

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): June 30, 2021

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 June 30, 2021, Ocuphire Pharma, Inc. (the “Company”) posted on its website an informational presentation regarding the results of its VEGA-1 Phase 2 trial in presbyopia. 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 June 30, 2021, the Company issued a press release regarding the results of its VEGA-1 Phase 2 trial in presbyopia. 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
<u>99.1</u>	Investor Presentation Materials, dated June 30, 2021.
<u>99.2</u>	Press Release, dated June 30, 2021.

SIGNATURE

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: June 30, 2021



VEGA-1 Phase 2 Topline Results Conference Call

June 30, 2021

Disclosures and Forward Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning Ocuphire Pharma, Inc.'s ("Ocuphire" or the "Company") product candidates and future milestones, including the potential for Nyxol to be a "best in class" presbyopia drop. These forward-looking statements are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) 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.

The Company makes no representation or warranty, express or implied, as to the accuracy or completeness of the information contained in or incorporated by reference into this presentation. Nothing contained in or incorporated by reference into this presentation is, or shall be relied upon as, a promise or representation by the Company as to the past or future. The Company assumes no responsibility for the accuracy or completeness of any such information. This presentation may not be reproduced or provided to any other person (other than your advisor) without our prior written consent. By accepting delivery of this presentation, you agree to the foregoing and agree to return this presentation and any documents related thereto and any copies thereof to us or to destroy the same if you do not make an investment in any securities. The information contained within this presentation shall not, except as hereinafter provided, without the prior written consent of the Company, be disclosed by you or your representatives in any manner whatsoever, in whole or in part, and shall not be used by you or your representatives other than for the purpose of evaluating the transaction described herein. By accepting delivery of this presentation you further acknowledge and agree aware of the restrictions imposed by the United States securities laws on the purchase or sale of securities by any person who has received material, nonpublic information from the issuer of the securities or any affiliate thereof and on the communication of such information to any other person when it is reasonably foreseeable that such other person is likely to purchase or sell such securities in reliance on such information for so long as the information remains material and non-public. 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.



Agenda and Participants

Phase 2 Trial Topline Readout As Planned In 2Q21

- Topline VEGA-1 Phase 2 Clinical Trial Results for Nyxol and Low-Dose Pilocarpine in Presbyopia
- Presbyopia Market Opportunity
- Future Milestones
- Q&A

Participants

Mina Sooch, MBA, President and CEO

Mitch Brigell, PhD, Head of Clinical Development

Jay Pepose, MD, Medical Advisory Board & Corporate Board Member

Susan Benton, Corporate Board Member

Charlie Hoffmann, MBA, VP of Corporate Development and Operations

Amy Rabourn, MAcc, VP of Finance

Ocuphire Pipeline & Upcoming Milestones

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

	Product Candidate	Indication	Development Stage				Anticipated Milestones
			Pre-clinical	Phase 1	Phase 2	Phase 3	
Ocuphire-Focused Development			Positive Data Readout				Initiated Phase 3 MIRA-2 trial 4Q20; Topline data reported in 1Q21 (n=185)
	0.75% Nyxol® Eye Drop	Reversal of Mydriasis (RM)					Initiate Phase 3 MIRA-3 trial 2H21; Data expected in early 2022 (n=330)
							Initiate Pediatric trial 2H21; Data expected in early 2022 (n=20)
	0.75% Nyxol® Eye Drop	Dim Light or Night Vision Disturbances (NVD)					Initiated Phase 3 LYNX-1 trial 4Q20; Data expected in 3Q21 (n=160)
	0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops	Presbyopia (P)					Initiated Phase 2 VEGA-1 trial 1Q21; Topline data reported in 2Q21 (n=150)
Partnering-Focused Development	APX3330 Oral Pill	Diabetic Retinopathy (DR)/ Macular Edema (DME)					Initiated Phase 2 ZETA-1 trial Apr21; Data expected by early 2022 (n=100)
	APX2009 Intravitreal	DME, Wet Age-Related Macular Degeneration (wAMD)					Next steps: IND enabling studies (with partner funding)

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



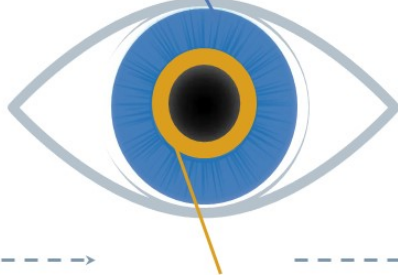
Product Profile: Nyxol + Low-Dose Pilocarpine (LDP) Combo

Moderate Use of Iris Dilator And Iris Sphincter Muscles To Improve Near Vision

0.75% Nyxol



**Iris Dilator
Muscle
Inhibition**



- Active ingredient approved decades ago 505(b)(2)
- Novel MOA on iris dilator with 24+ hour durability with moderate 1+mm pupil reduction
- Chronic daily dosing of Nyxol at bedtime demonstrated no daytime redness
- Well-tolerated with no systemic effects
- Stable, preservative-free, single use vial



0.4% LDP

**Iris Sphincter
Muscle
Activation**

- Active ingredient approved decades ago 505(b)(2)
- Known MOA on sphincter muscle with more potent miotic effects at approved doses (1%, 2%, 4%)
- Chronic daily dosing in daytime
- Low concentration avoids known tolerability issues:
 - headache and browache
 - redness
 - accommodative spasm causing loss of distance vision especially at night



Potential 'Best in Class' Presbyopia Drop

Topline Results From Vega-1 Were Positive...

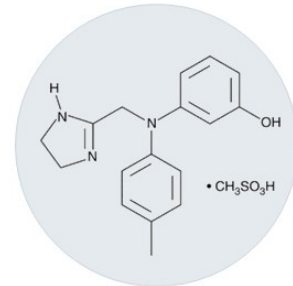
Nyxol + LDP Presbyopia Treatment is Differentiated:

- ✓ Statistically significant efficacy data
- ✓ Favorable safety profile
- ✓ Comfort and tolerability
- ✓ Fast onset
- ✓ Long duration
- ✓ Maintain good distance visual acuity (night/day)
- ✓ Novel tunable pupil modulation

Nyxol[®]



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



Phentolamine
Mesylate

Topline VEGA-1 Phase 2 Results

Randomized, Multi-Center, Double-Masked, Placebo-Controlled Study of the Safety and Efficacy of Nyxol (0.75% Phentolamine Ophthalmic Solution) + 0.4% Low Dose Pilocarpine (LDP) for the Treatment of Presbyopia

Clinical trial NCT#04675151

Objectives and Key Eligibility Criteria

VEGA-1 (OPI-NYXP-201) Phase 2 Trial Evaluating Nyxol + LDP for Treatment of Presbyopia

Key Objectives

PRIMARY

- To evaluate the efficacy of Nyxol + LDP to improve DCNVA compared to Placebo alone in presbyopia subjects

KEY SECONDARY

- To evaluate the ocular and systemic safety of Nyxol + LDP and each component individually
- To evaluate multiple secondary visual acuity and pupil diameter endpoints

Key Eligibility Criteria

INCLUSION

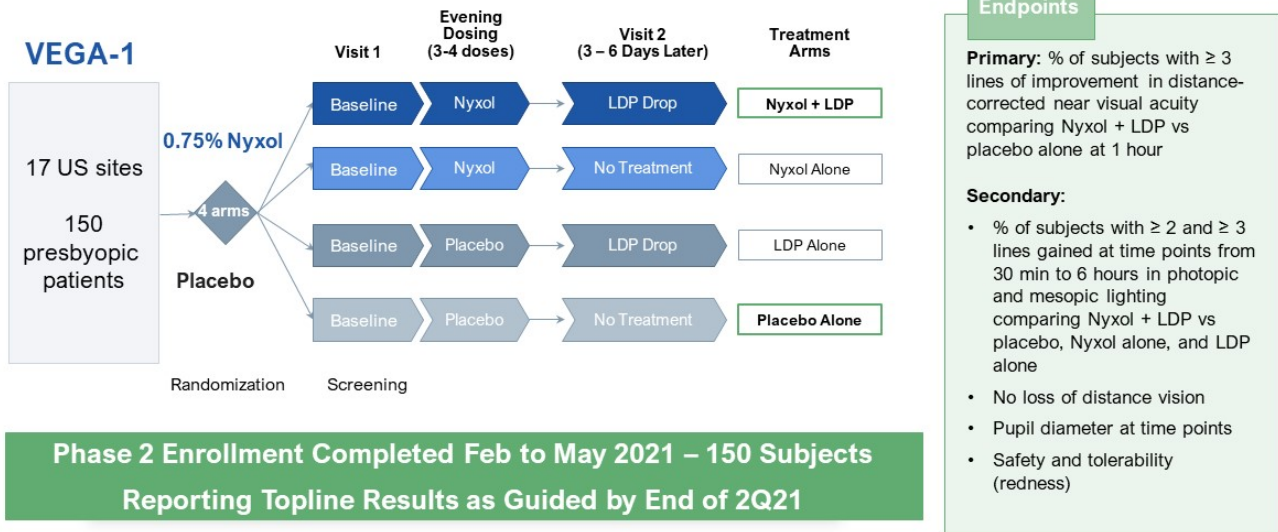
- Males or females ≥ 40 and ≤ 64 years of age.
- BCDVA of 20/20 or better under photopic conditions
- DCNVA of 20/50 or worse under photopic conditions
- Binocular best-corrected near VA is 20/25 or better

EXCLUSION

- Clinically significant ocular disease
- Recent or current evidence of ocular infection or inflammation in either eye

Presbyopia VEGA-1 Phase 2 Design

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



Patient Population – Subject Disposition

Per Protocol Population, mITT, And Safety Population Are Essentially Identical

	Placebo Alone N (%)	Nyxol Alone N (%)	LDP Alone N (%)	Nyxol+LDP N (%)	Total N (%)
All Randomized Population (ARP)	45	30	31	44	150
Safety Population (SP)	45 (100%)	30 (100%)	31 (100%)	44 (100%)	150 (100%)
Modified Intention to Treat Population (mITT)	44 (98%)	30 (100%)	31 (100%)	43 (98%)	148 (99%)
Per Protocol Population (PP)	43 (96%)	30 (100%)	31 (100%)	43 (98%)	147 (98%)
Completed Study	44 (98%)	30 (100%)	31 (100%)	43 (98%)	148 (99%)
Discontinued Study Early	1 (2%)	0	0	1 (2%)	2 (1%)

- 148/150 subjects completed the study (mITT)
- Only a single subject difference between mITT and PP population
- Per Statistical Analysis Plan, all analyses performed on PP population with results being nearly identical for mITT

Demographics (PP Population)

Treatment And Placebo Arms Were Balanced In This Phase 2 Clinical Trial

	Placebo Alone N=43	Nyxol Alone N=30	LDP Alone N=31	Nyxol+LDP N=43	Total N=147
Age (years): Median (Range)	52 (42-62)	54 (41-60)	52 (44-64)	53 (43-63)	53 (41-64)
Sex: Male n (%)	15 (35%)	7 (23%)	13 (42%)	5 (12%)	40 (27%)
Female n (%)	28 (65%)	23 (77%)	18 (58%)	38 (88%)	107 (73%)
Race: White n (%)	37 (86%)	26 (87%)	28 (90%)	40 (93%)	131 (89%)
African American n (%)	4 (9%)	0 (0%)	1 (3%)	0 (0%)	3 (2%)
Asian n (%)	2 (5%)	0 (0%)	6 (6%)	6 (6%)	11 (5%)
Other* n (%)	0 (0%)	1 (3%)	1 (3%)	0 (0%)	2 (1%)
Dark Iris Color: n (%)	18 (42%)	12 (40%)	12 (39%)	18 (42%)	60 (41%)
Light Iris Color: n (%)	25 (58%)	18 (60%)	19 (61%)	25.1 (58%)	87 (59%)

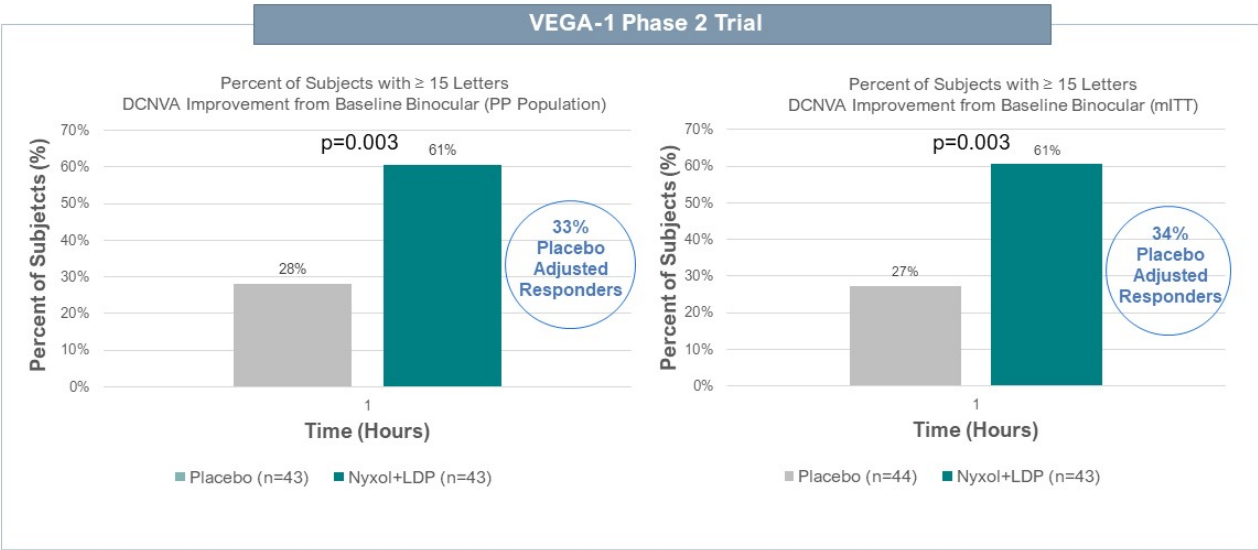
* includes American Indian or Alaska Native; Native Hawaiian or Other Pacific Islander

Baseline Characteristics Study Eye (PP Population)

Treatment Arms Were Balanced Across Key Ocular Measurements

	Placebo Alone N=43	Nyxol Alone N=30	LDP Alone N=31	Nyxol+LDP N=43	Total N=147
Baseline Characteristic					
Photopic DCNVA Mean Letters read-Binocular (Snellen Equiv.) 70 letters = 20/20	46 (20/63)	45 (20/63)	48 (20/63)	46 (20/63)	46 (20/63)
Photopic BCDVA Mean Letters read-Binocular (Snellen Equiv.) 55 letters = 20/20	62 (20/15)	61 (20/15)	60 (20/15)	61 (20/15)	61 (20/15)
Photopic Pupil Diameter Mean (mm)	4.3	4.5	4.3	4.3	4.3
Mesopic Pupil Diameter Mean (mm)	5.1	5.0	5.0	5.1	5.1
IOP (mmHg)	13.5	14.8	13.9	14.4	14.1

Primary Endpoint: % of Subjects ≥ 15 Letter Gain in Photopic DCNVA at 1 Hour
Primary Endpoint Was Met For Nyxol + LDP Gaining ≥ 15 Letters Near Vision In PP Population

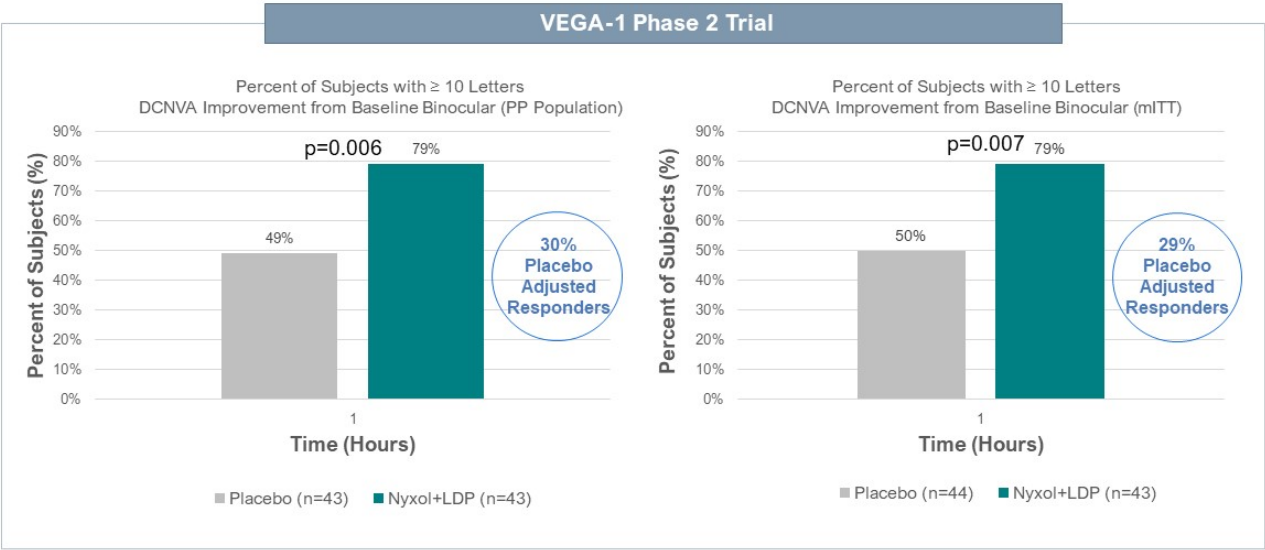


14 Source: VEGA-1 TLR Table 14.2.1.1 (mITT) and 14.2.1.2 (PP) Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point . 15 letters is 3 lines.

P

Secondary Endpoint: % of Subjects ≥ 10 Letter Gain In Photopic DCNVA At 1 Hour

Many Subjects Treated With Nyxol + LDP Gained A Clinically Meaningful ≥ 10 Letters

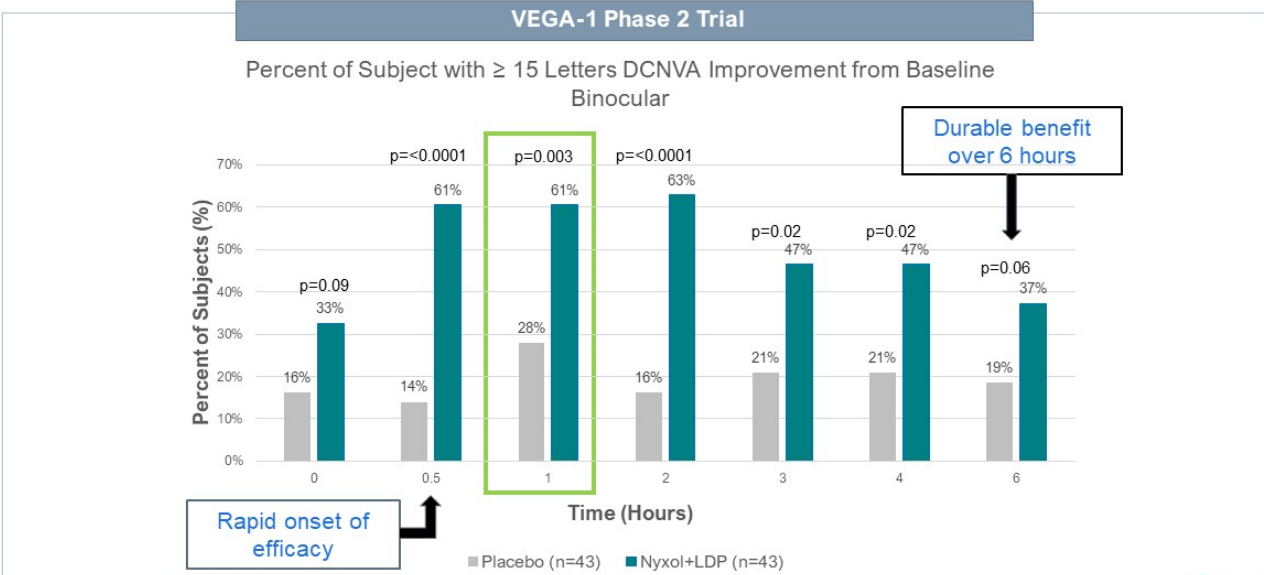


15 Source: VEGA-1 TLR Table 14.2.1.1 (mITT) and 14.2.1.2 (PP) Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point. 10 letters is 2 lines.

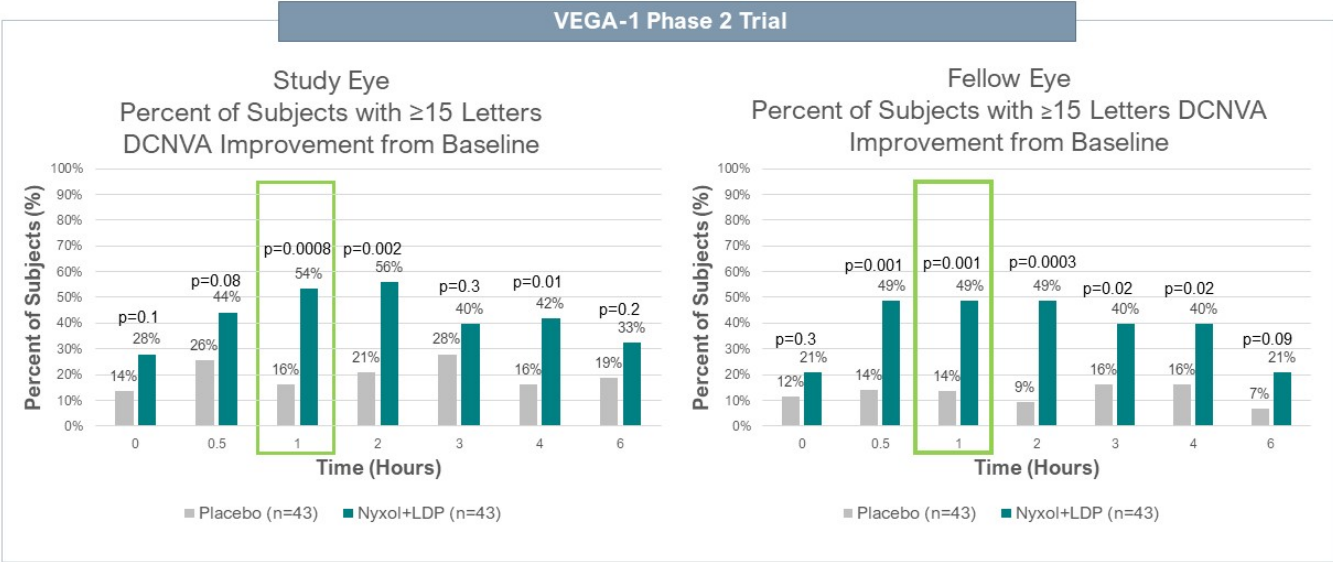


Secondary Endpoint: % of Subjects ≥ 15 Letter Gain At All Timepoints

Nyxol + LDP Had Strong Response With ≥ 15 Letter Gain From 30 Min To 6 Hours



Secondary Endpoint: % of Subjects ≥ 15 Letter Gain DCNVA (Monocular)
Similar Results Were Seen Monocularly For Study Eye And Fellow Eye On Primary Endpoint

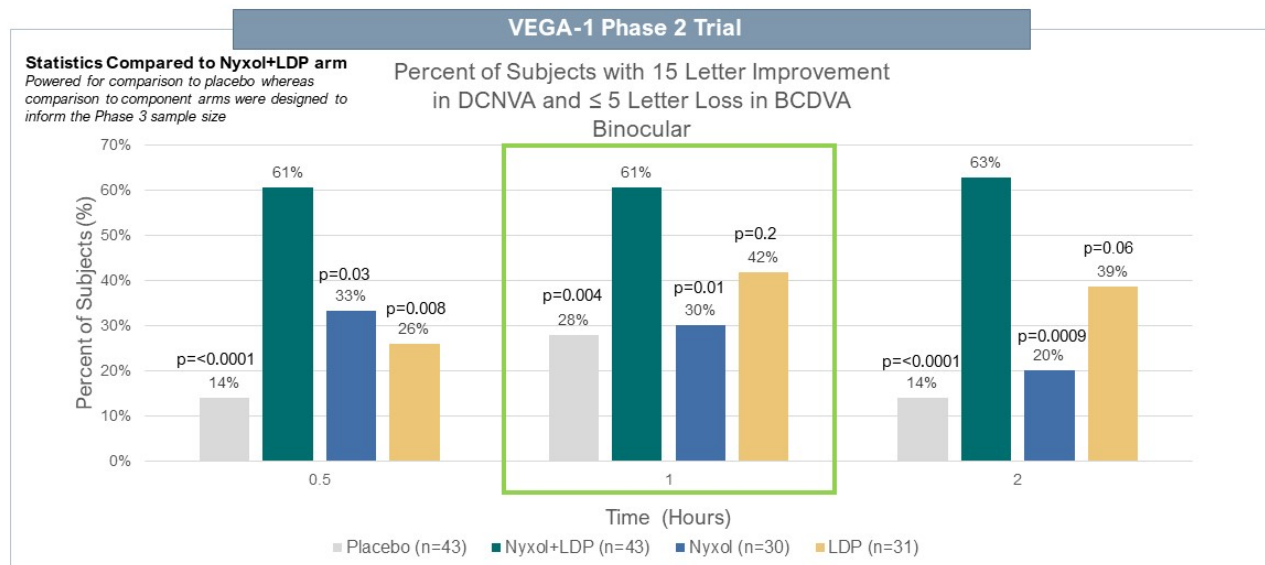


17 Source: VEGA-1 TLR Table 14.2.1.2 Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point (PP Population)

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2nd Endpoint: % of Subjects ≥ 15 Letter Gain In Near & ≤ 5 Letter Loss In Distance

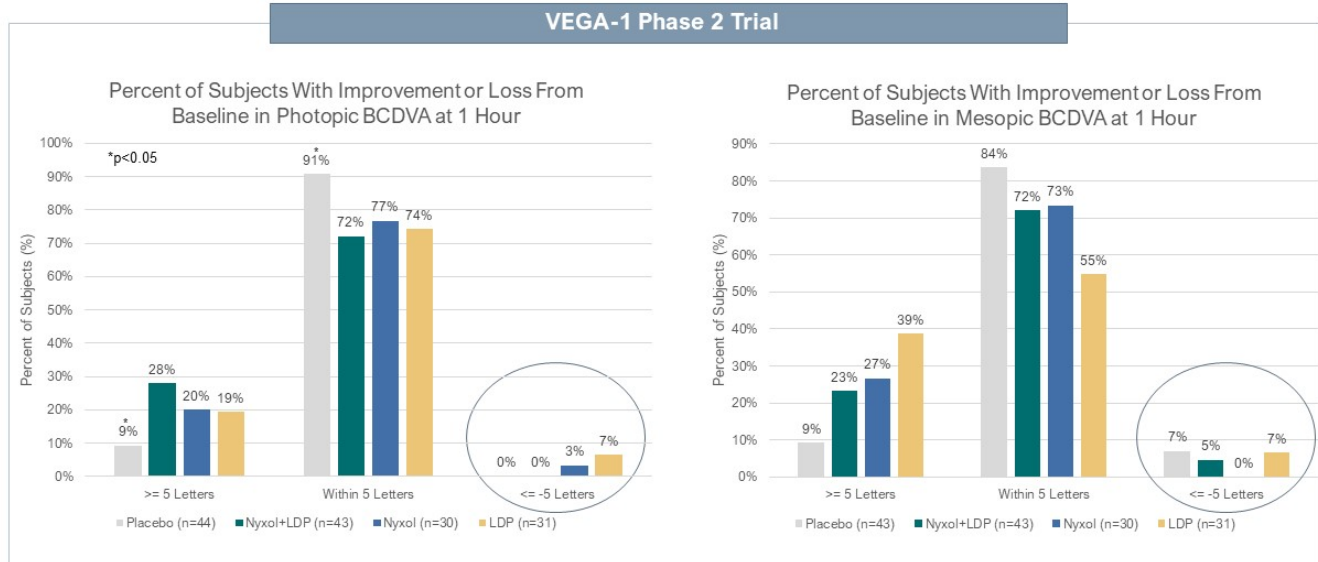
Phase 3 Approval Endpoint Also Showed Early Onset Of Near Vision Gain Without Loss of Distance



18 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)

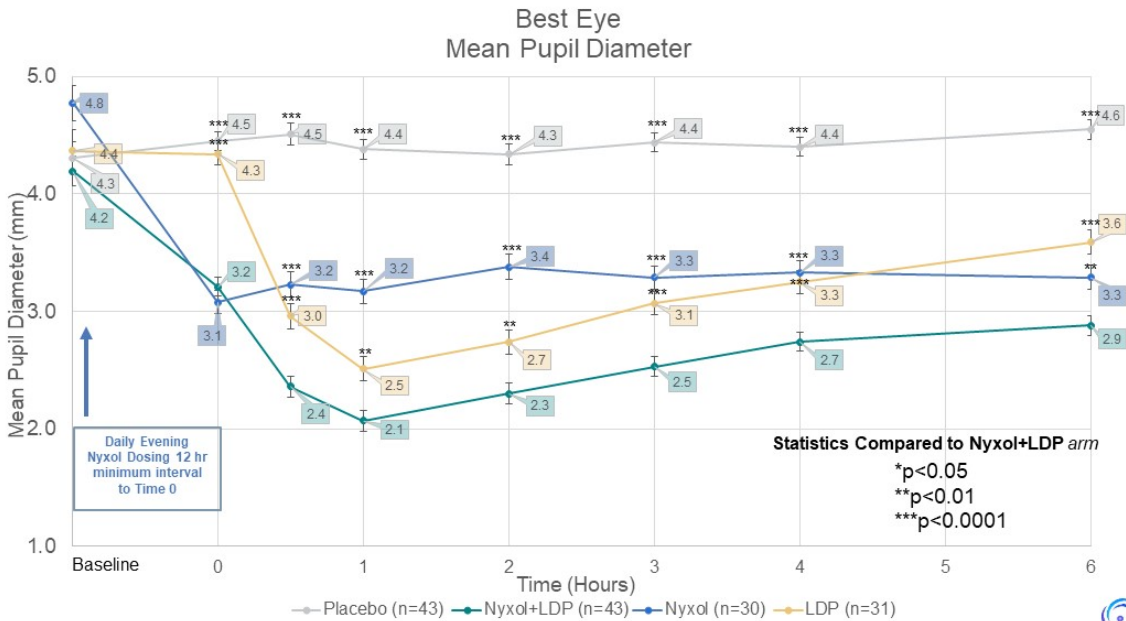
Change in Photopic and Mesopic BCDVA at the 1-Hour Timepoint

Treatment With Nyxol And/Or LDP Did Not Reduce BCDVA And Had A Modest Beneficial Effect



Secondary Endpoint: Mean Pupil Diameter Over Time

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



Secondary Endpoint: Safety Findings

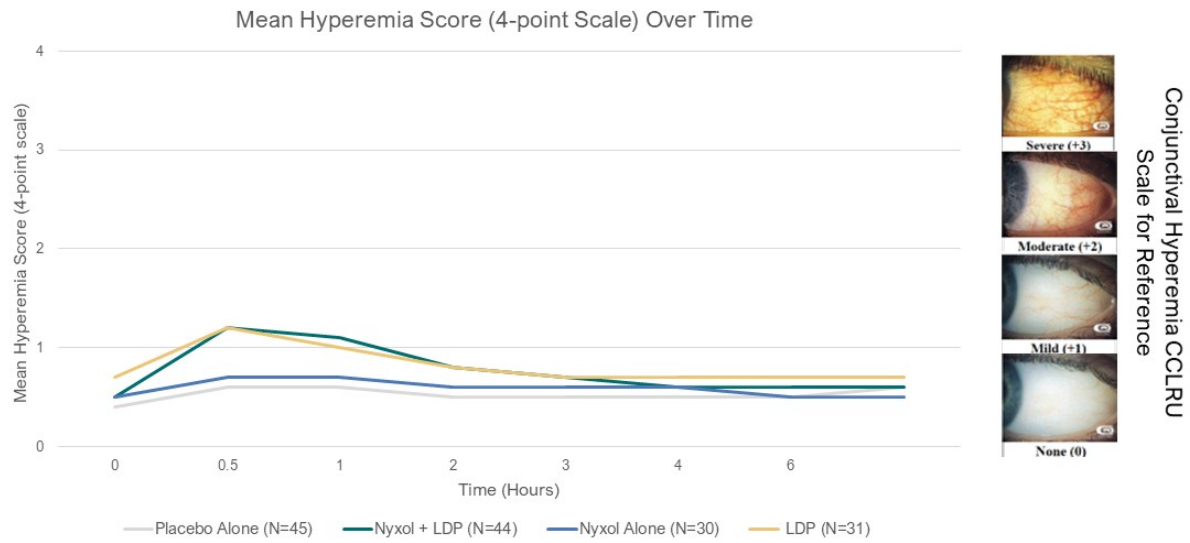
Nyxol+LDP Combination Was Well Tolerated With A Favorable Safety Profile In VEGA-1 Trial

	Placebo Alone n=45	Nyxol Alone n=30	LDP Alone n=31	Nyxol+LDP n=44
Total Treatment Emergent Adverse Events (n)	4	18	13	50
TEAEs by Severity (n [%])				
Mild	1 (2.2%)	6 (20%)	6 (19.4%)	13 (29.5%)
Moderate	1 (2.2%)	0 (0%)	0 (0%)	1 (2.3%)
Severe	0 (0%)	0 (0%)	0 (0%)	1 (2.3%)
AEs Occurring in ≥ 5% of subjects (n [%])				
Instillation Site Pain (Mild)	1 (2.2%)	3 (10%)	0 (0%)	4 (9.1%)
Instillation Site Erythema (Mild)	0 (0%)	3 (10%)	2 (6.5%)	5 (11.4%)
Conjunctival Hyperemia (Mild)	0 (0%)	2 (6.7%)	0 (0%)	2 (4.5%)
Eye Disorders (Mild)	1 (2.2%)	2 (6.7%)	4 (12.9%)	5 (11.4%)

- No deaths, no serious AEs, and 1 withdrawal due to AEs (on Nyxol alone)
- **0% Headaches or Browaches** reported for Nyxol+LDP and Nyxol alone
- Only 1 subject in LDP alone arm reported mild headache
- Almost all AEs were mild and most common was mild instillation site discomfort
- **Distance visual acuity not adversely affected (as shown earlier)**
- No change in IOP

Tolerability: Conjunctival Hyperemia (Redness) Score

Minor Change (0.5 Point) In Redness Score Over The First 2 Hours In LDP Arms



Summary of Positive VEGA-1 Phase 2 Results for Nyxol Eye Drops

Efficacy Data In Subjects With A Favorable Safety Profile In Presbyopia With Nyxol And Low Dose Pilocarpine

- **Met the primary endpoint** with statistical significance for binocular photopic near vision at 1 hour
 - 61% Nyxol + LDP gained 15 letters (3 lines) or more vs. 28% Placebo (33% Placebo Adjusted)
- **Met the Phase 3 co-primary endpoint** vs. placebo gaining 15 letters (3 lines) near vision with less than 5 letters of distance vision loss
- **Met many key secondary endpoints**
 - Rapid onset at 30 min
 - Durable near vision improvement through at least 6 hours
 - Nyxol+LDP was numerically better than each component through 2-hours
 - Sustained significant reduction in PD over at least 18 hours due the durability effects of Nyxol
 - Near vision efficacy seen monocularly and binocularly
 - Also, efficacy data in both light and dark iris colors
- **Favorable safety profile for Nyxol + LDP**
 - No serious AEs
 - No systemic AEs were observed in >5% subjects
 - No headaches, no browaches, and no blurry vision AEs were reported
 - Only mild, transient conjunctival hyperemia observed in <5% of subjects
- **Positive Phase 2 results lead to advancing Phase 3 presbyopia program**



Next Steps

Ocuphire Plans To Present Full Results At ASCRS In July And Move Into Phase 3

VEGA-1 Presbyopia Presentation by Dr. Pepose at ASCRS on Sunday July 25, 2021 at 8:45am

ASCRS Paper ID 76645 SPS-204 Presbyopia Correcting IOL Comparisons, New Treatments and Studies
MBCR - Level 2, Lagoon EF

MIRA-2 Reversal of Mydriasis Presentation by Dr. Pepose at ASCRS on Monday July 26, 2021 at 4:25pm

ASCRS Paper ID 76599 SPS-316 Corneal Diagnostic Studies
MBCR - Level 2, Lagoon EF

Advance into Phase 3 Presbyopia Registration
Trials in 2022 Towards a Potential NDA in 2023

Presbyopia Market Opportunity

Presbyopia – Chronic Opportunity

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

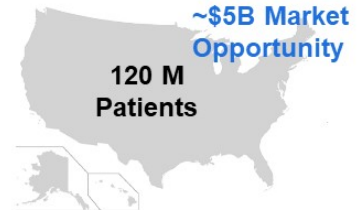
The Problem

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

“Effectively everyone over 40 will have the problems with reading.”

Physician KOL

No Currently Approved
Drug Therapies



Seeking Treatment Findings

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

Presbyopia – Chronic Opportunity

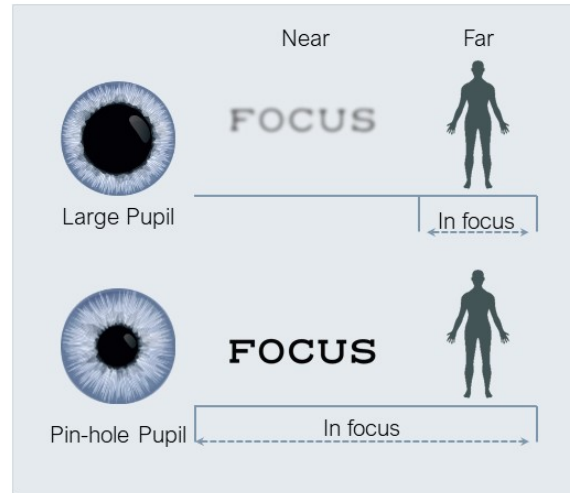
Pupil Modulation Eye Drops May Replace Reading Glasses

Nyxol's Potential Differentiated Solution

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

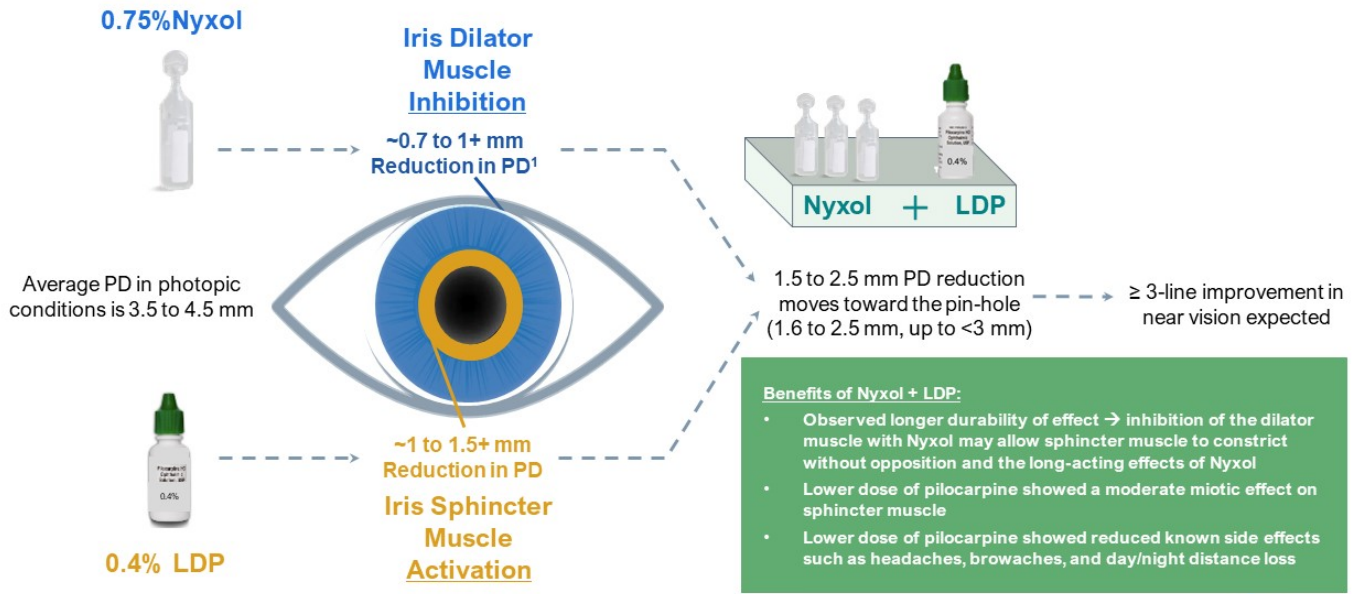
“This would just become part of my daily routine for my eyes to be able to see things up close. How convenient is that?”

Presbyopic Patient, age 49



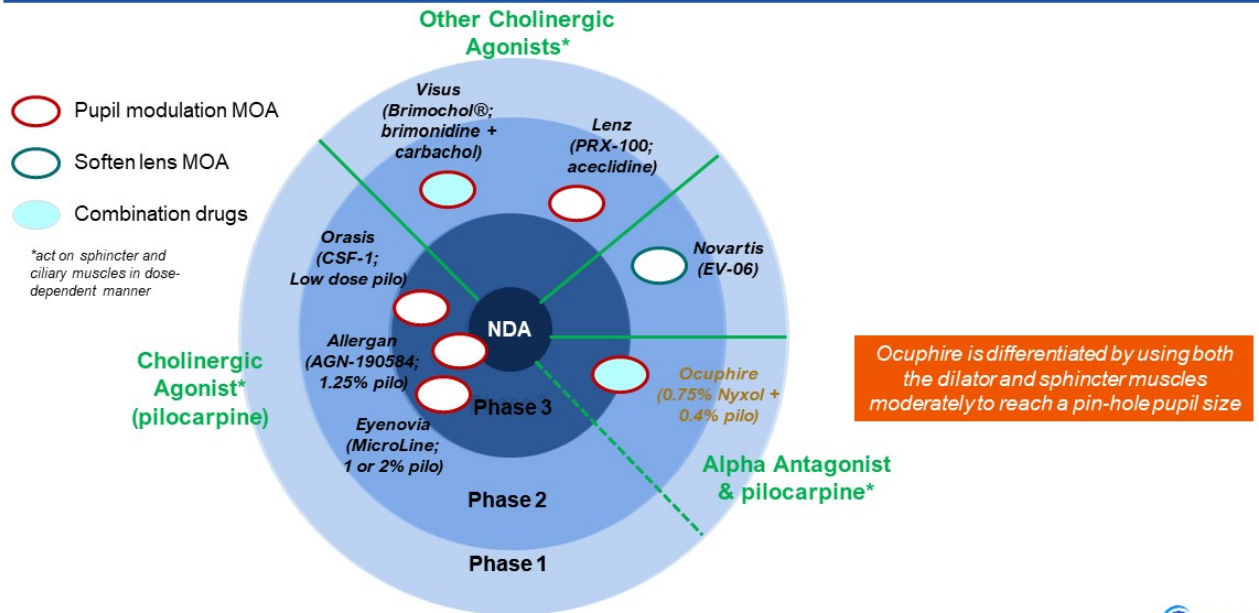
Synergistic Effects of Nyxol + Low-Dose Pilocarpine (LDP) Combo

Nyxol + LDP Demonstrated Efficacy and a Favorable Safety Profile in VEGA-1 Trial



Presbyopia Eye Drops Competitive Landscape

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



Potential 'Best in Class' Presbyopia Drop

Competitive Approaches Limited by Safety/Tolerability, Durability, and Poor Distance Night Vision

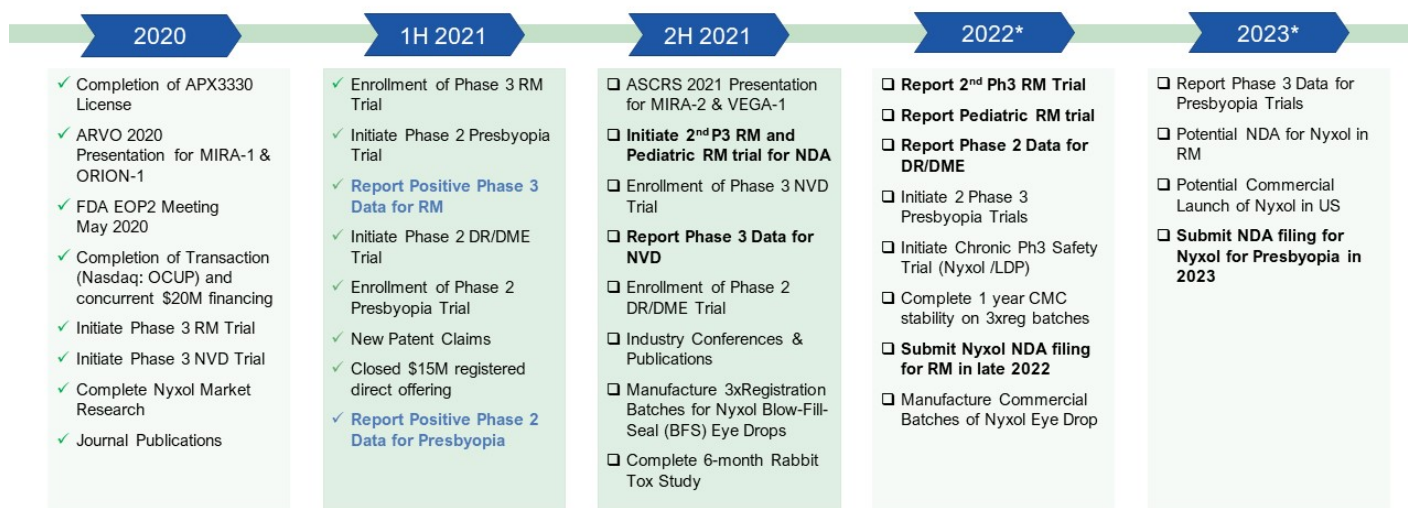
Nyxol + LDP Presbyopia Treatment is Differentiated:

- ✓ Statistically significant efficacy data
- ✓ Favorable safety profile
- ✓ Comfort and tolerability
- ✓ Fast onset
- ✓ Long duration
- ✓ Maintain good distance visual acuity (night/day)
- ✓ Novel tunable pupil modulation

Future Milestones

2021 to 2022 Ocuphire Cadence of Milestones

Multiple Data Catalysts On Path To NDA(s)



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

*Additional Studies for NVD and DR based on Data Readouts



Q&A

www.ocuphire.com
ir@ocuphire.com





Ocuphire's VEGA-1 Phase 2 Trial in Presbyopia Meets Primary and Secondary Endpoints

Met primary endpoint with statistical significance at 1 hour with 61% of subjects treated with Nyxol® plus low-dose pilocarpine (LDP) gaining ≥ 15 letters (3 lines) in near vision

Key secondary endpoints on visual acuity and pupil diameter showed statistical significance

Nyxol plus LDP showed a favorable safety profile

Plans to advance into Phase 3 registration trials

Conference call and live webcast @ 8.30 am ET today

FARMINGTON HILLS, Mich., June 30, 2021 -- Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of several eye disorders, today announced that the VEGA-1 Phase 2 clinical trial evaluating the efficacy and safety of Nyxol in combination with low-dose pilocarpine (LDP) in presbyopic subjects successfully met its primary and many secondary endpoints. On the strength of these results, Ocuphire plans to move into Phase 3. Given the rapid onset and sustained duration of efficacy, the favorable safety profile, and the potential tunability of treatment, Nyxol + LDP has the potential for differentiation and to be a best in class product for the treatment of presbyopia.

Highlights from the VEGA-1 Phase 2 Trial in Presbyopia:

Nyxol + LDP Met the Primary Endpoint

- 61% of subjects treated with Nyxol + LDP improved 15 letters or greater (≥ 3 lines) in photopic binocular near vision at 1 hour compared with 28% of subjects on placebo with statistical significance ($p = 0.003$ with placebo adjusted difference of 33%)

Nyxol + LDP Met Many Additional Efficacy Endpoints

- Met the Phase 3 co-primary endpoint vs. placebo gaining 15 letters (3 lines) near vision with less than 5 letters of distance vision loss
- Rapid onset of efficacy at 30 mins
- Durable near vision improvement through at least 6 hours
- Sustained significant reduction in pupil diameter over at least 18 hours due to the durable effects of Nyxol
- Near vision efficacy seen both monocularly and binocularly
- Efficacy in both light and dark iris colors

Nyxol + LDP Showed a Favorable Safety Profile

- No serious AEs, almost all AEs were mild
 - No headaches, no brow aches, and no blurry vision AEs were reported
 - Mild, transient conjunctival hyperemia (eye redness) observed in $<5\%$ of subjects
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Jay S. Pepose, MD, PhD, Director of the Pepose Vision Institute, Professor of Clinical Ophthalmology at the Washington University School of Medicine, and Ocuphire Medical Advisory Board and Corporate Board member commented, “The results from this Phase 2 VEGA-1 trial validate Nyxol’s mechanism of action on iris dilator muscle and the beneficial effects of smaller pupil size in treating presbyopia. These latest data support a clinical profile for Nyxol plus LDP combination that includes rapid onset of action and sustained duration of effect, while maintaining distance visual acuity in day and night conditions. All treatments were well tolerated and demonstrated a favorable safety profile. Taken together, we believe these attributes position Nyxol + LDP as a potential ‘best in class’ presbyopia treatment option.”

Presbyopia is a gradual, age-related loss of the eyes’ ability to focus on nearby objects. The global prevalence is estimated to be 2 billion. Approximately 120 million Americans live with presbyopia, a large prevalence that is expected to exceed 150 million by 2034. To assist with their near vision deficiencies, individuals with presbyopia use reading glasses and contact lenses, and in some cases undergo surgical interventions. However, there are currently no approved drug therapies for presbyopia in the United States. As there are several drawbacks to reading glasses and contact lenses, including inconvenience, eye strain, and night vision disturbances, eye drops are increasingly being explored as an alternative treatment modality.

Susan Benton of Ocuphire’s Board of Directors remarked, “The need for an eyedrop treatment is highlighted by industry leader Allergan and several other companies developing pharmacological treatment options for presbyopia. Ocuphire’s novel target product profile of a combination kit of Nyxol and LDP may offer rapid onset and long-lasting effects with ‘tunability’ as an option in that all patients are not the same (one size does not fit all). A combination kit option may provide a “range” of pupillary modulation that the doctor can customize to the patient to optimize their near vision. This ability to customize therapy will be more difficult for fixed-dose combinations and single-agent products.”

“We are thrilled with the positive outcome in VEGA-1, which showed that a combination of Nyxol and low-dose pilocarpine produced a statistically significant improvement in near visual acuity in subjects with presbyopia,” said Mina Sooch, MBA, President and CEO of Ocuphire Pharma. “We would like to thank all of the subjects and investigational sites that participated in our first presbyopia clinical trial for Nyxol. Presbyopia represents an area of considerable unmet need due to its rising prevalence worldwide and the limitations of currently available corrective methods. Based on the data generated thus far, we believe that Nyxol and LDP is novel in its mechanism of action and could become a leading pharmacological treatment option for presbyopia and potentially allow those afflicted to reduce their dependence on reading glasses. We plan to initiate our Phase 3 trials for presbyopia in 2022, building on our recent success of Nyxol for Reversal of Mydriasis with initiation of the second Phase 3 registration trial later this year.”

VEGA-1 Phase 2 Trial Design

The VEGA-1 Phase 2 clinical trial was designed to evaluate the efficacy and safety of Nyxol in combination with low-dose pilocarpine compared to placebo in presbyopic subjects. A total of 150 subjects (planned target was 140 to 152) were enrolled at 17 investigational sites in the US from mid-February to mid-May of this year. The Phase 2 trial was a randomized, double-masked, placebo-controlled study with 4 treatment arms. At the first visit, subjects were randomized to receive either Nyxol or placebo drops that were instilled at home near bedtime for 3 to 4 days prior to Visit 2; at Visit 2 subjects then received either low-dose pilocarpine or no treatment, with efficacy and safety measurements collected at multiple timepoints through 6 hours. The primary endpoint was the percentage of subjects with ≥ 15 letters of improvement in photopic binocular near vision (i.e. distance-corrected near visual acuity, DCNVA) at 1 hour on Visit 2 for Nyxol + LDP arm compared to placebo alone arm. The study was powered for comparison to placebo whereas comparison to component arms were designed to inform the Phase 3 sample size for a combination product approval. Secondary endpoints at multiple timepoints included Nyxol + LDP improvements of 3 lines of DCNVA without any loss of distance vision, pupil diameter, and improvements of DCNVA of 1 and 2 lines compared to placebo as well as to Nyxol and low-dose pilocarpine alone. For more information, refer to ClinicalTrials.gov Identifier: [NCT04675151](#).

Ocuphire collaborated closely with Oculis Development Services, a Rush, NY based clinical research organization and a subsidiary of iuvo BioScience, on the launch and execution of the VEGA-1 trial.

Detailed results of the VEGA-1 study will be presented by Dr. Pepose at the upcoming American Society of Cataract and Refractive Surgery (ASCRS) medical meeting: *VEGA-1 Presbyopia Presentation on Sunday July 25, 2021 at 8:45am (ASCRS Paper ID 76645)*.

Conference Call and Webcast (with slides)

Ocuphire management will host a conference call and webcast with slides, today at 8.30am ET. Details for the call are as follows:

Toll free (U.S.)	877-407-4018
International:	201-689-8471
Conference ID	13721064
Webcast:	http://public.viavid.com/index.php?id=145478

The webcast will also be available on the “Investors” tab of the Ocuphire corporate website tab, under [News & Events](#) and will be archived for 90 days.

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 several eye disorders. Ocuphire’s pipeline currently includes two small-molecule product candidates targeting front and back of the eye indications. The company’s lead product candidate, Nyxol® (0.75% phentolamine ophthalmic solution) Eye Drops, is a once-daily preservative-free eye drop formulation of phentolamine mesylate, a non-selective alpha-1 and alpha-2 adrenergic antagonist designed to reduce pupil size, and is being developed for several indications, including dim light or night vision disturbances (NVD), reversal of pharmacologically-induced mydriasis (RM), and presbyopia, and has been studied in 9 clinical trials including the recently completed Phase 3 trial in RM and Phase 2 trial in presbyopia. Ocuphire reported positive topline data in March 2021 for MIRA-2, a Phase 3 FDA registration study for treatment of RM. Nyxol is also currently in Phase 3 clinical development for NVD. Ocuphire’s second product candidate, APX3330, is an oral tablet designed to inhibit angiogenesis and inflammation pathways relevant to retinal and choroidal vascular diseases, such as diabetic retinopathy (DR) and diabetic macular edema (DME) and has been studied in 11 Phase 1 and 2 trials. APX3330 is currently enrolling subjects in a Phase 2 clinical trial in subjects with DR/DME. As part of its strategy, Ocuphire will continue to explore opportunities to acquire additional ophthalmic assets and to seek strategic partners for late-stage development, regulatory preparation, and commercialization of drugs in key global markets. Please visit www.clinicaltrials.gov to learn more about Ocuphire’s completed Phase 2 trials, recently completed Phase 3 registration trial in RM ([NCT04620213](#)), ongoing Phase 3 registration trial in NVD ([NCT04638660](#)), recently completed Phase 2 trial in presbyopia ([NCT04675151](#)), and Phase 2 trial in DR/DME ([NCT04692688](#)). For more information, please visit www.ocuphir.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 a potential Phase 3 trial in presbyopia, Nyxol + LDP’s potential to be a ‘best in class’ presbyopia treatment option, and the market and commercial potential of Nyxol + LDP. 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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