARMA

2021: The Time for Presbyopia Drops

Headlines from Academia and Industry Articles with an Early First Approval for Vuity™

September 22, 2021 | 11 min read

Treatment landscape for presbyopia evolving toward noninvasive options

Presbyopia treatment options now and on the horizon

Refractive September 2021

Clinical Ophthalmology

Dovepress

REVIEW

Presbyopia – A Review of Current Treatment Options and Emerging Therapies

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 PHYSICIAN

NOVEMBER 2021

Presbyopia PHYSICIAN

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 Conni 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

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-Correcting Eyedrops Move Ahead

Presbyopia Treatment Market Size Projected to Rise Lucratively by 2026 end BioSpace

Ocuphire PHARMA

Sources: Academic review articles, journals, and publications between July 2021 to December 2021

Nyxol® and Nyxol + Low Dose Pilocarpine Presbyopia Eye Drops

Differentiated MOA with Two Potential Product Labels for Functional Near Vision Improvement

0.75% Nyxol

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

0.4% LDP

- Pilocarpine (cholinergic agonist)
- Known MOA on sphincter (and ciliary) muscle
- Potent miotic at approved doses (1%, 2%, 4%)
- Low concentration avoids known safety issues:
  - Headache, brow ache, and redness
  - Accommodative spasm causing loss of distance vision especially at night

Nyxol as a Single Agent for Presbyopia
Single Durable Drop

Optimal Pupil Target is 2-3 mm

Nyxol with LDP as Adjunctive Therapy for Presbyopia
Two Drops Tunable Option

Source: Nyxol® data from 12 completed trials; Pilocarpine product label and literature

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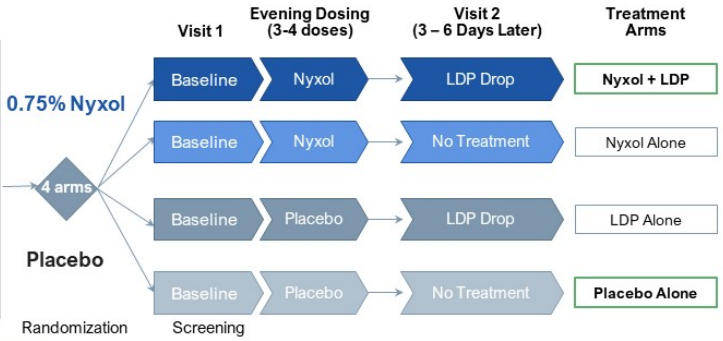
Presbyopia VEGA-1 Phase 2 Trial

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

VEGA-1

17 US sites

150 presbyopic patients



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 in June 2021 and Jan 2022

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:

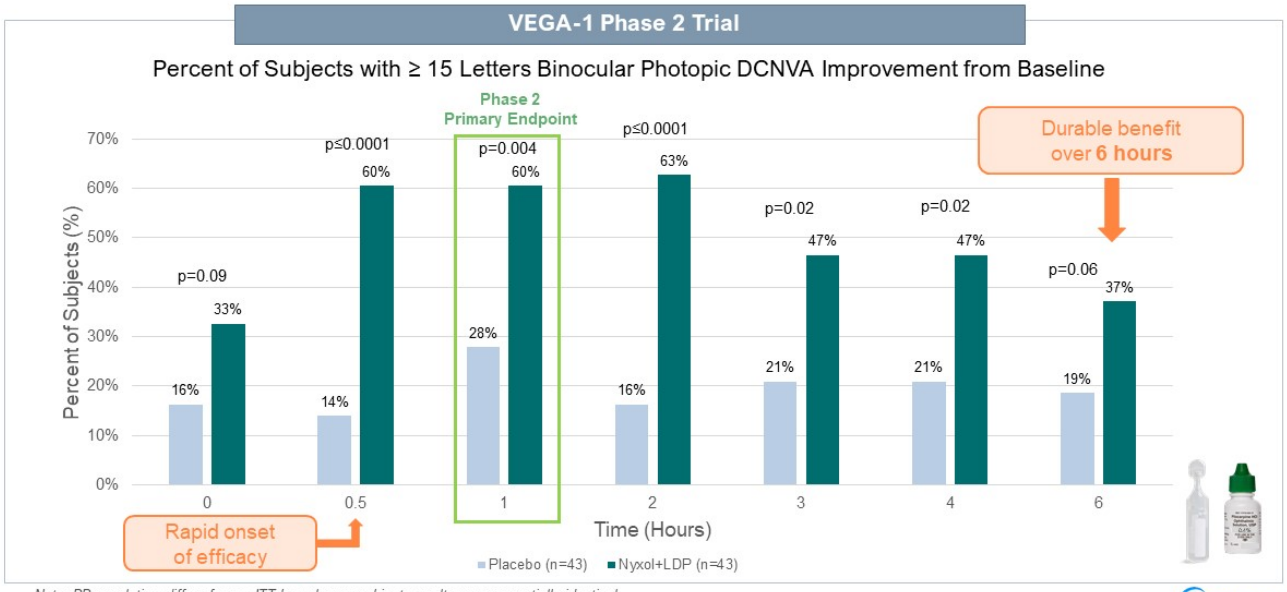
- % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours in photopic lighting comparing Nyxol + LDP vs placebo, Nyxol alone, and LDP alone
- No loss of distance vision
- Pupil diameter at time points
- Safety and tolerability (redness)

Clinical trial NCT#04675151. DCNVA = distance-corrected near visual acuity . BCDVA = best corrected distance visual acuity

Ocuphire PHARMA

VEGA-1: Nyxol+LDP Met Primary & Secondary Endpoints

60% Patients with Nyxol+LDP had ≥ 15 Letter Near Gain with Fast Onset & Durable Responses



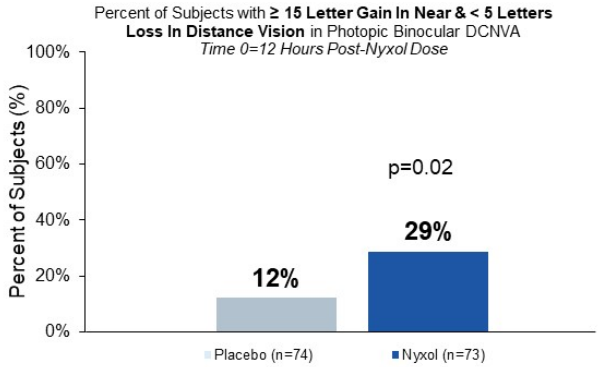
Note: PP population differs from mITT by only one subject; results were essentially identical.

26 VEGA-1 TLR Table 14.2.1.2

VEGA-1: Planned P3 Efficacy Endpoint Met by Nyxol and Nyxol+LDP

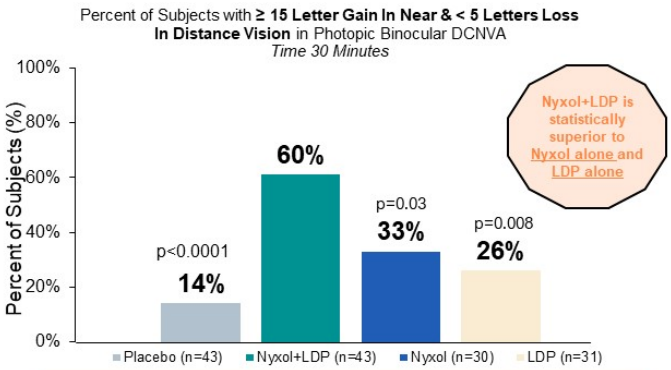
Nyxol Single Drop and LDP Combination Provide Statistically Significant 3-line Near Vision Gain

1 **Nyxol as a Single Drop for Presbyopia**



53% of subjects achieved ≥ 10 letter improvement in DCNVA at 12 hours (p=0.005 vs placebo) and a similar trend at other time points

2 **Nyxol with LDP Adjunctive Therapy**

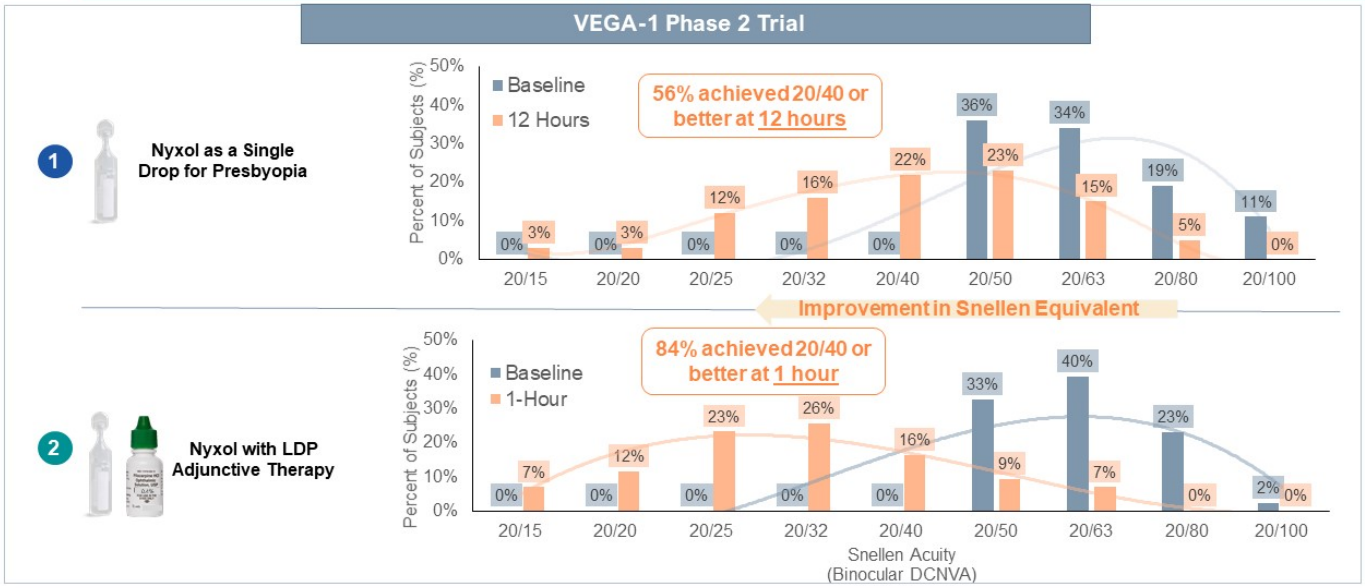


79% of subjects achieved ≥10 letter improvement in DCNVA at 1 Hour (p=0.005 vs placebo) and a similar trend at other time points

VEGA-1 TLR Table 14.2.2.2.1; Table 14.2.2.2; Table 14.2.1.7; Table 14.2.1.2

VEGA-1: Improvement in Functional Near Vision

Nyxol and Nyxol with LDP Both Provide Durable Improvement in Functional Near Vision



Similar trend was seen at all timepoints
Baseline Inclusion: Photopic DCNVA of 20/50 or worse
Source: VEGA-1 TLR Table 14.2.24.1 Percent of Subjects with Photopic DCNVA by Time Point (PP Population)

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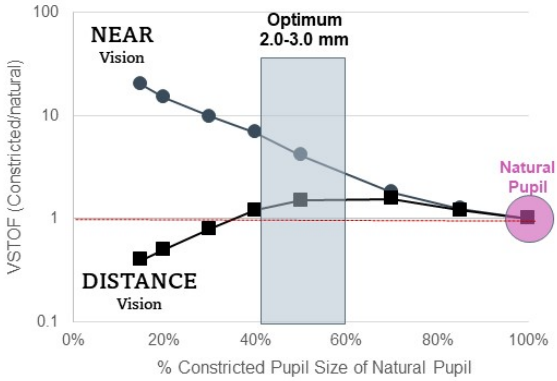
What is the Optimal Pupil Size?

Literature Highlights New Drops to Treat Presbyopia Achieve Optimal Pupil Diameter of 2-3 mm

Photopic Lighting (100 -1000 lux)
Natural Pupil Size ~ 4 mm



Effect of Target Luminance on Optimum Pupil Diameter for Presbyopic Eyes

Renfeng Xu*, Larry Thibos†, and Arthur Bradley‡

"A fixed **2- to 3-mm** small pupil or a 30% pupil miosis can both produce near visual acuity gains without significant losses to distance acuity or image quality, and therefore can be considered as optimal for a presbyope experiencing a wide range of light levels."

- Optometry and Vision Science, November 2016

CATARACT SURGERY

WHAT IS THE OPTIMAL PUPIL SIZE?

This question is becoming increasingly relevant as small-aperture IOLs and pupil-modulating drops are developed to treat presbyopia.

BY JAY S. PEPOSE, MD, PHD, AND RENFENG "RENA" XU, MD, PHD

"The impact of pupillary modulation on the functional depth of field differs among patients with refractive error versus those who are truly emmetropic."

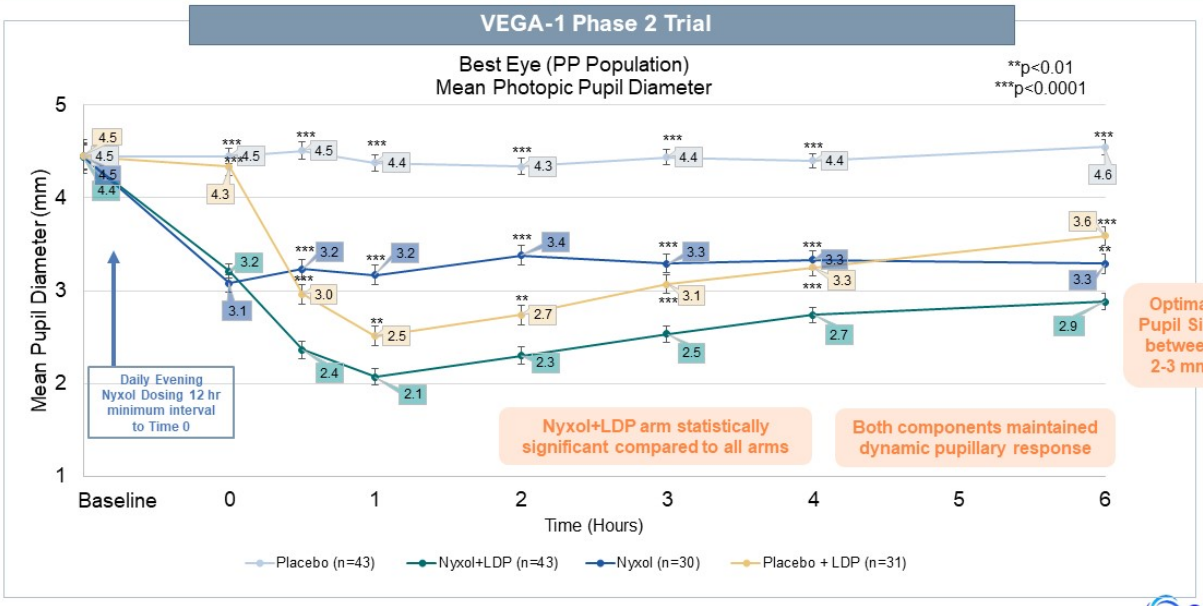
- Cataract & Refractive Surgery Today (CRST), January 2022

Source: Xu et al, OVS 2016; Pepose & Xu CRST article 2022, Effect of Target Luminance on Optimum Pupil Diameter for Presbyopic Eyes

Ocuphire PHARMA

VEGA-1: Mean Pupil Diameter Over Time

Achieved Optimal Pupil Size in Nyxol+LDP and Nyxol Alone Consistent with Near Vision Gains



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

Summary Of Positive VEGA-1 Phase 2 Results

Nyxol and Nyxol + LDP has Demonstrated Efficacy Response & Well Tolerated Safety Profile

Well-Controlled, Multi-Center Phase 2 Trial Evaluating Nyxol & Nyxol+LDP

1 Nyxol as a Single Drop *Single Durable Drop*		2 Nyxol with LDP Adjunctive Therapy *Two Drops Tunable Option*
Met planned P3 endpoint at 12 hours (29%; p=0.02)	**Efficacy**	Met primary endpoint at 1 hour (60%; p=0.004)
Durable near vision gain at 12 and 18 hours	**Durability**	Durable near vision gain through at least 6 hours
56% (12 hours post-dose)	**Functional Vision** ***(20/40 or better)***	84% (1-hour post-dose)
Sustained PD reduction at least 18 hours	**Reduction in PD**	Sustained PD reduction at least 6 hours
• Ages 40-64 • 20/50 or worse DCNVA • Light and dark irides	**Breadth of Patients Showed Efficacy**	• Ages 40-64 • 20/50 or worse DCNVA • Light and dark irides

Efficacy

Safety

Nyxol and Nyxol+LDP Pooled Safety Findings

- No serious AEs, most AEs were mild
- No headaches, no brow aches, and no blurry vision AEs were reported
- No loss in distance vision under photopic and mesopic lighting
- ~5% mild, transient redness
- No change in IOP

PP Population, VEGA-1 Trial

*Trend toward statistical significance even in smaller Nyxol arm from time 0 to time 6 hours (n=30); larger sample size for all arms planned in Phase 3 program

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Potential 'Best in Class' Presbyopia Drop(s)

Nyxol and Nyxol+LDP Combination Data Differentiate on Efficacy, Safety, and Durability

Product Attributes*	VUITY™		Ocuphire	
			Nyxol	Nyxol+LDP
1) Efficacy (≥ 3-Line Gain w/o loss of 1 line in DCNVA - Primary Endpoint Responders)*	**26-31% (3 hours)**	*Caveats of cross-trial comparisons for VUITY™ and Nyxol/LDP. Differences include age, severity of near vision loss, lighting conditions, doses, timing, and # of patients*	**29% (12 hours)**	**60% (1 hour)**
2) Safety: Loss of Distance in Mesopic	**No Significant Loss**		**No Significant Loss**	**No Significant Loss**
3) Tolerability: Headaches and Conjunctival Hyperemia	**>5% Headaches >5% redness**		**No Headaches <5% mild redness**	**No Headaches ~5% mild redness**
4) Durability (% responders at the longest timepoint)	**18% at 6 hours**		**37% at 18 hours**	**37% at 6 hours**

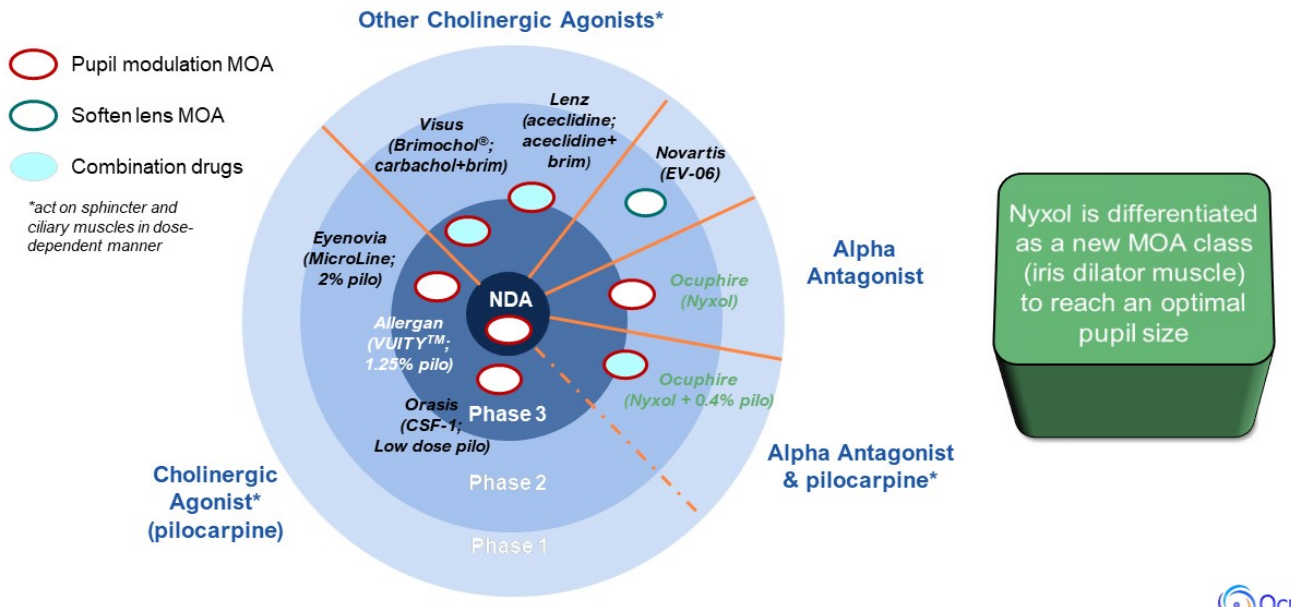
Nyxol's Potential Differentiated Solution

Placebo Adjusted Values for Vuity ™ were 15-23% in Gemini 1 & 2; Placebo Adjusted Nyxol was 16% and Nyxol+LDP was 33% (all stat significant)

Source: Nyxol Data: ASCRS (July 2021) Abstract# 76645 (Phase 2) and VEGA-1; Abstract 74336 (Phase 3). VUITY™ Data FDA Label and AAO 2021 Presentation.

Presbyopia Eye Drops Competitive Landscape

Nyxol Creates a New, Differentiated MOA Class; Nyxol+LDP Offers Tunability Option



Nyxol is differentiated as a new MOA class (iris dilator muscle) to reach an optimal pupil size

Corporate Websites, Grzybowski, A, Markeviciute A, Zemaitiene R. A Review of Pharmacological Presbyopia Treatment. 2020

Presbyopia is a Burgeoning Market Opportunity

Vuity™ Approval Sets the Stage for Market Development by Large Pharma to Build a Large Market

The Problem

- Lens loses ability to view objects up close as we age
- Dependence on reading glasses for intermittent and prolonged use, with inability to see near and far at same time
- Aesthetics and inconvenience

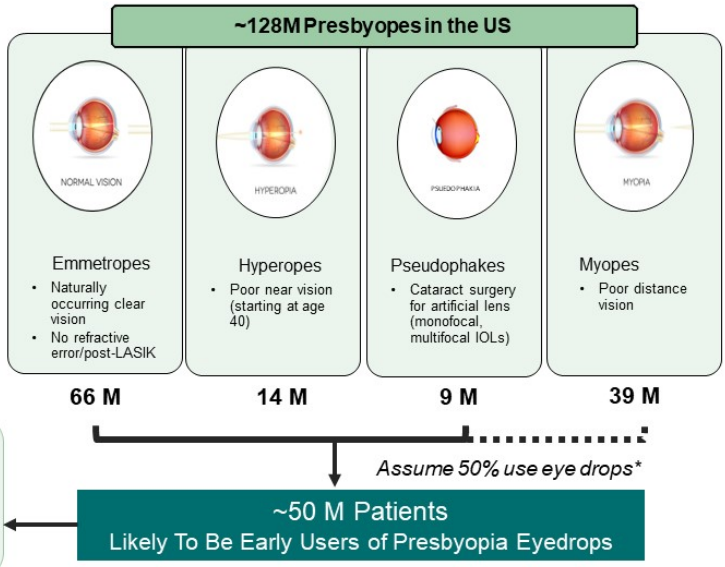
100%

of adults over the age of 40 years are at risk of developing presbyopia[3]

FDA Approval of Vuity™ positive for the presbyopia eyedrop market

Private Cash Pay Vuity™ List Price $79

~$10B - $20B
Estimated US Presbyopia Market Opportunity



Source:
1. Global Prevalence of Presbyopia, 2018, Fortune Business Insights Reading Glasses Forecast 2016-2027, Cataract & Refractive Surgery Today, 2021, NEI 2010 data.
2. Vitale S. et. Al. JAMA Ophthalmology, 2008, Vision problems, US, Arch. Ophthal, 2014, Vision Monday.
3. NEI/NIH https://www.nei.nih.gov/sites/default/files/health-pdfs/Presbyopia.pdf

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*

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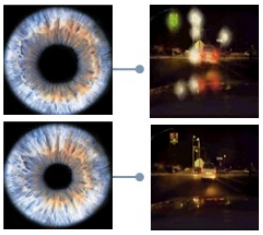
NVD

Market Opportunity in Dim Light or Night Vision Disturbances

No Approved Treatments with Ripe Opportunity for Growth

The Problem

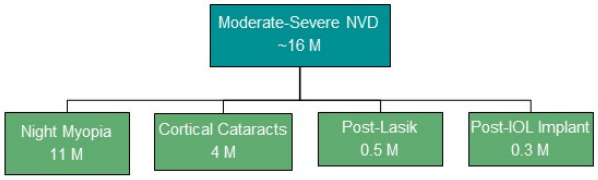
- Peripheral imperfections scatter light when pupils enlarge in dim light, causing halos, starbursts, and glare that impair vision
- The imperfections may be caused by LASIK surgery, IOL implants, certain types of cataracts (cortical), and natural reasons (especially with age)
- Symptoms cannot be properly corrected by any type of lens (reading glasses, contact lenses) or surgical procedures



Before

After

No Approved Treatments



Seeking Treatment Findings	
Patients willing to try a new eye drop treatment	67%

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

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

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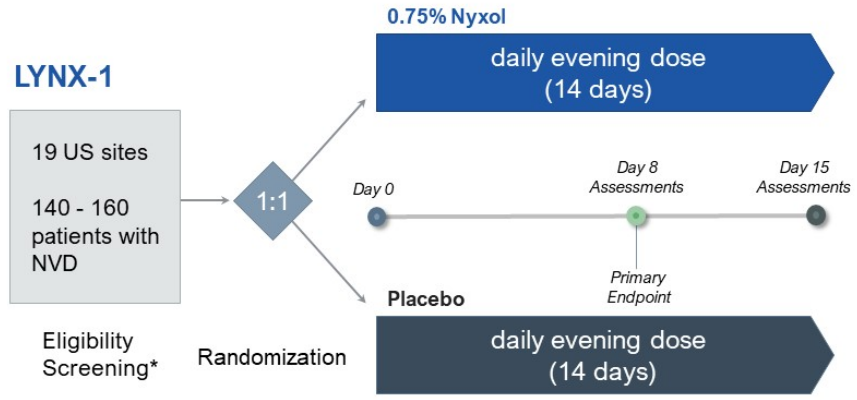
GlobalData Market Research Report, 2020; Photos are illustrative

NVD LYNX-1 Phase 3 Registration Design

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



Phase 3 Initiated in Dec 2020; 145 Patients Enrolled

Top Line Results Reported May 19, 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):

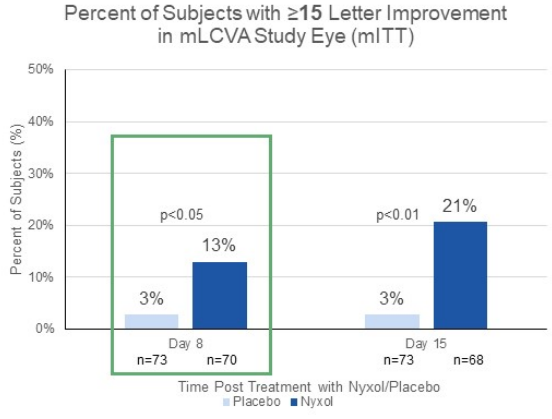
- Pupil diameter
- Visual acuity measures (distance and near)
- Safety and tolerability (redness)

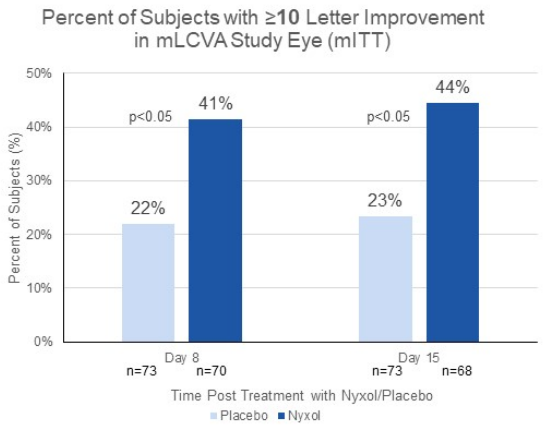
Note: Inclusion Criteria includes subjects with baseline mesopic LCVA of 20/63 or worse

LYNX-1: Nyxol Met Primary Endpoint

Significantly Higher % of Nyxol Treated Subjects Gained ≥15 Letter and ≥10 Letter From Baseline

LYNX-1 Phase 3 Trial



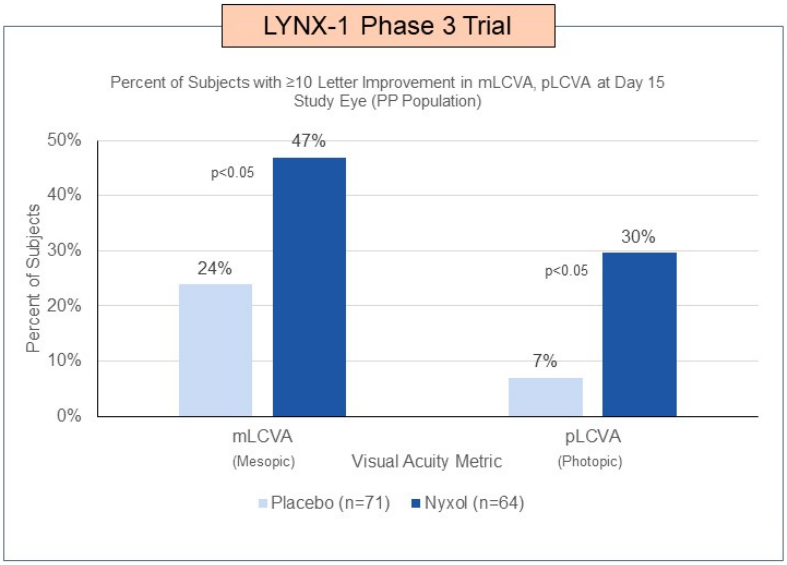


Source: LYNX-1 topline data

LYNX-1: Improvement in Distance Vision

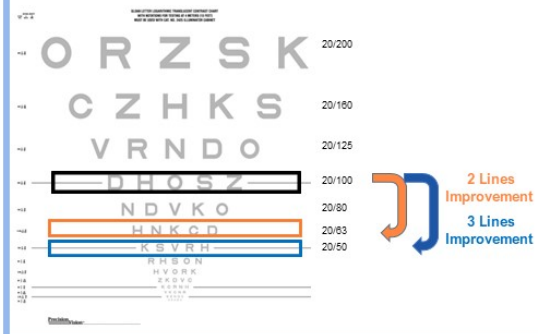
Nyxol Provides Meaningful Low Contrast Vision Benefit Across Lighting Conditions at Day 15

LYNX-1 Phase 3 Trial



FDA Accepted Endpoint For Contrast Sensitivity Assessment Tested in Dim Light (Mesopic) and Bright Light (Photopic) Conditions

5% Low Contrast Visual Acuity (LCVA) Chart



Source: LYNX-1 topline data

Summary of Positive LYNX-1 Phase 3 Results For Nyxol Eye Drops

Data Support a Favorable Benefit/Risk Profile For Subjects with NVD

Efficacy

- Met primary endpoint at Day 8 with 13% of subjects gaining 15 or more ETDRS letters of mesopic low contrast distance visual acuity vs. 3% on placebo ($p<0.05$)
- Nyxol's 3 line efficacy increased after 14 days of evening dosing, with 21% responders compared to 3% on placebo ($p<0.01$)
- Nyxol statistically significantly reduced pupil diameter by a mean of ~1 mm on Day 8 and Day 15
- Significant improvements in low contrast distance vision under photopic conditions were also observed
- Efficacy was seen with light and dark irides
- Nyxol demonstrated benefit in mesopic high contrast near vision

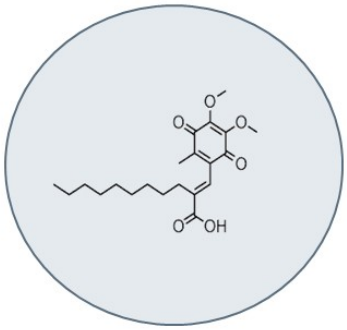
Safety

- No deaths or serious AEs
- AEs occurring in >5% of Nyxol treated subjects included: Instillation site irritation (9% vs 0% placebo), Installation site pain (13% vs 0% placebo), Dysgeusia (11% vs 0% placebo) and conjunctival hyperemia (9% vs 3% placebo)
- 84% of the AEs considered related to Nyxol were mild
- No statistical difference in conjunctival hyperemia between treatment arms with evening dosing at Day 8 and Day 15

Source: mITT Population, LYNX-1Trial

APX3330

ORAL TABLET



DR — Diabetic Retinopathy

DME — Diabetic Macular Edema

Ocuphire PHARMA

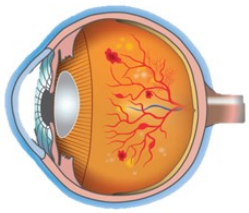
Clinical Unmet Need in Diabetic Retinal Diseases

Increasing Prevalence of DR with No Early Intervention Options

The Problem

- DR/DME are major causes of vision loss in working aged adults
- Diabetic population expected to increase dramatically worldwide
  - Losing vision is one of diabetic patients' top concerns
- Approved therapies for DR are effective but require IVT injection
- **DR patients are not routinely treated with approved injectable anti-VEGF drugs until they develop center-involved DME or PDR**
  - DR progresses resulting in vision loss
- **Early, noninvasive intervention targeting DR represents a therapeutic unmet need**

Growing Incidence of Diabetes and DR	
Diabetes	34 M US >450 M WW
DR	7 M US >150 M WW



US Projected Market in DR*

DR/DME affects about 1 in 4 people with type 1 and type 2 diabetes

$10+B
Oral Rx Revenues

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

Source:
1. American Diabetes Association; International Diabetes Federation; Healthline; *Ocuphire internal analysis and assumptions;
2. Das UN. DME, retinopathy and age-related macular degeneration as inflammatory conditions. Arch Med Sci. 2016;12(5):1142-1157. doi:10.5114/aoms.2016.61918
3. Patient survey adapted from Lions International Foundation and International Diabetes Foundation-Europe; Meltzer 2000

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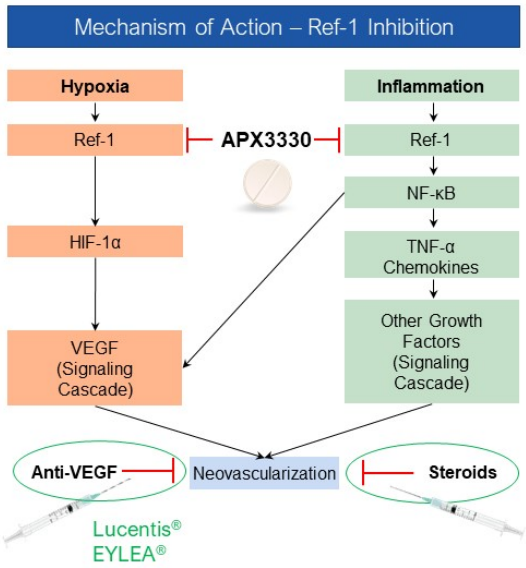
APX3330 History and Ref-1 Inhibition Mechanism

Ref-1 Involved in Multiple Key Pathways that Contribute to Diabetic Retinopathy and DME



- 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 in 11 Phase 1 and 2 trials
  - Similar oncology origin as approved anti-VEGFs
- MOA uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1
- Extensively studied in over 20 in-vitro and animal studies with favorable efficacy and safety

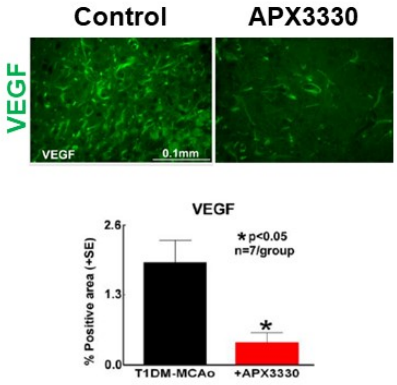
Logsdon et al (2018), Li et al (2014).

DR
DME

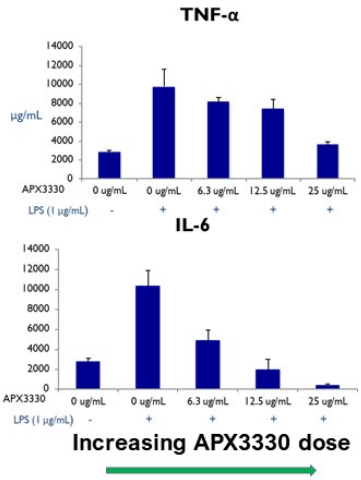
In vitro Validation of APX3330 Mechanism of Action

APX3330 Reduces VEGF Levels and Inflammatory Cytokines; Provides Neuronal Protection

APX3330 reduces VEGF protein expression in preclinical stroke model

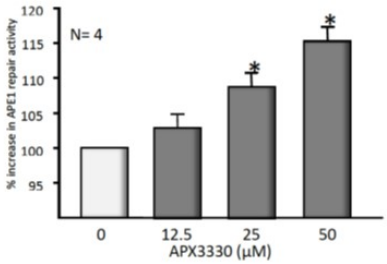


APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages



Increasing APX3330 dose

APX3330 increases DNA oxidative repair and neuronal protection



APX3330 enhances Ref-1 endonuclease activity in dorsal root ganglion neurons

Source:
1. Tao Yan *et al*. APX3330 Promotes Neurorestorative effects after stroke in type one diabetic rats. Aging and Disease. Vol 9, Oct 2018
2. Apurinic/Apyrimidinic endonuclease 1 regulates inflammatory response in macrophages.
3. Jedinak A, Dudhgaonkar S, Kelley MR, Sliva D. Anticancer Res. 2011 Feb;31(2):379-85. PMID: 21378315
4. Fehrenbacher, J. C., Guo, C., Kelley, M. R. & Vasko, M. R. DNA damage mediates changes in neuronal sensitivity induced by the inflammatory mediators, MCP-1 and LPS, and can be reversed by enhancing the DNA repair function of APE1. Neuroscience 366, 23-35, doi:10.1016/j.neuroscience.2017.09.039 (2017).

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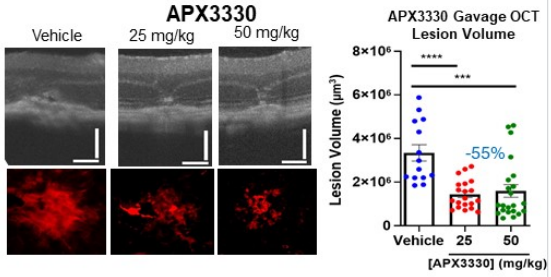
DR
DME

Preclinical Data: Oral APX3330 Blocks Neovascularization

Lesion Volume Decrease with Oral APX3330 in Murine Laser CNV Model Similar to EYLEA® Data

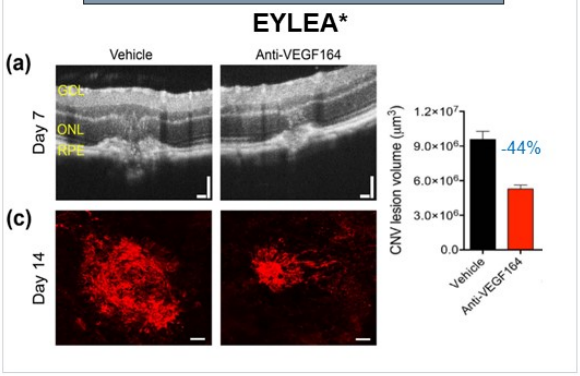
L-CNV Mouse Retina Model

Lesion Size and Corresponding Fluorescent Stains in L-CNV Models Treated with APX3330 at **25 mg/kg oral gavage**



Silva et al, 2021

L-CNV Mouse Retina Model



- ✓ Efficacy was also seen after single intravitreal injection of 20µM APX3330 in mouse L-CNV model**
- ✓ Efficacy was also seen after dosing intraperitoneal injection of 50 mg/kg twice daily, 5 days on/2 days off, for 2 weeks in mouse L-CNV model***
- ✓ Efficacy was also seen after single intravitreal injection of 20µM APX3330 in Vldlr $^{-/-}$ mice model****

Source:
1. Silva et al. ARVO 2021 Annual Meeting
2. *Published data on EYLEA. This study was performed independently from APX3330 study and is a cross-study comparison.
3. **Li 2014; *** Pasha 2018; ****Jiang 2011 (Vldlr -/- : Very Low-Density Lipoprotein receptor knock-out mice)

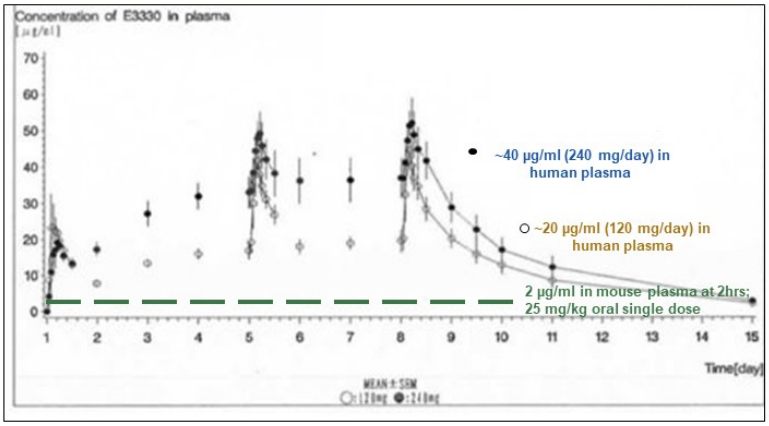
Ocuphire PHARMA

DR
DME

Phase 1/2 Clinical Trials: PK Data Supporting the ZETA-1 Trial

APX3330 is Bioavailable and Reaches the Retina via Oral Administration

Plasma levels with 120 and 240 mg/day APX3330 dosing is multiple times higher than plasma concentrations for mouse efficacy ➔ planned clinical dose is 600 mg/day



Oral administration of APX3330 reaches the retina

Mouse — 25 mg/kg APX3330 oral gavage measured in mouse retina[1]

Rat — 10 mg/kg APX3330 oral gavage measured in rat eye[2]

Human — 300 mg BID (600 mg/day total)

Established PBPK model predicts APX3330 reaches sufficient human retinal concentrations[3]

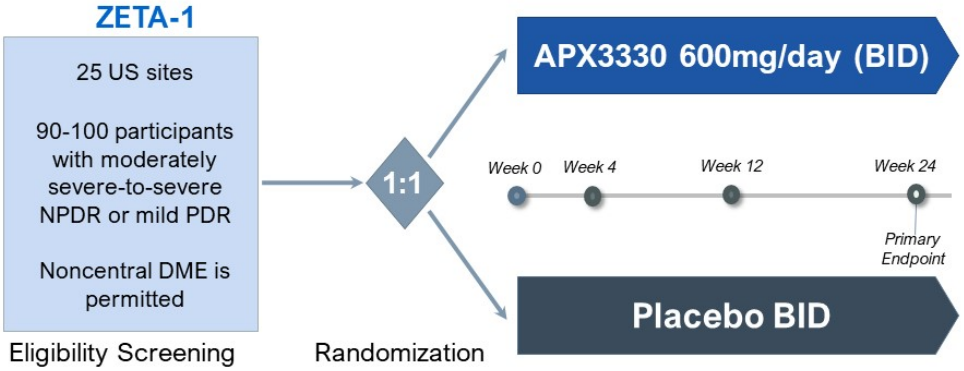
Source:
Eisai PK clinical data APX_CLN_0002 (left panel)

1. Apexian preclinical data
2. Eisai preclinical data
3. Silva et al. Presented at the ARVO 2021 Annual Meeting

Ocuphire Pharma

DR/DME ZETA-1 Phase 2b Design

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



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 Enrolled 103 DR Patients from April 2021 to March 2022

Top Line Expected in 2H 2022

NPDR = non-proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
PDR = proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
ZETA-1 Clinical Trial is Sponsored by Ocuphire Pharma https://clinicaltrials.gov/ct2/show/NCT04692688?term=ZETA-1&draw=2&rank=1

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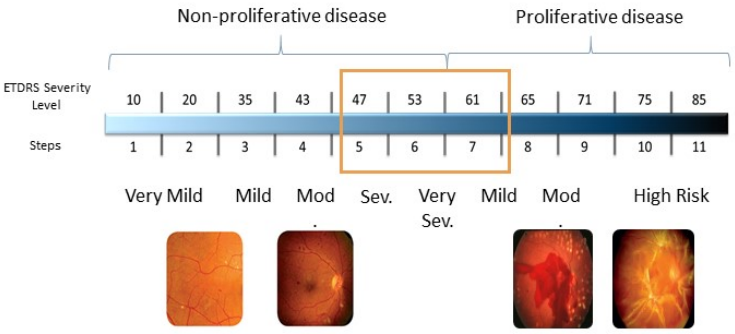
Why DRSS is an Important Endpoint?

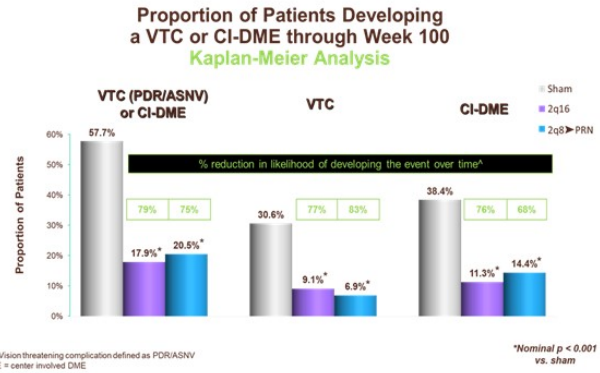
DR DME

FDA Accepted Endpoint for EYLEA® in PANORAMA Pivotal DR Trial - 2 Step Improvement on the DRSS Score at Week 24

Diabetic Retinopathy Severity Scale (DRSS)



PANORAMA: Reduction of DRSS Significantly reduces the incidence of Vision Threatening DR



Risk of vision-threatening events increases with worsening step progression

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DR
DME

Masked Safety Findings from Ongoing ZETA-1 Trial

Favorable Safety Profile (as of 3/17/2022) Observed with 600 mg Oral Daily Doses in Diabetic Subjects

APX3330 Masked Safety Data ZETA-1 Trial

103	**>4500**	**43**	**7**	***Safety profile consistent with that seen in prior studies with APX3330***
Randomized Diabetic Subjects	Subject-Days of at **600mg/day** APX3330 Exposure	Subjects with AEs (96 total events)	SAEs, all unrelated to study medication	

- **96 TEAEs in 43/103 (42%) subjects**
  - **19/96 AEs were considered probably or possibly related to study medication**
    - 14 Mild AEs (74%) in 12 subjects
    - 5 Moderate AEs in 4 subjects
      - Diarrhea[1], DME[2], urticaria, and blurry vision and vitreous hemorrhage (both in same subject)
    - No severe related AEs
  - **77/96 AEs were not related, unlikely related or unknown (3) to study medication**
    - 48 mild, 23 moderate, 5 severe, 1 unknown severity
- **2 subjects[1,2] withdrew from study due to moderate AEs**
- **7 treatment emergent SAEs in 6 subjects**
  - **None of these SAEs were related to study medication**
    - Cholecystitis, dyskinesia, progression of multivessel coronary artery disease, COVID-19, transient ischemic event, and cellulitis and left leg cellulitis (both in same subject)
- **No major organ toxicities** (liver, heart, kidney, brain, lung) or vital sign abnormalities (blood pressure or heart rate) were observed

1. Vasovagal near syncope same subject considered unrelated to study medication
2. DME possibly study medication related (APX3330 or placebo)
Note: ZETA-1 Interim Data as of database 3/18/22 with complete monitoring before final database lock; assumes 50% subjects on APX333

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DR
DME

APX3330 Product Candidate Profile for Multiple Retinal Indications

Oral, First-In-Class Ref-1 Inhibitor with Favorable Human Safety Data

APX3330: Well-tolerated Oral Dose up to 600mg/day Twice Daily Dosing

Expected Efficacy Data	Favorable Safety Profile
Improving Eye Health in Diabetics ↓ Inflammation ↓ Abnormal Angiogenesis	**>6600 Subject-exposure days* at ≥600 mg/day dose**
Enhance Compliance & Exposure Oral pill may reduce the burden of frequent anti-VEGF injections	**Few Systemic Adverse Effects** • < 5% Mild Gastrointestinal (diarrhea) • < 5% Mild Skin Rash (reversible)
	No Organ Toxicity (Liver, Cardiovascular {BP, HR}, Kidney, Neurologic, Pulmonary)
	No Ocular Effects • No observed ocular AEs

*Phase 1 and Phase 2 clinical trials by Eisai, Apexian and Ocuphire (*includes ~34 subjects from ongoing ZETA-1 study)

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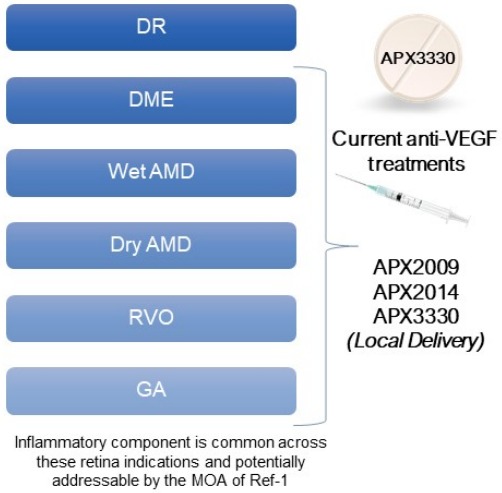
Broad Opportunities to Treat Retinal Diseases with APX Platform

APX3330 May Treat Patients Across Retinal Diseases as Single Agent or Adjunctive Therapy

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 to reduce intravitreal injection burden
- **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



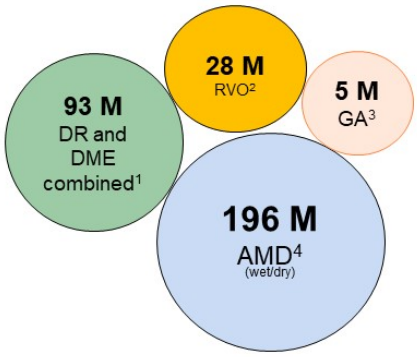
Inflammatory component is common across these retina indications and potentially addressable by the MOA of Ref-1

Large Global Market Opportunity in Retinal Disease

DR DME

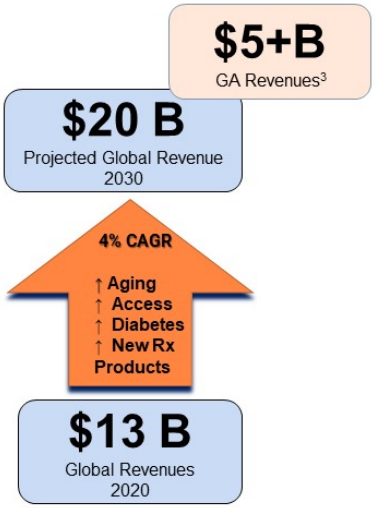
Retinal Global Markets Served by Anti-VEGF Injections Alone are Greater than $10B+ Today

Global Disease Prevalence (Patients)



$10+B
Oral Rx Revenues5

Anti-VEGF Injectable Global Revenue6



Source:
1. Nancy M. Holekamp, Overview of Diabetic Macular Edema, 2016, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6513508/pdf/jogh-09-010427.pdf https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6513508/pdf/jogh-09-010427.pdf;
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6513508/pdf/jogh-09-010427.pdf
3. Boyer DS et al., Retina 2017 2 2. Wong WL, et al. Lancet Glob Health. 2014;2:e106-16; Global Data AMD Global Drug Forecast and Market Analysis, JAMA Ophthalmology, Gibson 2012
4. https://www.brightfocus.org/macular/article/age-related-macular-facts-figures
5. Ocuphire internal analysis and assumptions
6. Market Scope 2020

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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
SynDevRx
Goldman Sachs

Mina Sooch, MBA
President & CEO and Founder

HARVARD BUSINESS SCHOOL
Gemphire Therapeutics
Apjohn Ventures
MONITOR
ProNAi

Amy Rabourn, CPA
VP, Finance

MICHIGAN ROSS
Gemphire Therapeutics
Pfizer
NeuroBo Pharmaceuticals
pwc

Ronil Patel, MS
Senior Director BD and Market Strategy

FLORIDA TECH
BETALIQ
RevitaLid
PointGuard Partners LLC
OCULOS Integrated Insight

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

UF UNIVERSITY of FLORIDA
Gemphire Therapeutics
ESPERION
Cerenis THERAPEUTICS
Pfizer

Mitch Brigell, PhD
Head, Clinical Development and Strategy

KANSAS STATE UNIVERSITY
aerpio
Pfizer
NOVARTIS

Barbara Withers, PhD
VP, Clinical and Regulatory Strategy

WAYNE STATE UNIVERSITY SCHOOL OF MEDICINE
aerpio
UBC
Pfizer

Bindu Manne
Head, Market Development and Commercialization

UNC PEMBROKE
Takeda
Shire
MERCK
Ocular Therapeutix
equinox
ThromboGenics

Chris Ernst
Global Head, QA and Manufacturing

NORTHERN KENTUCKY UNIVERSITY
aerpio
Akebia Therapeutics
MEDPACE

Laura Gambino
Director, Project Management

EASTERN MICHIGAN UNIVERSITY
aerpio
Akebia Therapeutics
Pfizer

Drey Coleman
VP, Clinical Operations

OCULOS Integrated Insight
SIRION Therapeutics
UCF
Ocuphire Pharma

Ocuphire's World-Class Medical Advisory Board

Fortunate for the Insights of Leading KOLs & Drug Candidate Co-Founders

PeposeVision

Refractive Specialist

Jay Pepose, MD, PhD
UCLA School of Medicine

CEI
Cincinnati Eye Institute

Refractive Specialist

Ed Holland, MD
Loyola University Chicago

elCON Medical

Refractive Specialist

Eliot Lazar, MD
Georgetown University

Cleveland Clinic
Cole Eye Institute

Retinal Specialist

Peter Kaiser, MD
Harvard Medical School

The Midwest Center for Sight

Refractive Specialist

James Katz, MD
University of Illinois

OCLI

Refractive Specialist

Marguerite McDonald, MD
Columbia University

Indiana University
Melvin and Bren Simon Cancer Center

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

Retina-Vitreous Associates Medical Group

Retinal Specialist

David Boyer, MD
Chicago Medical School

Jacksoneye

Refractive Specialist

Mitch Jackson, MD
University of Chicago

ChuVision

Refractive Specialist

Y. Ralph Chu, MD
Northwestern University

New England Retina Consultants

Retinal Specialist

David Lally, MD
Vanderbilt University

RETINA Consultants of America

Retinal Specialist

David Brown, MD
Baylor University

Minnesota Eye Consultants

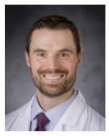
Refractive Specialist

Thomas Samuelson, MD
University of Minnesota

arcscan

Refractive Specialist

Jack Holladay, MD
University of Texas



Duke Eye Center

Retinal Specialist

Michael Allingham, MD, PhD
University of North Carolina

Ophthalmic Consultants of Boston
Excellence in Eye Care

Retinal Specialist

Jeffrey Heier, MD
Boston University

Kentucky Eye Institute

Optometry

Paul Karpecki, OD
Indiana University

Eye Care Associates of Nevada

Optometry

Douglas Devries, OD
University of Nevada

Ocuphire Pharma

Ocuphire Board of Directors

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

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Chair, Board Director

University of San Diego
VELOSBIO
zentalis
ONCTERNAL therapeutics
RetroSense THERAPEUTICS

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

HARVARD BUSINESS SCHOOL
Gemphire Therapeutics
Apjohn Ventures
MONITOR
ProNAi

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Washington University in St. Louis
Olin Business School
Allergan
RetroSense THERAPEUTICS
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Board Director

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PeposeVision INSTITUTE
Wilmer Eye Institute
Washington University in St. Louis

James Manuso, PhD/MBA
Board Director

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astex pharmaceuticals
Talfinium Investments, Inc.
GALENICA

Richard Rodgers, MBA
Board Director

CARLSON SCHOOL OF MANAGEMENT
UNIVERSITY OF MINNESOTA
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Abraxis BioScience

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Board Director

USF MUMA COLLEGE OF BUSINESS
Théa let's open our eyes
Shire
BAUSCH+LOMB

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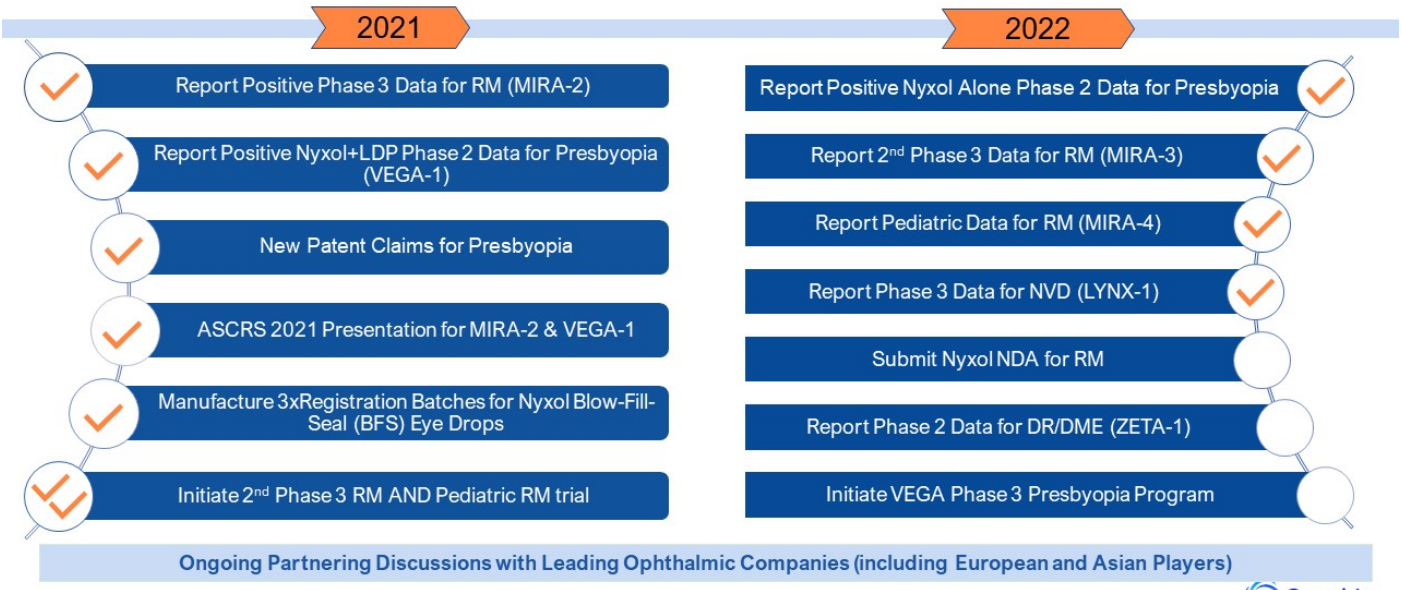
Track Record of Achieving Milestones ➔ Exciting 2022 News Cadence

Multiple Late-Stage Data Catalysts Expected in 2022 for Potential First NDA Approval in 2023



Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)

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OCUP – Market Snapshot

Active Trading Volume and Sufficient Cash Runway Into 2Q 2023

Ticker	OCUP	
Price	$2.21	As of 5-17-22
Market Cap	$43 M	As of 5-17-22
Shares Outstanding	19.3 M	As of 10Q (5-13-21)
Cash	$19.2 M	As of 3-31-22 (unaudited)
Cash Runway	Sufficient into 2Q 2023	Guidance as of 10K (3-24-22)
Average Daily Volume	~192 K	As of 5-17-22 (YTD Avg)
Short Interest	298K; 1.6% of Float	As of 4-29-22

Research Analyst Coverage on OCUP	
John Newman	Canaccord Genuity
Kristen Kluska	Cantor Fitzgerald
James Molloy	Alliance Global Partners
Soumit Roy	Jones Trading
Matthew Caufield	H. C. Wainwright

Source: FactSet

Ocuphire Pharma


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Restore Vision & Clarity
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Ocuphire Pharma
Click here to view Ocuphire Pharma's
Investor R&D Day Recording

Ocuphire Announces Positive Topline Results from LYNX-1 Phase 3Trial Evaluating Nyxol® Eye Drops for Night Vision Disturbances

Met FDA-agreed Primary Endpoint with More Nyxol Subjects Gaining 3 Lines of Low Contrast Distance Vision under Dim Light Conditions Compared to Placebo

First to Demonstrate Efficacy in Phase 3 Trial for the Large Unmet Need of Treating Night Vision Disturbances (NVD) in Subjects Experiencing Glare, Starbursts, or Halos

Benefit to Distance Vision in Dim Light Conditions Further Differentiates Nyxol from Other Presbyopia-Correcting Drops

Sixth Consecutive Positive Efficacy Readout in Last 15 Months with Nyxol Across Multiple Indications for Reversal of Mydriasis, Presbyopia, and now NVD

FARMINGTON HILLS, MI, May 19, 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 announced positive topline results from the LYNX-1 Phase 3 pivotal clinical trial investigating its product candidate Nyxol® for night (or dim light) vision disturbances (NVD). Across 12 US clinical trials with approximately 1100 subjects, over 650 subjects have now been exposed to Nyxol.

NVD is a condition in which unfocused rays of light derived from imperfections (or higher order ocular aberrations) in the periphery of the cornea manifest as reduced image quality when the pupil dilates in dim light conditions. Patients with NVD experience glare, halos, starbursts, and decreased contrast sensitivity. The effects of NVD can be mitigated by moderately reducing pupil diameter to eliminate some of the aberrations and their scattering effect, without impeding the ability to see in dim light due to reduced retinal illumination.

“We are pleased with this demonstrated efficacy of Nyxol in patients with NVD,” stated Mina Sooch, MBA, founder and CEO of Ocuphire Pharma. “LYNX-1 represents our sixth consecutive positive data readout for Nyxol in several indications and is a critical milestone towards future product registration. In alignment with our overall clinical priorities, and while we plan for a future LYNX trial as needed next year, we will focus on the pivotal trials for presbyopia and on the NDA submission and pre-commercial activities for Nyxol in reversal of mydriasis (RM). Importantly, the LYNX-1 trial results provide additional support for the safety and vision improvement benefits of Nyxol in RM and presbyopia in dim light conditions. I am very proud of our team’s track record of excellent execution. We are committed to making a difference for millions of patients with vision problems and are proud of the disruptive innovation we bring to the ophthalmic space. In that regard, we look forward to yet another late-stage clinical data readout in 2022 from the study of oral APX3330 for diabetic retinopathy.”

Highlights of LYNX-1 NVD Phase 3 Results

LYNX-1 is a registration trial for Nyxol in this chronic NVD indication, and was designed as a randomized, double-masked, placebo-controlled, Phase 3 study to evaluate the safety and efficacy of Nyxol compared to placebo. In the trial, 145 study participants who experienced vision impairment under dim light conditions were randomized to receive either Nyxol or placebo, self-administered in each eye daily, at or near bedtime, over 14 days. The primary endpoint was the gain of 3 lines (or 15 letters) or more of distance vision improvement on a low contrast chart in dim light conditions.

Baseline demographics and ocular characteristic means were well-balanced across Nyxol and placebo treatment arms. Highlights of the patient population include a mean age of 46 years with participants ranging from 19 to 70 years old; subjects with a mix of light and dark irides; mean baseline mesopic pupil diameter of 6.1 mm; and mean distance visual acuity of only 17 letters (20/100 Snellen) under mesopic low contrast conditions.

Summary of LYNX-1 Data

- The FDA-agreed primary endpoint was met, with a statistically significant greater percentage of Nyxol-treated subjects having gained 15 or more letters of mesopic low contrast distance visual acuity (mLCVA) at Day 8, compared to placebo (13% vs 3%; $p<0.05$)
- Key secondary efficacy endpoints were also met with statistical significance:
    - The effect of Nyxol increased at Day 15, with 21% of subjects gaining 15 or more letters of mLCVA compared to 3% placebo ($p<0.01$)
    - Nyxol significantly increased the percentage of subjects gaining 10 or more letters of mLCVA at both Day 8 with 41% vs. 22% placebo ($p<0.05$) and at Day 15 with 44% vs. 23% ($p<0.05$)
- Nyxol showed a favorable safety and tolerability profile:
    - There were no serious adverse events
    - Adverse events occurring in Nyxol-treated subjects were predominantly mild in severity and were consistent with those observed in previous trials

Jay Pepose, M.D., Ph.D., Chief Medical Advisor and Board member said, “In the past, patients with night vision disturbances sometimes puzzled eye care professionals because their complaints often impacted the quality of vision far more than the quantity of vision as assessed in the office using standard high contrast charts. In the LYNX-1 study, after 14 days of dosing, a remarkable 21% of subjects achieved the 3 line improvement, the high bar set by the FDA. Moreover, 44% of subjects gained a clinically meaningful 2 line improvement in mesopic low contrast vision - a test of image quality that is sensitive to higher order aberrations and induced spatial phase shifts seen in patients with night vision disturbances. The unique 24-hour duration of Nyxol’s effect in reducing pupil diameter makes this a convenient option for evening dosing for these patients, who find nighttime driving and other dim light activities challenging. In distinction to some other classes of miotics, the mechanism of action of Nyxol obviates any increased risk of retinal tears or detachment in this cohort of patients, many of whom have longer axial lengths and are therefore at higher retinal detachment risk. An additional safety attribute of Nyxol is that it does not make the pupil too small, which can markedly impact retinal illumination and thereby reduce retinal neural contrast and distance vision.”

Marguerite McDonald, M.D., F.A.C.S., Clinical Professor of Ophthalmology at New York University’s Langone Medical Center and Tulane University Health Sciences Center, and member of Ocuphire’s Medical Advisory Board said, “I applaud Ocuphire for its commitment to pursue a treatment option for NVD. It is a common condition that has previously been largely unrecognized. I consider the results of the LYNX-1 study to be groundbreaking. As a refractive surgeon who has been involved with the development of Nyxol since its inception, I am happy to have a potential treatment option for my patients who suffer from NVD. NVD is currently patient-reported, including people of all ages who are post-LASIK, post-corneal ulcer, post-radial keratotomy, post-corneal transplant, tear-film instability or dry eye disease, keratoconus, or post-cataract surgery with multifocal or extended depth of focus intraocular lens implants. Eyecare professionals currently do not have the tools to actively manage NVD. Once a treatment becomes available, eyecare providers will begin to address this condition, and we expect that this market may grow, as was the case when Restasis® was approved for dry eye treatment.”

Ocuphire Pharma plans to present LYNX-1 topline data and additional data at upcoming medical conferences. For more information about the LYNX-1 trial, please visit www.clinicaltrials.gov (NCT04638660).

Night Vision Disturbances Market Opportunity

According to GlobalData market research, approximately 38 million individuals in the US are believed to suffer from NVD, also referred to as dim light vision loss, with an estimated 16 million having moderate-to-severe NVD that may be directly addressable with a pupil modulation approach. The market size findings from the in-depth physician and patient surveys were larger than previously projected for this new unmet ophthalmic indication. Upon interview of patients who self-report NVD, 25% completely avoid driving at night. Furthermore, 67% of those that report moderate or severe NVD would be willing to try an eye drop treatment option. Seventy-five percent (75%) of physicians surveyed said they expect the diagnosis to increase once a treatment becomes available.

Despite many addressable patients with moderate-to-severe NVD, there is no FDA-approved treatment on the market for NVD. Pupil modulation by Nyxol through inhibition of the iris dilator muscle may offer symptomatic relief for these patients.

About Ocuphire Pharma

Ocuphire is a publicly-traded (NASDAQ: OCUP), clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of refractive and retinal eye disorders. The Company's lead product candidate, Nyxol® eye drops (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 12 completed clinical trials. Ocuphire has reported positive data from MIRA-2, MIRA-3 registration trials and MIRA-4 pediatric safety trial for the treatment of RM. Ocuphire also reported positive topline data from a Phase 2 trial of Nyxol for treatment of presbyopia, both Nyxol as a single agent and Nyxol with low dose pilocarpine ("LDP") 0.4% as adjunctive therapy. The Company recently reported positive topline results from LYNX-1 Phase 3 trial of Nyxol 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. The Company recently announced the completion of enrollment in a Phase 2b clinical trial of APX3330 to treat DR/DME (ZETA-1). Please visit www.clinicaltrials.gov to learn more about Ocuphire's ongoing APX3330 Phase 2b trial in DR/DME (NCT04692688) and completed Nyxol trials: Phase 3 registration trial in NVD (NCT04638660), Phase 3 registration trials in RM MIRA-2 (NCT04620213), MIRA-3 (NCT05134974), MIRA-4 pediatric safety study (NCT05223478), and VEGA-1 Phase 2 trial in presbyopia (NCT04675151). As part of its strategy, Ocuphire will continue to explore opportunities to acquire additional ophthalmic assets and seek strategic partners for late-stage development, regulatory preparation, and commercialization of drugs in key global markets. 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, the success and timing of planned regulatory filings (including NDA filings), the market for NVD and other indications, the timing and results of potential future clinical trials, business strategy, pre-commercialization activities, and commercialization of Ocuphire's product candidates. 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.

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