UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

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

Date of Report (Date of earliest event reported): January 31, 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 1200 **Farmington Hills, Michigan**	**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 January 31, 2022, Ocuphire Pharma, Inc. (the "Company") will present new data and updates on its APX3330 and Nyxol clinical programs at its previously announced Virtual Investor R&D Day on January 31, 2022. The presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and are 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 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Investor Presentation Materials, dated January 31, 2022.

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: January 31, 2022

Exhibit 99.1

Ocuphire PHARMA

Restore Vision & Clarity

Ocuphire Pharma Investor R&D Day

January 31, 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, cash runway, and future clinical trials in RM, presbyopia, NVD and DR/DME, including the potential for Nyxol to be a "best in class" presbyopia drop. These forward-looking statements are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) the success and timing of regulatory submissions and pre-clinical and clinical trials, 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 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 Investor R&D Day 1/31/22 Agenda & Speakers

Speakers	Agenda	Time (EST)
 Ocuphire **Mina Sooch, MBA** President & CEO and Founder	**Introductions & Company Overview** **Closing Remarks**	10:00 am – 10:10 am 12:10 pm – 12:15 pm
 Indiana University  Cleveland Clinic Cole Eye Institute  Retina-Vitreous Associates Medical Group **Mark Kelley, PhD** **Peter Kaiser, MD** **David Boyer, MD**	**I. APX3330 DR/DME Program** ★★★ New Data	10:10 am – 10:50 am
 Kentucky Eye Institute  Jacksoneye  Ocuphire Head of Commercialization **Paul Karpecki, OD** **Mitchell Jackson, MD** **Bindu Manne**	**II. Nyxol Reversal of Mydriasis Program**	10:50 am – 11:30 am
 PeposeVision Institute  the Midwest Center for Sight **Jay Pepose, MD, PhD** **James Katz, MD**	**III. Nyxol Presbyopia Program** ★★★ New Data *Corey Davis, LifeSci Advisors will moderate Q&A*	11:30 am – 12:10pm Ocuphire

Company Overview

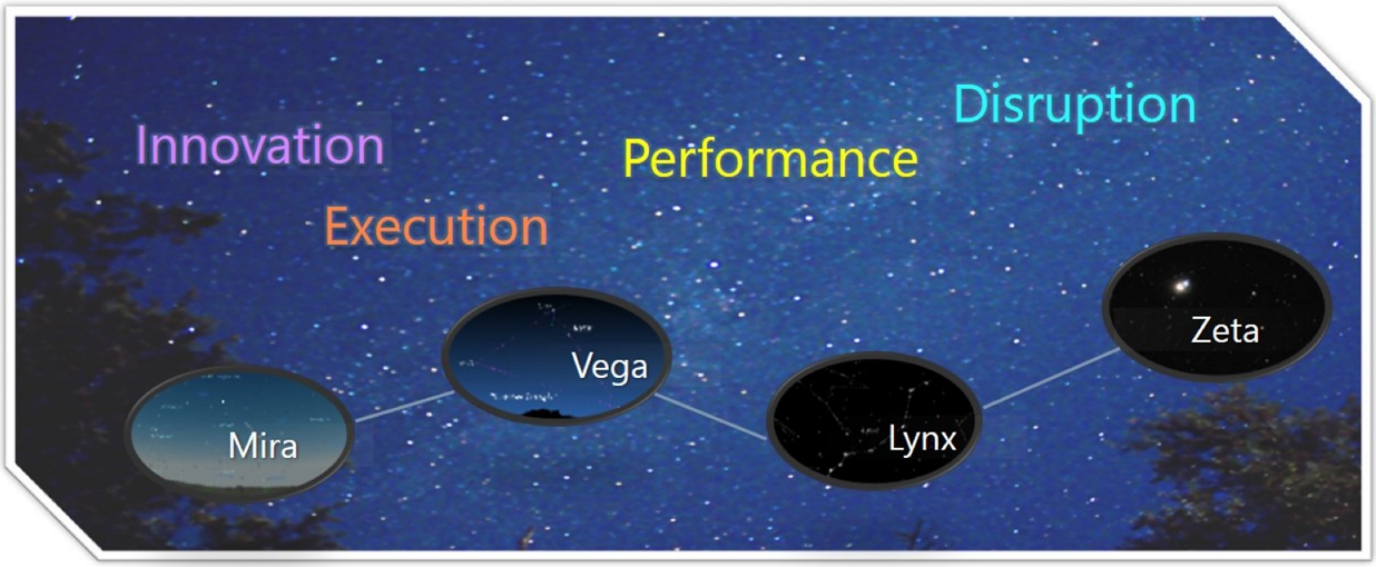
Presenter: Mina Sooch, CEO, Founder of Ocuphire Pharma

Mina Sooch
M.B.A
Harvard University

- Over 25 years of pharmaceutical and biotech experience as CEO, entrepreneur, venture capitalist and strategy consultant
- Successful track record of hundreds of millions of capital raise and leading private/public biotech companies
- Experience across multiple diseases (cardiovascular, oncology, renal, NASH, CNS, etc.) prior to ophthalmology
- Recipient of numerous awards including Deal Makers of the Year in 2016 and Alumni Commencement Speaker WSU College of Engineering in 2021

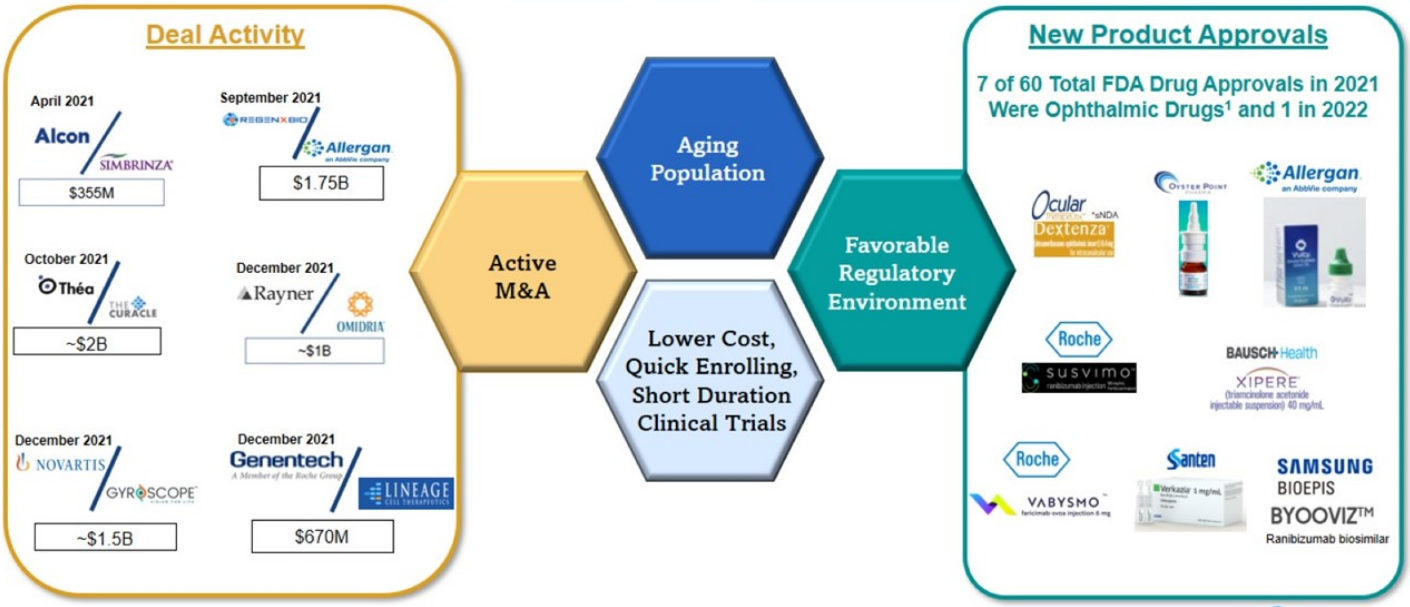
Ocuphire Pharma

Restoring Vision and Clarity for Your Eyes, Today and Tomorrow



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; OIS Year in Review 2021; Company press releases

Ocuphire Pharma

Nyxol & APX3330: Drug Development History and Patents

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

Refractive

Nyxol®
Novel α1/ α2 Blocker
505(b)(2)

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

Presbyopia P

Reversal of Mydriasis RM

Night Vision Disturbances NVD

Retina

APX3330
Oral REF-1 Inhibitor
New Chemical Entity

11	>340	Exposure in Humans 365	Patents to 2034+
Phase 1 & Phase 2 Trials	Subjects Dosed	Days	

Diabetic Retinopathy DR

Diabetic Macular Edema DME

Source: Eisai and Apexian Data

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Ocuphire Pipeline & Clinical Milestones

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

Product Candidate	Indication	Anticipated Milestones
0.75% Nyxol® Eye Drop	Reversal of Mydriasis (RM)	❑ MIRA-3 Phase 3 data expected in early 2022 (n=330) ❑ MIRA-4 Pediatric safety study data expected in early 2022 (n=20)
0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops	Presbyopia (P)	❑ VEGA Phase 3 program planned to initiate in mid 2022
0.75% Nyxol® Eye Drop	Dim Light or Night Vision Disturbances (NVD)	❑ LYNX-1 Phase 3 data expected in early 2022 (n=140)
APX3330 Oral Pill	Diabetic Retinopathy (DR)/ Macular Edema (DME)	❑ ZETA-1 Phase 2b data expected in 2H22 (n=90-100)
APX2009 (Intravitreal or Local Delivery)	DME or Wet Age-Related Macular Degeneration (wAMD)	❑ Seeking partner funding for IND enabling studies and further development

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

- **Differentiated, Late-Stage Pipeline for Front and Back of the Eye**
  - ✓ Nyxol with > 330 patients treated across 9 trials (505(b)(2) regulatory pathway)
  - ✓ APX3330 with > 340 patients treated across 11 trials (NCE development pathway)
  - ✓ Nyxol and APX3330 achieved promising clinical data and favorable safety profile across multiple Phase 1, 2, and 3 trials
- **Poised for Commercial Success in Multiple Large Unmet Markets**
  - ✓ Addressing 4 large markets with unmet needs: RM, Presbyopia, NVD, and DR/DME
  - ✓ Successful trial execution with 2 recent positive Phase 3 and Phase 2 data read-outs for Nyxol in RM and Nyxol + LDP Presbyopia, respectively
  - ✓ Stable, small-molecule drugs with commercial scalability
  - ✓ Robust and growing IP portfolio: US and global issued thru 2034 for both assets as well as new 2039 Nyxol patent issued for presbyopia
- **Many Catalysts in 2022 with Track Record of Execution**
  - ✓ $24.5 million cash reported at 12-31-21 sufficient for operations into 2Q 2023
  - ✓ Highly experienced management, Board and KOLs with broad ophthalmic and biotech drug development and commercialization success
  - ✓ Lower-cost, fast-enrolling, shorter-duration clinical trials
  - ✓ Favorable, precedent regulatory environment for ophthalmic drug approval
  - ✓ Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and HCW

DR
DME

Ocuphire PHARMA

I. APX3330 Program Update

INDIANA UNIVERSITY
MELVIN AND BREN SIMON CANCER CENTER

Mark Kelley, PhD
Founder
Apexian/APX3330

Cleveland Clinic
Cole Eye Institute

Peter Kaiser, MD
Harvard Medical School

Retina-Vitreous Associates Medical Group

David Boyer, MD
Chicago Medical School

DR
DME

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APX3330 Chemistry and MOA

Presented by: Mark Kelley, PhD

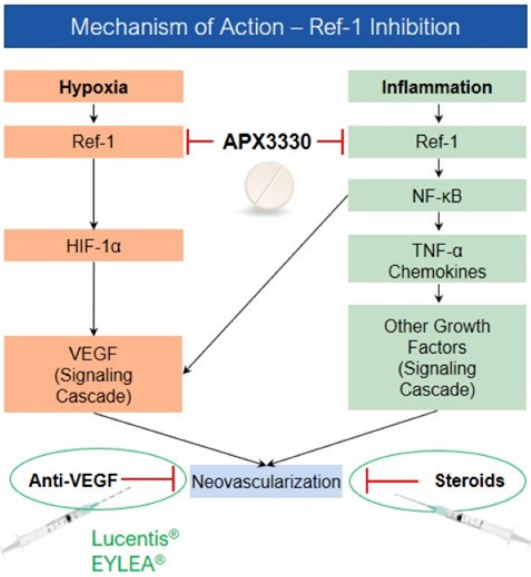
INDIANA UNIVERSITY
MELVIN AND BREN SIMON CANCER CENTER

Mark Kelley, PhD
Louisiana State University

- Chief Scientific Officer and Founder of Apexian Pharmaceuticals
- Discovered and has developed the redox-specific inhibitors of Ref-1 for over 20 years
- Associate Director of Basic Science at Indiana University Simon Comprehensive Cancer Center
- Betty and Earl Herr Professor of Pediatric Oncology Research, Indiana University
- Fellow, American Association for the Advancement of Science

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
  - Similar oncology origin as approved anti-VEGFs
- MOA uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1

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

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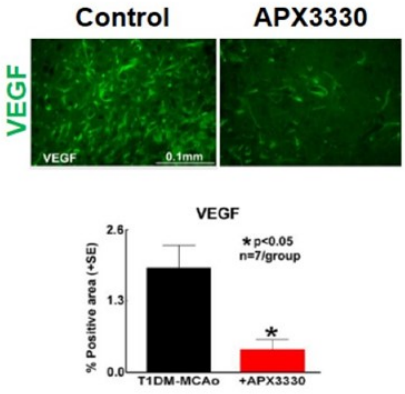
DME

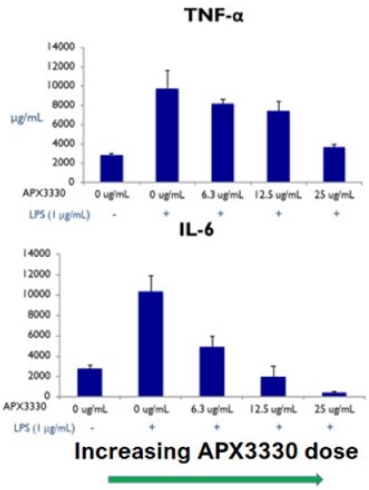
In vitro Validation of APX3330 Mechanism of Action

APX3330 Reduces VEGF levels and Inflammatory Cytokines; Provides Neuronal Protection

APX3330 reduces VEGF protein expression in preclinical stroke model

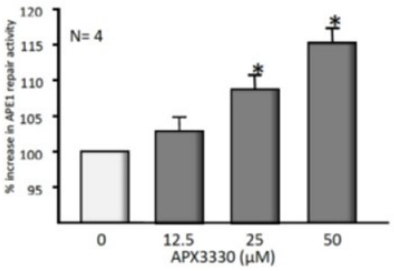


APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages



Increasing APX3330 dose

APX3330 increases DNA oxidative repair and neuronal protection



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

-Tao Yan *et al.* APX3330 Promotes Neurorestorative effects after stroke in type one diabetic rats. Aging and Disease. Vol 9, Oct 2018

-Apurinic/Apyrimidinic endonuclease 1 regulates inflammatory response in macrophages. Jedinak A, Dudhgaonkar S, Kelley MR, Sliva D. Anticancer Res. 2011 Feb;31(2):379-85. PMID: 21378315

-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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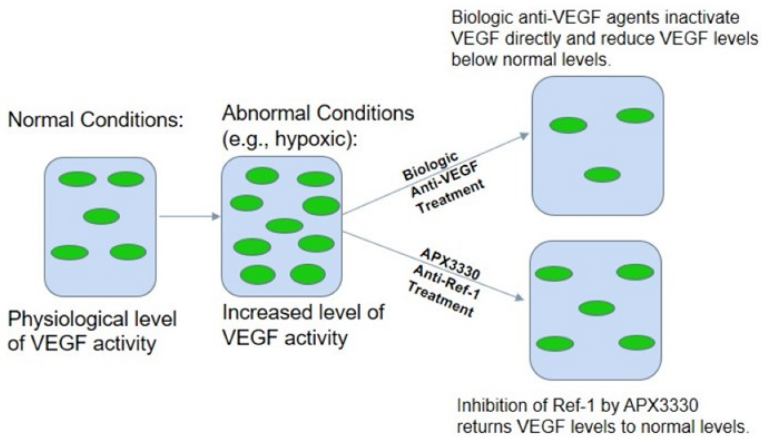
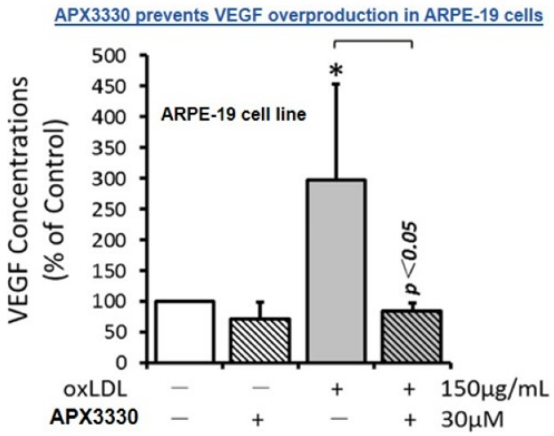
APX3330 VEGF Effects in Normal Cells

APX3330 Restores Normal Levels Unlike Biologic Anti-VEGFs that Reduce VEGF Below Normal





- **VEGF is a growth factor that is necessary for normal function of multiple cell types including vascular endothelium and neurons ➔ By returning VEGF levels to normal, APX3330 can reduce neovascularization, vascular leakage and the inflammatory response without adverse systemic effects**
- **The safety profile of APX3330 to date in over 300 subjects has not shown any of the adverse effects that has been seen with systemic administration of anti-VEGF biologics such as cardiovascular pathology, hypertension, arteriothrombotic events, or renal dysfunction**

Kamba 2007; Girardi 2010; Li 2014; APX3330 Investigator Brochure

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APX3330 Preclinical & IND-Enabling Studies

DR DME

Extensively Evaluated in Over 20 Studies by Large Japanese Pharma Eisai

Extensively Studied in Over 20 In-Vitro and Animal Studies with Favorable Efficacy and Safety

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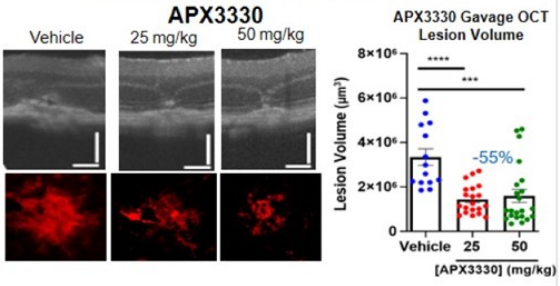
DME

Preclinical Data: Oral APX3330 Blocks Neovascularization

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

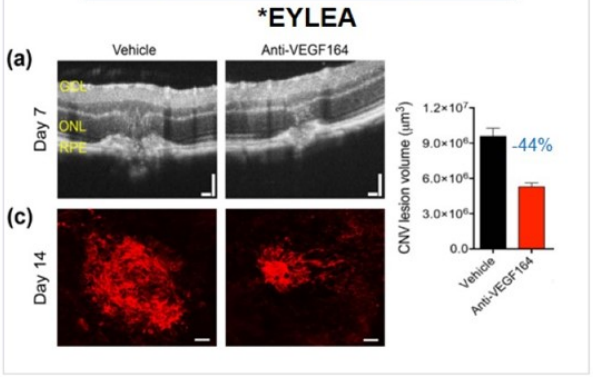
L-CNV Mouse Retina Model

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******

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

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APX3330 Human PK and Safety Summary

Presented by: Peter Kaiser, MD

Cleveland Clinic
Cole Eye Institute

Peter Kaiser, MD
Harvard Medical School

- Chaney Family Endowed Chair in Ophthalmology Research, Professor of Ophthalmology, Cleveland Clinic Lerner College of Medicine and Cole Eye Institute
- Clinical research expert, serving as a Study Chairman of 5 major, multi-center, international trials, and principal investigator for numerous studies for AMD, DR, and other retinal disorders.
- Major contributions to medical literature having authored 7 textbooks, more than 250 peer-reviewed papers
- Recognized by American Academy of Ophthalmology and American Society of Retina Specialist with Senior Achievement Awards.

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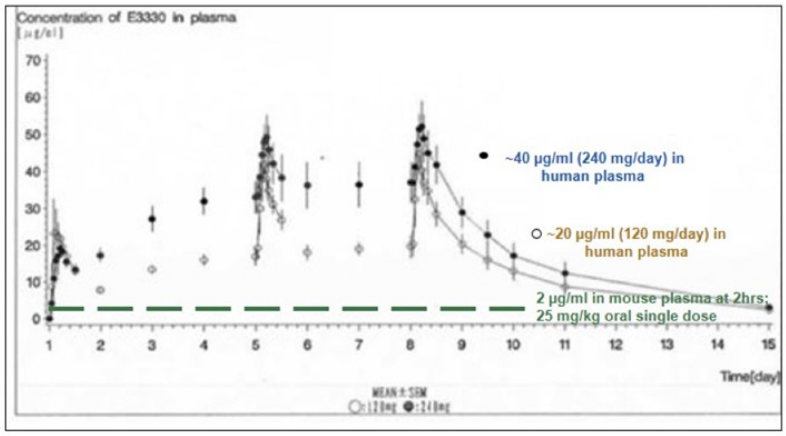
DME

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

APX3330 has Oral Bioavailability and a Sustained PK Profile



- **Favorable Oral Bioavailability**
- **Sustained Pharmacokinetic Profile**
  - T_{max} 3-4 hours
  - Linear dose-proportional PK
  - Dose-proportional increase in C_{max}/AUC exposure
  - Half-life elimination of 45 hours (steady state [SS] 5-6 days)
  - Meals have no clinically meaningful impact on the PK of orally administered APX3330
- **Sufficient APX3330 Exposure**
  - Plasma levels observed after 120 and 240 mg/day dosing is multiple times higher than what was required for efficacy in preclinical studies ➔ planned clinical dose is 600 mg/day

1. Apexian preclinical data (unpublished)
2. APX3330 Investigator Brochure
3. Eisai PK clinical data APX_CLN_0002

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

DR DME

APX3330 Reaches the Retina via Oral Administration

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

Rat

Orally administered, radiolabeled APX3330 reaches high levels in rat eye

Mouse

25 mg/kg APX3330 oral gavage measured in mouse retina

Human

Human clinical dose: 300 mg BID (600mg/day total)

Established PBPK model using human data predicts APX3330 reaches sufficient human retinal concentrations

APX3330 is orally bioavailable & detectable in mouse and rat retina

Preclinical PK and PBPK human modeling support 600 mg/day dosing for clinical development

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

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Subject Exposure Across 11 Prior Clinical Trials

Over 2000 Subject-Days of Exposure at ≥600 mg/day

11 Trials Prior to ZETA-1		
Dose:	**≥600 mg/day APX3330**	**<600 mg/day** APX3330**
Total Subjects	**34* Subjects**	**328* Subjects**
Subject-Days of Exposure	**2078 Subject-days**	**17961 Subject-days**
Subjects with ≥21 days of exposure	**16 Subjects**	**245 Subjects**
Subjects with >300 days of exposure	**3 Subjects**	**N/A**

*18 subjects in dose escalation trials received doses <600mg/day and ≥600mg/day and are included in both columns, resulting in greater than 340 subjects;

**Many of the subjects between 20-240

* Eisai and Apexian Phase 1 and Phase 2 clinical trials (subject to final safety database)

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DME

Safety Summary From Phase 1 and Phase 2 Studies

Low AEs Across 11 Trials, <5% Mild Drug Related AEs, Discontinuations Similar Across Arms

Integrated Overall Summary of Adverse Events in Eisai Phase 2 Studies (Hepatitis)

	APX3330 20-240 mg (N=236)		Placebo (N=68)	
	n (%)	# events	n (%)	# events
Any event	40 (16.9%)	52	11 (16.2%)	15
Mild or Moderate adverse Events	39 (16.5%)	50	9 (13.2%)	13
Serious adverse events	1 (0.4%)	2	2 (2.9%)	2
Adverse events leading to discontinuation	10 (4.3%)	16	5 (7.4%)	7

% = proportion of subjects relative to N, where n = number of subjects with an event and N = the number of subjects in the enrolled population.
Note: This table was generated by Eisai which has slightly different event and sample size counts than the Ocuphire analysis. Ocuphire will be creating an integrated safety database. The overall conclusions between the Eisai and Ocuphire analyses are the same.

Totals Across ALL Phase 1 and Phase 2 Studies (Among Healthy Subjects, Hepatitis Patients, and Oncology Patients)

	APX3330	Placebo
Diarrhea/Soft Stool (mild)	14/346 (4%)	2/95 (2%)
Rash/Pruritis (mild)	14/346 (4%)	1/95 (1%)

Phase 1 and Phase 2 Clinical Trials performed by Eisai and Apexian

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APX3330 Product Candidate Profile for Multiple Retinal Indications

DR DME

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
 	
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 Significant 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 and Apexian

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DME

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APX3330 Addressing Unmet Needs in Retina

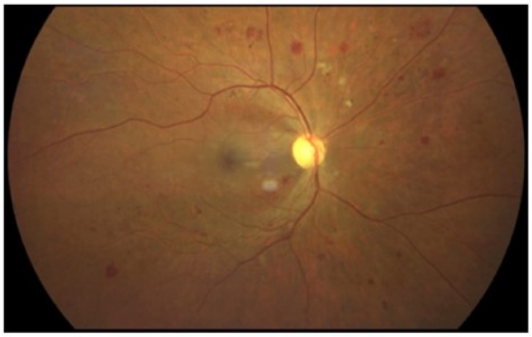
Presented by: Peter Kaiser, MD

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
- 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**



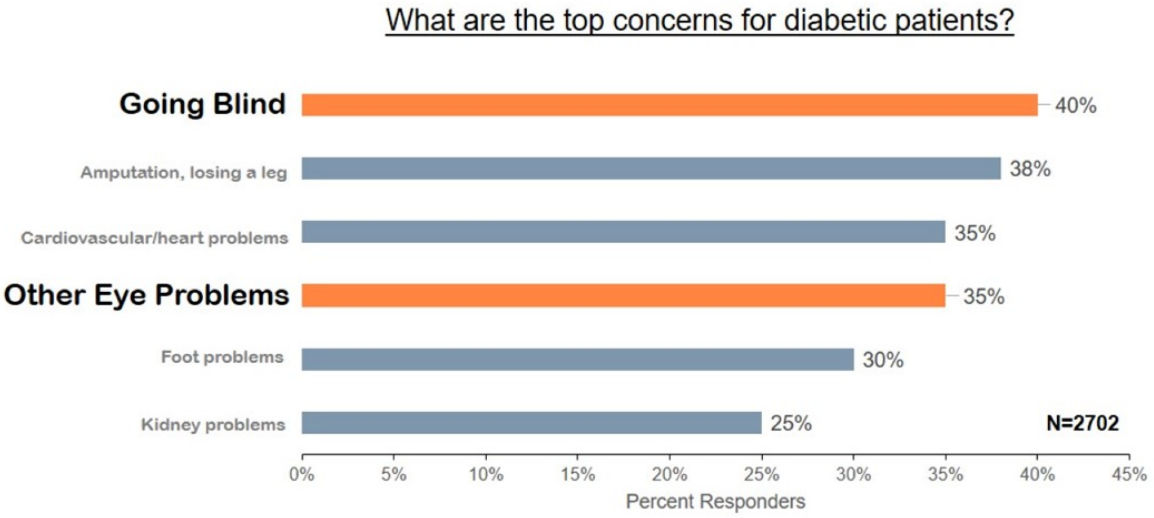
Growing Incidence of Diabetes and DR	
Diabetes	34 M US >450 M WW
DR	7 M US >150 M WW

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

American Diabetes Association; International Diabetes Federation; Healthline
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

Diabetic Retinopathy is a Progressive, Vision Threatening Disease

Losing Vision is Diabetic Patients Top Concern



Source: Patient survey adapted from Lions International Foundation and International Diabetes Foundation-Europe; Meltzer 2000

Key Clinical Landscape in Diabetic Retinopathy (and DME)

Intravitreal Injection the Focus for Drugs in Development; Ocuphire Pioneering an Oral Option

Company	Drug	Target/MOA	Route of Administration	Pre-clinical	Ph1	Ph2	Ph3	Commercial	2021 Annual Sales (US/Ex-U.S.)
Regeneron/Bayer	Eylea (aflibercept)	VEGF-A/B; PlGF	Intravitreal (DR & DME)	✓	✓	✓	✓	✓	~$6 B/ ~$4 B
Roche/Novartis	Lucentis (ranibizumab)	VEGF-A	Intravitreal (DR & DME)	✓	✓	✓	✓	✓	~$1.5 B/~$2 B
Roche	Ranibizumab PDS	VEGF-A	Surgical/Refill (DME)	-	✓	✓	✓	✓ Oct 2021	
Roche	Faricimab	VEGF-A x Ang2	Intravitreal (DME)	✓	✓	✓	✓	✓ Jan 2022	
Kodiak	KSI-301	VEGF	Intravitreal (DR & DME)	✓	✓	N/A	○		
Kalvista	KVD001	Plasma Kallikrein	Intravitreal (DME)	✓	✓	✓			
Eli Lilly	LY333531	Protein Kinase C inhibitor	Oral (DR)	✓	✓	✓	X 2006		
Ocuphire	**APX3330**	**Ref-1 inhibitor**	**Oral (DR)**	✓	✓	○			
Bayer	BAY1101042	Guanylate Cyclase activator	**Oral (DR)**	✓	✓	○			
Alkahest	AKST4290	CCR3 Eotaxin inhibitor	Oral (DR)	✓	✓	○			
Roche	RG7774	CB2 Receptor	Oral (DR)	✓	✓	○			
Boehringer Ing.	BI 1467335	AOC3	Oral (DR)	✓	✓	X 2021			
Rezolute	RZ402	Plasma Kallikrein	Oral (DME)	✓	✓				
OcuNexus	HCB 1019	Connexin 43 (inflammasome)	Oral (DR)	✓	✓				
OcuTerra	OTT166	Integrin inhibitor	Eyedrop (DR)	✓	✓				

ORAL Rx

✓Completed
○ Recruiting
X Discontinued/Failed study

Guggenheim report (2020); www.clinicaltrials.gov; Company websites

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DR
DME

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ZETA-1 Phase 2b Clinical Trial (APX3330 in DR)

Presented by: David Boyer, MD

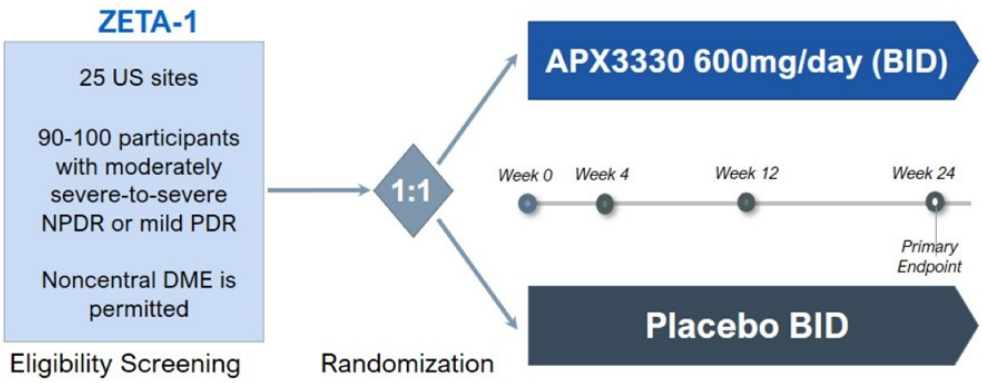
Retina-Vitreous Associates Medical Group

David Boyer, MD
Chicago Medical School

- Board-certified Ophthalmologist specializing in treatment of retinal and vitreous diseases
- Widely-published author and internationally recognized lecturer on retinal research and innovative approaches
- Investigator in numerous innovative product retinal trials over the last 35 years

DR/DME ZETA-1 Phase 2b Design

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



Phase 2b Initiated in April 2021

Top Line Expected in 2H22

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

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)
https://clinicaltrials.gov/ct2/show/NCT04692688?term=ZETA-1&draw=2&rank=1

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Key Eligibility Criteria in ZETA-1

Given Bilateral Treatment with Oral, Patient Criteria Allows DME in Fellow Eye

INCLUSION

- Moderately-severe to severe NPDR or mild PDR in study eye as confirmed by reading center
- BCVA ≥ 20/63 in study eye

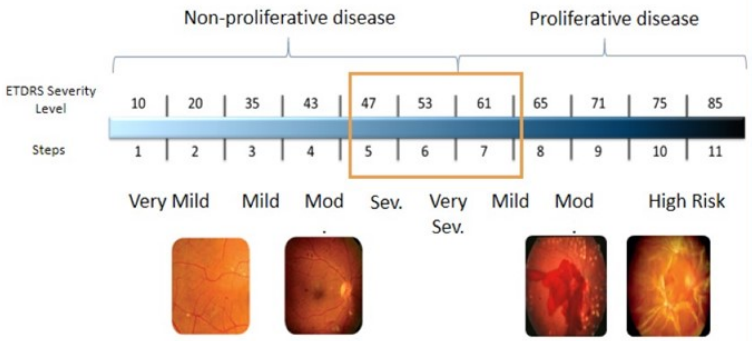
EXCLUSION

- Retinopathy from causes other than diabetes in study eye
- Presence of center involved diabetic macular edema (DME) defined as a central subfield thickness (CST) ≥ 320 µm on SD-OCT or the presence of intra- or subretinal fluid within the central subfield
  - **Center involved DME in the fellow eye is allowed**
- Prior treatment in study eye with focal/grid laser photocoagulation within the past year, PRP at any time, systemic or intravitreal anti-VEGF agents within last 6 months in study eye
- HbA1c ≥ 12.0%
- Clinically significant systemic disease (e.g., uncontrolled diabetes, myasthenia gravis, cancer, hepatic, renal, endocrine, or cardiovascular disorders) that might interfere as deemed by Investigator

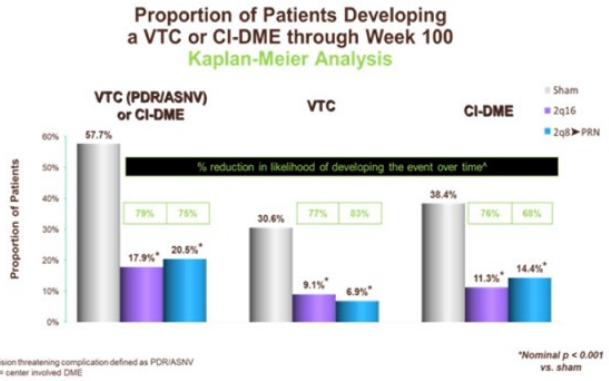
Why DRSS is an Important Endpoint?

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)



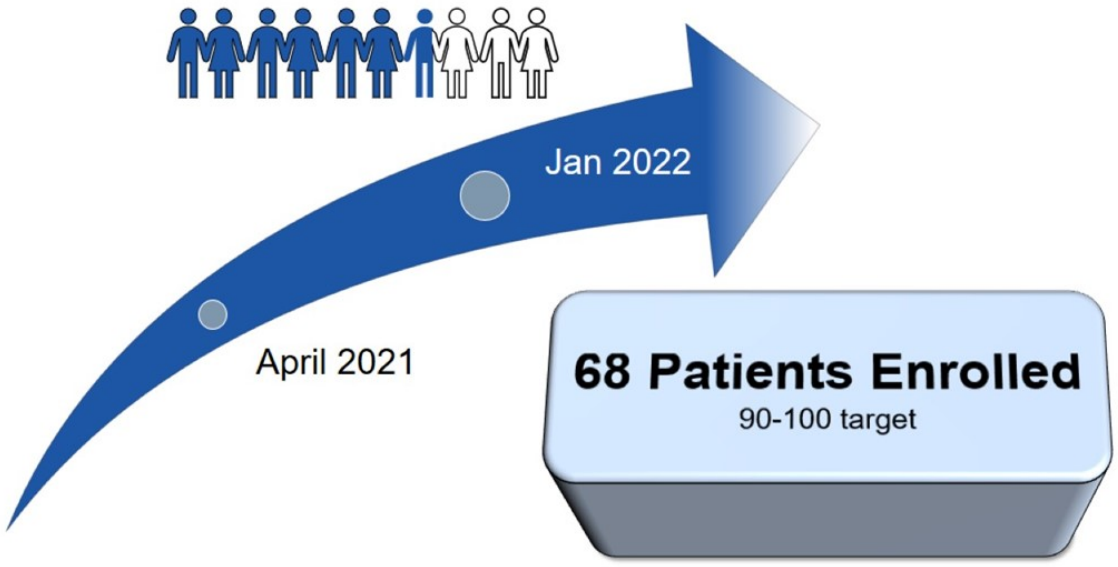
PANORAMA: Reduction of DRSS Significantly reduces the incidence of Vision Threatening DR



Risk of vision-threatening events increases with worsening step progression

Enrollment Update on ZETA-1

~70% Completion of Enrollment in 24-week Phase 2b Trial



DR
DME

Comparison of Subject Exposure Before and After ZETA-1

Subject-Days of Exposure at 600 mg/day Substantially Increases Exposure Data

	≥600 mg/day		<600 mg/day**
	Prior to ZETA-1	To Date*	Prior to ZETA-1
Total Subjects	**34 Subjects**	+34 **68 Subjects**	**328 Subjects**
Subject-Days of Exposure	**2078 Subject-days**	+3727 **5805 Subject-days**	**17961 Subject-days**
Subjects with ≥21 days of exposure	**16 Subjects**	+27 **43 Subjects**	**245 Subjects**
Subjects with >300 days of exposure	**3 Subjects**	**3 Subjects**	**N/A**

*Assumed 50% of ZETA-1 patients are on active treatment
**Many of the subjects between 20-240 mg/day

*Interim Zeta-1 Data as of 01-12-22; * Eisai and Apexian Phase 1 and Phase 2 clinical trials (subject to final safety database)

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Baseline Characteristics for ZETA-1 Trial (Interim)

Typical Demographics for Diabetic Population

Parameter	Total N = 68
Age (years): mean (range)	55 (24-81)
Sex: Male n (%) **Female** n (%)	34 (50%) 34 (50%)
Weight (kg): mean (range)	84 (54-123)
BMI (kg/m²): mean (Range)	30 (21-40)
Systolic BP (mmHg): mean (range)	137 (100-172)
Diastolic BP (mmHg): mean (range)	80 (53-104)
Heart rate (BPM): mean (range)	76 (51-96)

Source: ZETA-1 Demographics and Baseline Characteristics

Masked Safety Findings from Ongoing ZETA-1 Trial

DR
DME

Favorable Safety Profile (as of 1/12/2022) Observed with 600 mg Oral Daily Doses

APX3330
Masked Safety Data
ZETA-1 Trial

68	**>3700**	**28**	**6**
Randomized Subjects	Subject-Days of Exposure (50% on APX3330)	Subjects with AEs (52 total events)	SAEs, all unrelated to study medication

- 52 TEAEs in 28 subjects
  - **6/52 AEs were considered probably or possibly related to study medication**
    - 4 Mild (vertigo, rash, pruritus, frequent bowel movements); 2 moderate (DME*, diarrhea**)
  - 46/52 AEs were 'not' or 'unlikely' related (32 mild, 14 moderate)
- 6 SAEs in 6 subjects
  - None of these treatment emergent events were related to study medication
    - Cellulitis , dyskinesia, transient ischemic event, COVID-19, progression of multivessel coronary artery disease, cholecystitis
- Only 2 subjects have withdrawn from study due to AEs: vasovagal near syncope** considered unrelated to study medication and DME* possibly study medication related (APX3330 or placebo)

*same subject; **same subject
Note: ZETA-1 Interim Data as of database 1/12/22 with complete monitoring before final database lock

Source: ZETA-1 trial

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Takeaways: Masked Interim Safety Findings from ZETA-1 Trial

- ~70% completion of enrollment in 24-week ZETA-1 Phase 2b Trial
- No major organ toxicities (liver, heart, kidney, brain, lung) or vital sign abnormalities (blood pressure or heart rate) were observed
- Incidence of mild rash and diarrhea in the diabetic patient population is lower than previously observed in hepatitis patients

Review of masked safety data for 600 mg/day daily dose is consistent with the favorable safety profile seen in previous studies with APX3330

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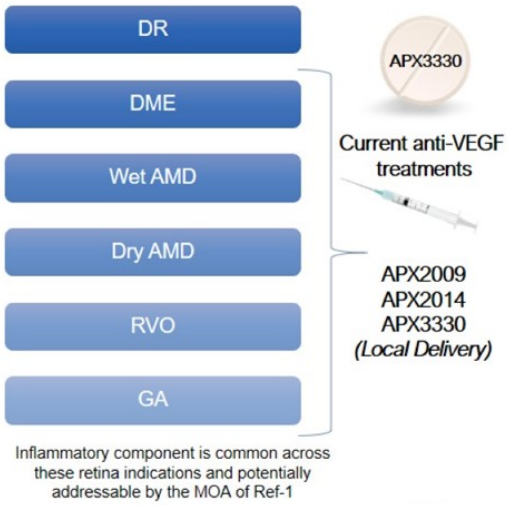
Broad Opportunities to Treat Retinal Diseases with APX Platform

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

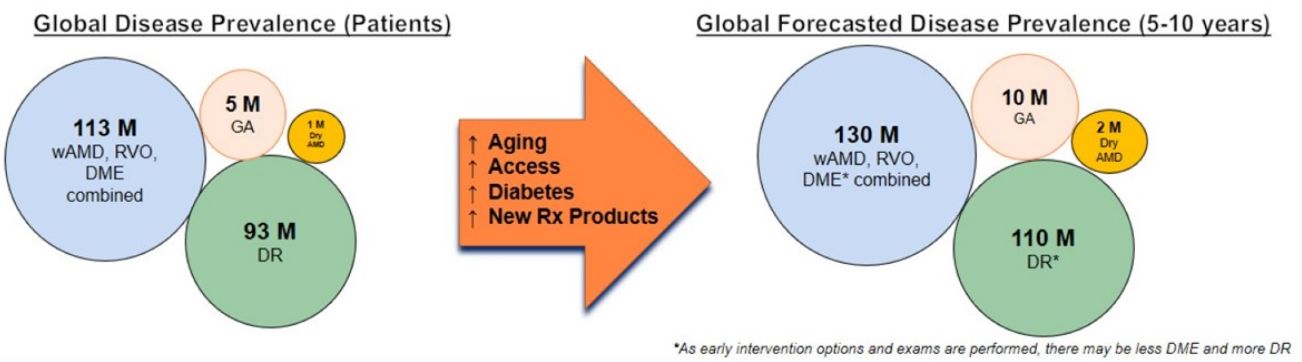


Inflammatory component is common across these retina indications and potentially addressable by the MOA of Ref-1

Large Global/US Market Opportunity in Retinal Disease

DR
DME

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



*As early intervention options and exams are performed, there may be less DME and more DR

Market Scope 2020
J Glob Health. 2019 Jun; 9(1): 010427
Tilahun M et. al, Prevalence of Diabetic Retinopathy and Its Associated Factors among Diabetic Patients at Debre Markos Referral Hospital, Northwest Ethiopia, 2019: Hospital-Based Cross-Sectional Study. Diabetes Metab Syndr Obes. 2020;13:2179-2187

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What's Important?

APX3330 has the Potential to be 1st Line of Therapy for DR Patients

Efficacy Signal

Percent of patients on APX3330 with a ≥ 2 step improvement on the DRSS score at week 24 **compared to placebo** in 2 well-controlled, multi-center clinical trials

Safety

Approval depends on a product's benefit outweighing its risks in the intended population as demonstrated in, multi-center, 2 years clinical trial

Non-Invasive Treatment Option

FDA does not require comparative arm of approved anti-VEGF injections such as Eylea for DR

FDA Guidance

Physician/ Patients

Efficacy Signal

- Clinically meaningful decrease in diabetic retinopathy severity with APX3330
- Early intervention with oral may reduce progression to vision threatening DR into DME

Safety

- No major organ toxicities
- Well-tolerated (e.g., AEs acceptable if mild and infrequent for oral)

Non-Invasive Treatment Option

- Eylea®, although approved, is currently not used as standard of care because of the treatment burden for asymptomatic DR patients
- Ability to be prescribed by all eye care doctors
- Oral option increases global access, especially in underserved regions

Eylea® label; APX3330 Investigator Brochure, ZETA-1 clinical trial

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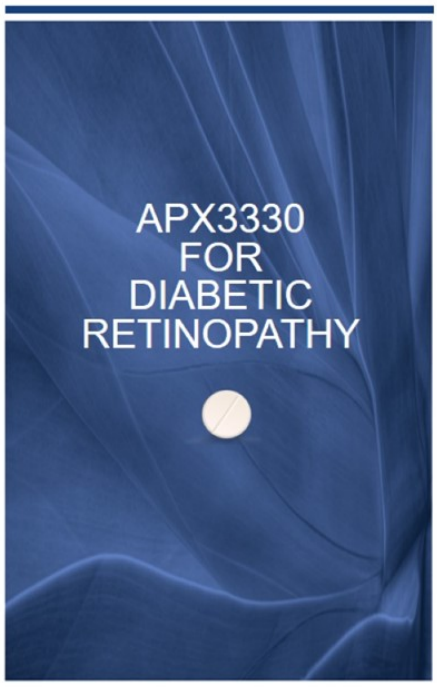

Question & Answer

Summary of APX3330 Program

	APX3330 is a **novel orally administered** drug initially being developed for DR/DME
	**APX3330 targets Ref-1 which plays a role in signaling under both ischemic and inflammatory conditions**, both of which are relevant to diabetic eye disease; resulting in inhibiting clinically validated pathways downstream of Ref-1(e.g., VEGF and inflammation)
	**ZETA-1's masked safety findings as of 01/12/2022 support favorable safety profile of APX3330 as an oral treatment option for DR** consistent with 11 prior Phase 1 and 2 clinical trials
	APX3330 randomized, double-masked, placebo-controlled, multi-center ZETA-1 Phase 2b trial enrollment on track at **68 subjects (of 90-100 subjects) with results expected in second half of 2022**
	Oral APX3330 has potential **utility as adjunctive treatment with anti-VEGF injections for other retinal vascular/inflammatory diseases** such as DME, GA, RVO and AMDs; future opportunities with APX2009/2014 pipeline locally or orally delivered

RM

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II. Nyxol Reversal of Mydriasis Overview

KENTUCKY EYE INSTITUTE

Paul Karpecki, OD
Indiana University

Jacksoneye
seeing beyond your imagination

Mitchell Jackson, MD
University of Chicago

Ocuphire PHARMA

Bindu Manne
Head of
Commercialization

RM

Ocuphire PHARMA

Reversing Dilations: Addressing an Unmet Need with α1 Blocker **Nyxol**

Presented by: Paul Karpecki, OD

KENTUCKY EYE INSTITUTE

Paul Karpecki, OD
Indiana University

- Director of Cornea Services for Kentucky Eye Institute, Gaddie Eye Centers, Midwest Center for Sight
- Associate Professor at the Kentucky College of Optometry and Board Member of Optometry Giving Sight
- Medical Director for KEPLR Vision and Dry Eye Institutes of Kentucky and Indiana
- Chief Medical Editor for Review of Optometry, Chairman of the NTT Conferences

Problem: Dilated Eyes for Exams and Procedures

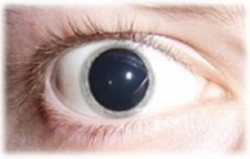
Patients Report Significant Side Effects after Dilated Eye Exam

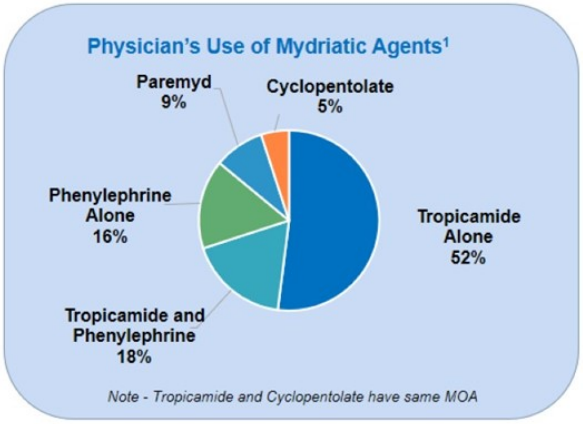
The Problem

Pharmacologically-induced pupil dilation is a necessary tool for routine ophthalmoscopy…

…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

1. GlobalData Market Research Survey; Oraverse and Regitine Label

RM

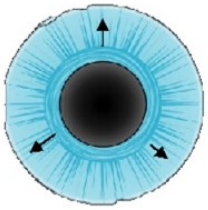
Current Off-Label Landscape for RM

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

2 Classes of Mydriatic Agents

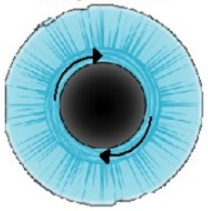
Phenylephrine (α1 agonist)

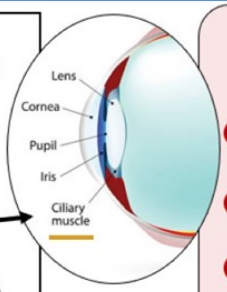
Sympathetic (primarily α1) innervation stimulates the iris dilator muscles



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

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

**** 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 that does not affect the ciliary muscle

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

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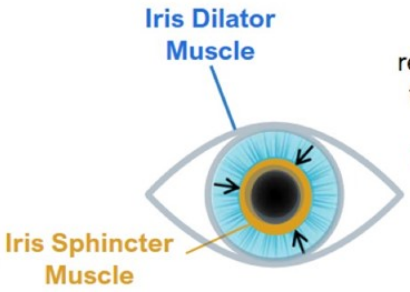
Nyxol's Differentiated MOA as an Alpha-1 Blocker

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*

Nyxol Product Candidate Profile

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

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

Effective	Favorable Safety Profile	Durable
Nyxol Improves Vision by Decreasing Pupil Size (1 to 1.5mm) ↑ Near & Distance Visual Acuity ↑ Contrast Sensitivity (night)	**No Systemic Effects** No Changes in Blood Pressure No Changes in Heart Rate **Well-Tolerated Topical Effects** Mild, Transient, Reversible Eye Redness **IOP Unchanged or Decreased** **No Headaches** Favorable safety profile vs competitors	**Effects Last ≥ 24 Hours** Chronic daily dosing of Nyxol at bedtime reduced pupil size for up to 24 - 36 hours With nighttime use, patients wake up without eye redness

RM

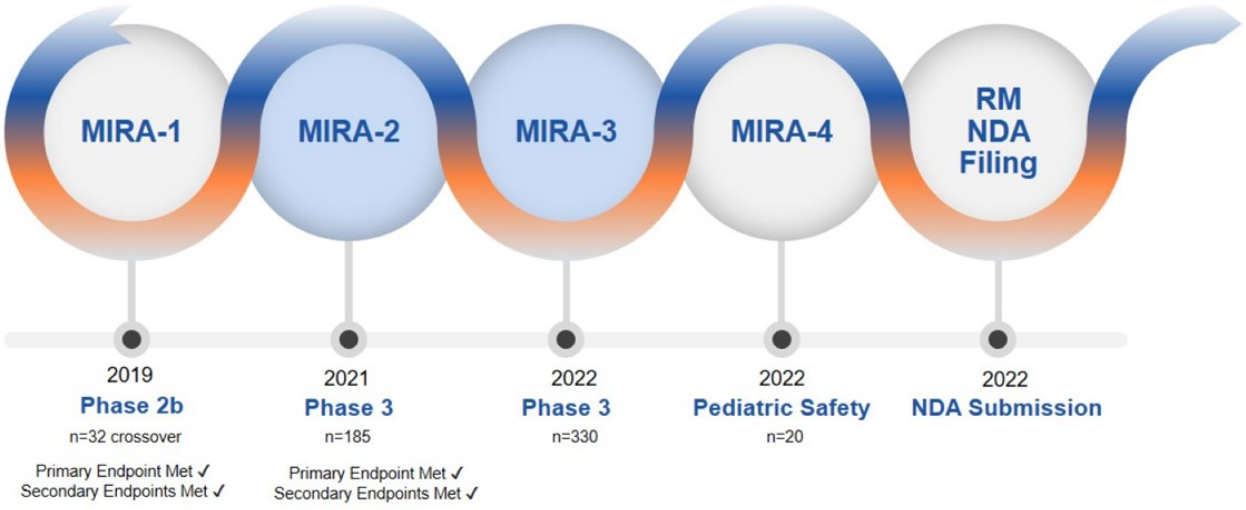
Ocuphire PHARMA

Nyxol Clinical Data for Reversing Dilations

Presented by: Paul M. Karpecki, OD

MIRA Program Evaluating Nyxol for the Reversal of Mydriasis

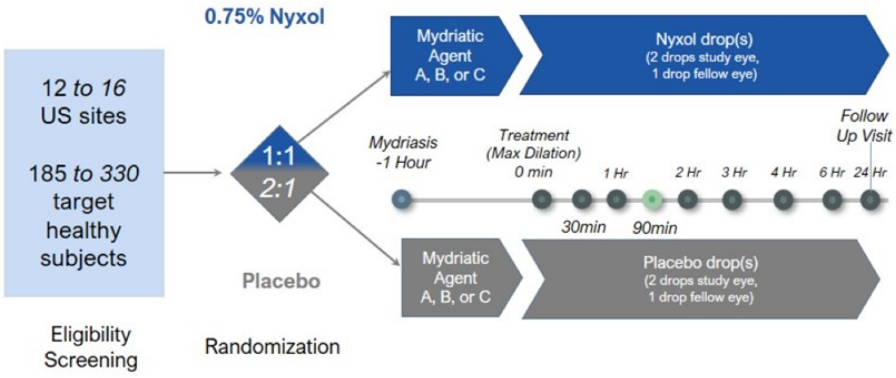
Efficient Clinical Programs have Positioned Ocuphire to Target NDA Filing in Late 2022



RM

MIRA-2/3 Phase 3 Registration Trial Design

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



Enrollment MIRA-3 Started in 4Q21

Topline Results Expected in Early 2022

Endpoints

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

Secondary:

- % of subjects returning to baseline at 0min, 30min, 1h, 90 min 2h, 3h, 4h, 6h, 24h (overall, by mydriatic agent, by iris color)
- Mean change in pupil diameter at all timepoints
- Accommodation (Tropicamide/Paremyd)
- *Visual acuity & discomfort w/ glare*
- *Pupillary light reflex*
- Safety and tolerability (redness)

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

Ocuphire

MIRA-2: Participant Characteristics

MIRA-2 Study was Balanced Across Both Nyxol and Placebo Groups

	MIRA-2 Phase 3 Trial		
	Nyxol n=94	**Placebo n=91**	**Total n=185**
Age (years): Median (Range)	31 (12-70)	30 (13-73)	31 (12-73)
Sex: Male n (%) **Female** n (%)	36 (38%) 58 (62%)	36 (40%) 55 (60%)	72 (39%) 113 (61%)
Race: White n (%) **African American** n (%) **Asian** n (%) **Other^** n (%) *^includes American Indian or Alaska Native; Native Hawaiian or Other Pacific Islander*	70 (75%) 17 (18%) 6 (6%) 2 (2%)	74 (81%) 16 (18%) 3 (3%) 1 (1%)	144 (78%) 33 (18%) 9 (5%) 3 (2%)
Dark Iris Color: n (%)	49 (52%)	46 (51%)	95 (51%)
Light Iris Color: n (%)	45 (48%)	45 (50%)	90 (49%)
Baseline Pupil Diameter Mean (mm)	5.09	5.18	5.13
Max Dilated Pupil Diameter Mean (mm)	7.21	7.20	7.20
Accommodation Median (diopters)	7.28	7.41	7.41

Note: 14 pediatric subjects 12-17 years old were enrolled in the trial; Race is more than 100% given subjects could check more than one category.

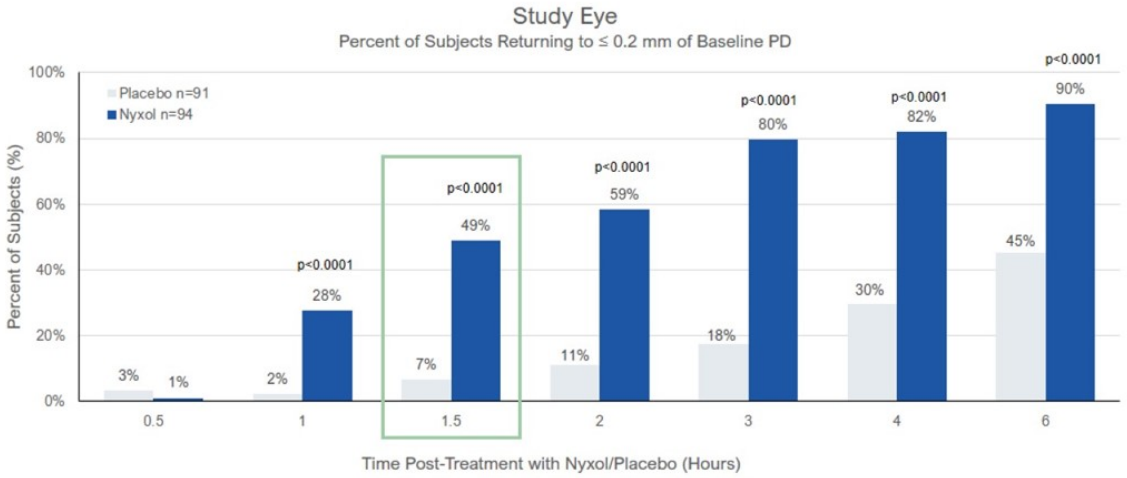
Source: MIRA-2 TLR table #14.1.2.3 (mITT)

MIRA-2: Phase 3 RM Trial Met Primary Endpoint

49% of Patients Returned to ≤ 0.2mm of Baseline at 90 Minutes

MIRA-2 Phase 3 Trial

Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD) at Every Timepoint



Source: MIRA-2 Trial Table 14.1.2.1, mITT Population (same as Safety Population)

*Data includes three of the most common mydriatics used in practice (Phenylephrine, Tropicamide, Paremyd)

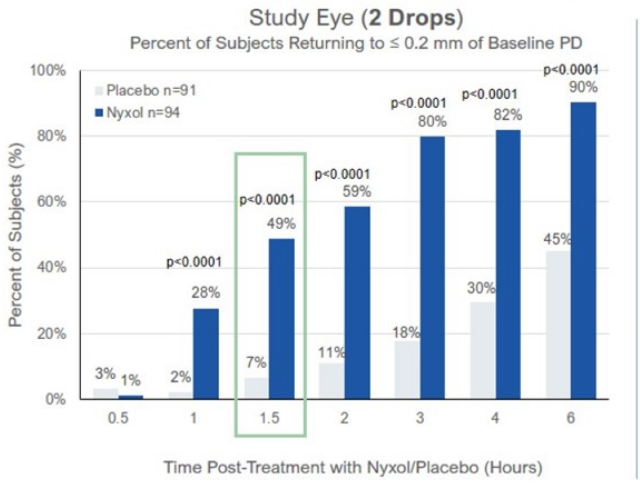
RM

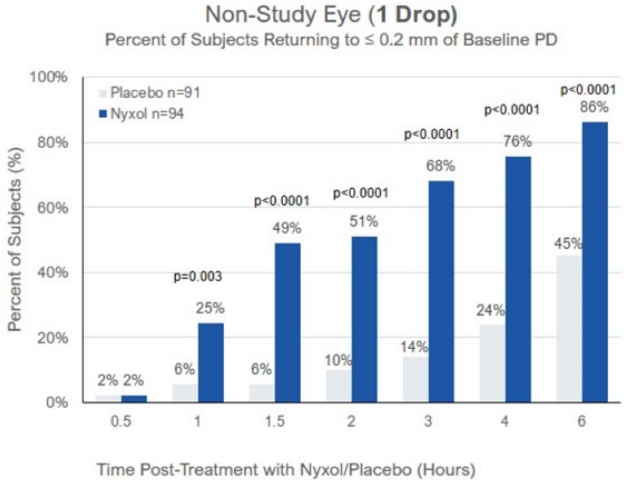
MIRA-2: Study Eye and Non-Study Eye

Similar Rapid Return to Baseline Pupil Size Results with 1 or 2 Drops of Nyxol

MIRA-2 Phase 3 Trial

1 or 2 Drops Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD) at Every Timepoint





Source: MIRA-2 Trial Table 14.1.2.1, mITT Population (same as Safety Population)

*Data includes three of the most common mydriatics used in practice (Phenylephrine, Tropicamide, Paremyd)

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MIRA-2: Responders Returning to Baseline Pupil Size by Iris Color

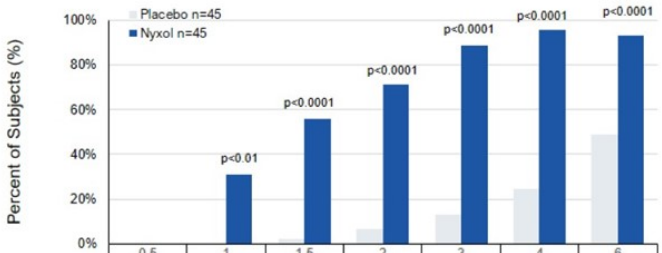
Nyxol Works in Subjects with Both Light and Dark Irides, with a More Vigorous Response in Light Irides

MIRA-2 Phase 3 Trial

Nyxol Reverses Dilation in Light and Dark Irides

Light Irides (Study Eye)

Percent of Subjects Returning to ≤ 0.2 mm of Baseline

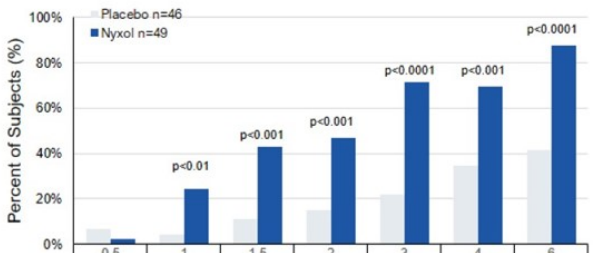


	0.5	1	1.5	2	3	4	6
Placebo n=45	0%	0%	2%	7%	13%	24%	49%
Nyxol n=45	0%	31%	56%	71%	89%	96%	93%

Time Post-Treatment with Nyxol/Placebo (Hours)

Dark Irides (Study Eye)

Percent of Subjects Returning to ≤ 0.2 mm of Baseline



	0.5	1	1.5	2	3	4	6
Placebo n=46	7%	4%	11%	15%	22%	35%	41%
Nyxol n=49	2%	25%	43%	47%	71%	69%	88%

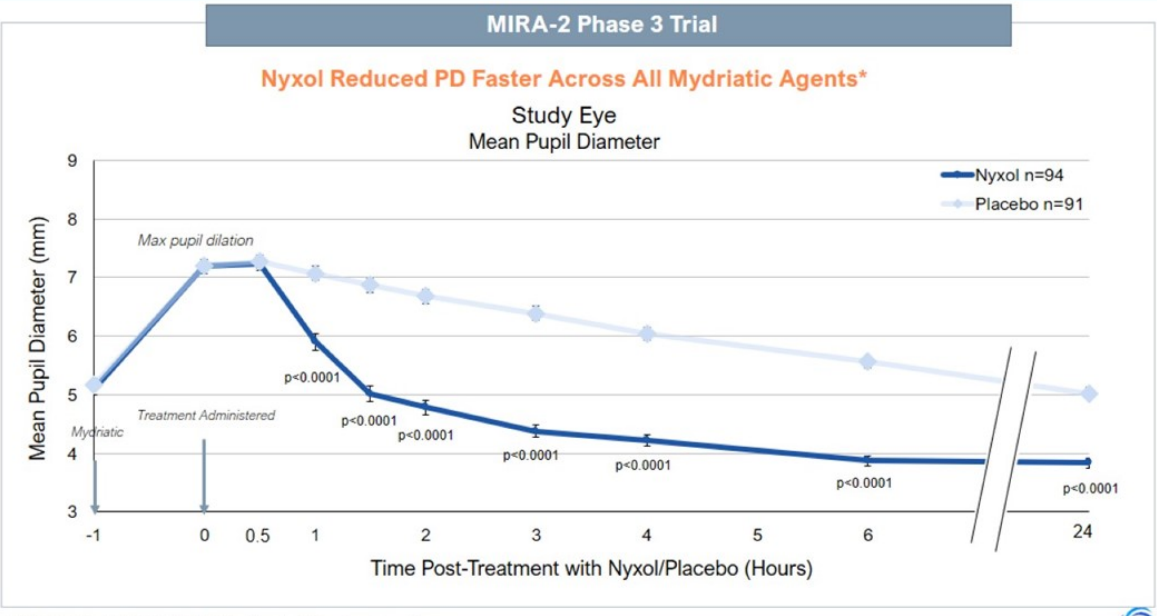
Time Post-Treatment with Nyxol/Placebo (Hours)

Source: MIRA-2 TLR table #14.2.1.6 (mITT)

*Data includes three of the most common mydriatics used in practice (Phenylephrine, Tropicamide, Paremyd)

MIRA-2: Mean Pupil Size Over Time After Maximum Pupil Dilation

Nyxol Treatment Significantly Reduced PD Starting at 1 Hour Post-Dose through 24 Hours



Source: MIRA-2 TLR table #14.2.2.1 (mITT). Standard Error bars are shown.

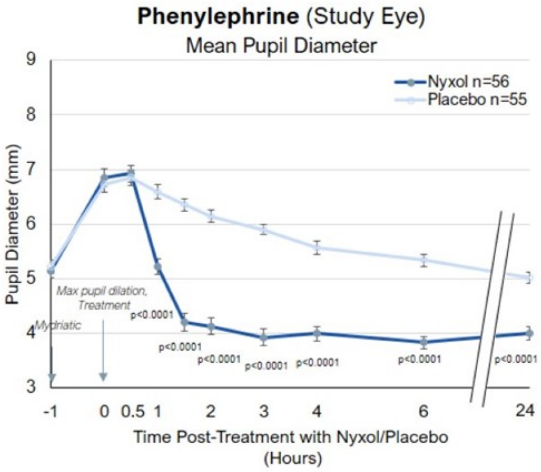
*Data includes three of the most common mydriatics used in practice (Phenylephrine, Tropicamide, Paremyd)

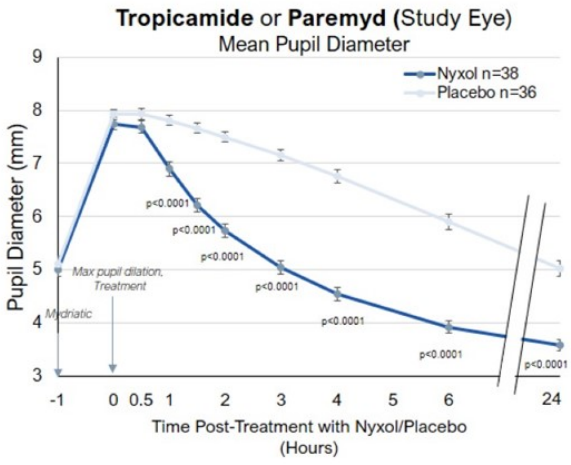
MIRA-2: Mean Pupil Diameter Over Time by Mydriatic Agent

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

MIRA-2 Phase 3 Trial

Nyxol Reduced PD Faster Across All Mydriatic Agents





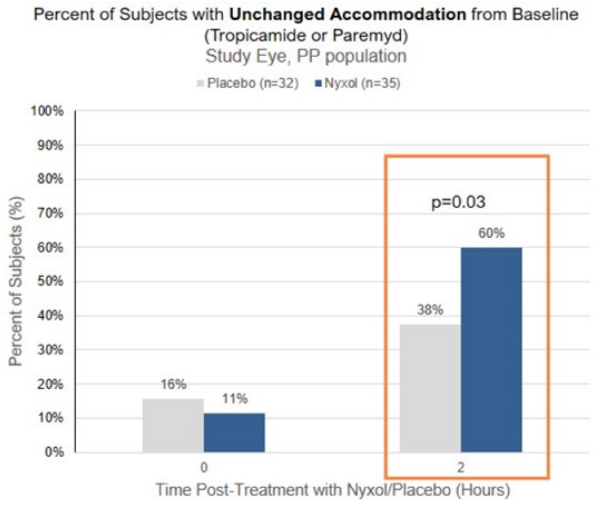
Source: MIRA-2 TLR table #14.2.2.3 (mITT). Standard Error bars are shown.

RM

MIRA-2: Gain of Visual Function (Accommodation)

Nyxol Demonstrates a Faster Return to Baseline Accommodation

MIRA-2 Phase 3 Trial



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

Accommodation

- **Definition:** Changing optical power to maintain a clear image or focus on an object as the distance varies
- Inhibition of the cholinergic system dilates the pupil (mydriasis) and relaxes the ciliary muscle, which adjusts the lens shape and thickness, worsening accommodation (cycloplegia) and causing latent refractive errors to manifest
- Mydriatic agents including Tropicamide and Paremyd inhibit the cholinergic system; not seen with Phenylephrine

Nyxol

✓ Nyxol, a non-selective, alpha-1 antagonist, constricts the pupil enhancing depth of focus by blocking unfocused peripheral light, independent of the ciliary muscle

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

Patel (2011). Pseudoaccommodation. International Ophthalmology Clinics, 51(2), 109–118.

Ocuphire Pharma

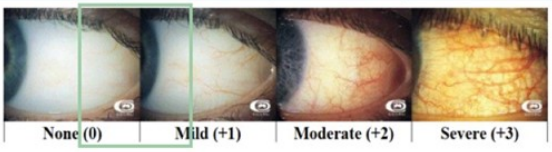
MIRA-2: Safety Findings (After Dilation with Mydriatic Agent)

Nyxol was Well Tolerated with a Favorable Safety Profile

	Nyxol n=94	Placebo n=91	Total n=185
Total Treatment Emergent Adverse Events (n)	113	31	144
TEAEs by Severity (n [%])			
Mild	47 (50%)	15 (17%)	62 (33%)
Moderate	3 (3%)	0 (0%)	3 (2%)
Severe	0 (0%)	0 (0%)	0 (0%)
AEs Occurring in ≥ 5% of subjects (n [%])			
Instillation Site Discomfort	36 (38%)	8 (9%)	44 (24%)
Conjunctival Hyperemia	12 (13%)	0 (0%)	12 (7%)
Conjunctival Hyperemia (mean [SD])			
Baseline (-1 hour)	0.7 (0.6)	0.7 (0.5)	--
60 minutes after instillation of Nyxol	1.7 (0.5)	0.5 (0.5)	--
4 Hours after instillation of Nyxol	1.2 (0.7)	0.5 (0.5)	--

- There were no deaths, serious AEs, or withdrawals due to AEs
- 94% of the AEs in the Nyxol group were **mild**
- Installation site discomfort was 97% mild; No burning, no stinging, no ptosis upon installation
- From a baseline mean of 0.7, the mean hyperemia score increased by approximately 1.0 unit (on a 4-point scale) at 60 minutes post-dose and decreased steadily thereafter

Conjunctival Hyperemia Grading Scale (CCLRU)



Source MIRA-2 Safety Population TLR table 14.3.1.1.; MIRA-2 table 14.3.1.2.2 System Organ Class; MIRA-2 table 14.3.3.2 Hyperemia Score by Time Point

NDA Submission Targeted in Late 2022

Ongoing Activities Sets Ocuphire on Path to a Potential Regulatory Approval in 2023

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

Preservative-Free
Single Unit Vial (5-pack)

Nyxol®

Topline Results Expected in Early 2022

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

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

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

Regulatory Approval
Submit NDA by Late 2022

What's Important?

Nyxol has the Potential to be the only FDA-Approved Treatment Option to Reverse Dilation

Efficacy Signal

- Statistically significant percent of subjects on Nyxol compared to placebo returning to baseline (within 0.2 mm) photopic pupil diameter (PD) at 90 min demonstrated in 2 well-controlled, multi-center clinical trials
- Precedent set with RevEyes Approval

Safety

- Well-tolerated drop
- No significant ocular or systemic AEs or SAEs

Label Expansion

- Opportunity to expand label with ongoing pediatric trial in kids 3 years and up given safety shown in dental reversal approval for phentolamine

Efficacy Signal

- Compelling magnitude of response compared to placebo with statistical significance
- More rapid response with Nyxol vs. placebo
- Works in all iris colors
- Works across all commonly used mydriatic agents

Safety

- No systemic side-effects such BP, HR, headache
- Mild, transient hyperemia is acceptable and common in R_X drops

Patient Experience

- Patients desire more rapid return to normal activities
- Patients actively asking for 'reversal' drops
- Patients want a comfortable experience post-dilation
- Patients more likely to maintain their annual exams if option to reverse dilation is presented

RM Market Opportunity and Commercialization

Presented by: Mitchell Jackson, MD

Jacksoneye
seeing beyond your imagination

Mitchell Jackson, MD
University of Chicago

- Founder and CEO of Jacksoneye in Illinois
- 29 years of experience as a Comprehensive Ophthalmologist
- 2021 - Best Cataract Surgeon in America
- 2021 - Top 50 Global Key Opinion Leaders (KOL)

Patients are Vocal About the Negative Effects of Mydriasis

"**I hate having my eyes dilated**" generated thousands of results on Google, Social Media and Patient Forums

"It takes all day or sometimes overnight to return to normal! I have too much to do!"

"I hate going to the eye doctor. Ruins my whole day."

"I HATE having my eyes dilated. Every time=migraine"

"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."

"Ever since I was a little kid, I have hated getting my eyes dilated. I hate trying to walk, let alone try to drive in the sun with dilated eyes."

"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.'

Quotes are from anonymous patients

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Importance of Dilations

Dilated Eye Exam Remains the Recommended Standard of Care

Advocacy

AMERICAN ACADEMY OF OPHTHALMOLOGY · AMERICAN ACADEMY of OPTOMETRY · CDC · American Diabetes Association. · AMERICAN OPTOMETRIC ASSOCIATION · NIH National Eye Institute

Patient Types For Dilation	Reasons Patients Decline	Non-Dilated Exam
• Patients with or at-risk for glaucoma, diabetes, AMD, etc. • Patients undergoing cataract evaluation • Patients undergoing refractive evaluation (includes first or annual exams) • Patients receiving anti-VEGF injections • Anyone over the age of 60 or other risk populations	• Blurry vision • Photophobia • Headaches • Loss of accommodation • Allergic reactions • Digital strain • Phobia • Lifestyle • Work	• Ultra-Widefield Imaging (UWFI) Tool • Barriers: - Capital Equipment Cost - Training time - Cost to patient $40-80 - Not a replacement for a dilated exam - Dilated exam is standard of care

$35 B+
Societal cost of major visual disorders among U.S. residents aged 40+

63%
of participants who had eye disease were not aware

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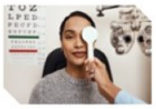
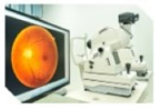
Source: American Academy of Ophthalmology, Comprehensive Adult Medical Eye Evaluation Preferred Practice Pattern, 2020

Bottom-Up Calculation of Annual Dilated Eye Exams

~101 Million Annual Dilated Eye Exams are Performed in the US

Demand Side Estimate

	Number of Providers (X)	Average Number of Weekly Exams (Y)	Estimated % Patients Dilated (Z)	Total (X*Y*Z) * 48 wk/yr
 Optometrists	46,000	59	40%	~52 M
 Ophthalmologists	18,000	88	50+%	~38M
 Retina Specialists	3,000	150	50%	~11 M

Supply Side Validation: Based on the ~2 million total units of mydriatic agents sold in 2020, we calculated the total number of dilated eye exams to be ~125 million patients, consistent with demand side estimates.

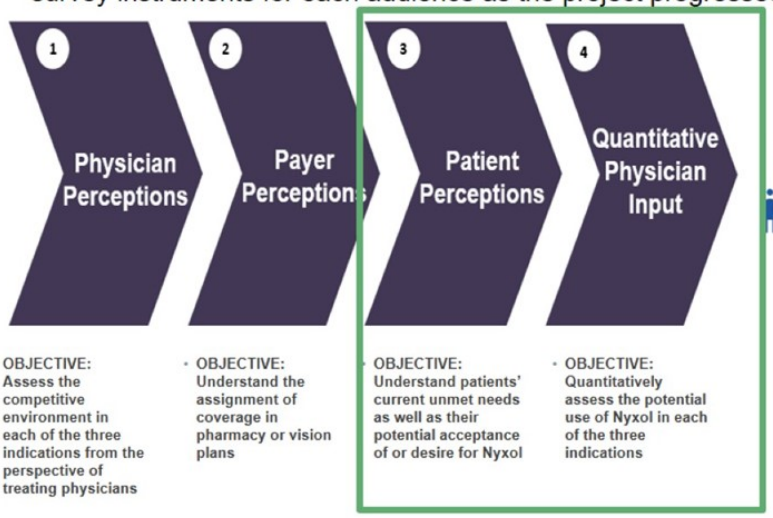
*IQVIA 2020 sales data; KOL Interview; GlobalData market research; and AOA Excel and Jobson Medical Information
'Bottom-Up Calculation' assumes 48 total work weeks in a year
Supply side validation assumed each unit (bottle) has ~10 mL fill volume and each patient gets 2-4 drops

RM

Market Research Methodology by GlobalData

Market Research Conducted in 2H 2020 for RM, Presbyopia, and Night Vision Disturbances

GlobalData conducted this research in 4 phases of primary research, which allowed us to inform the survey instruments for each audience as the project progressed



>200 Total Patients Surveyed

- Reversal of mydriasis (N=190)
- Presbyopia (N=134)
- Dim Light Vision Disturbance (N=120)

120* Optometrists & Ophthalmologists Surveyed

(N=69 Optometrists; N=51 Ophthalmologists)

* Retina specialist were not surveyed

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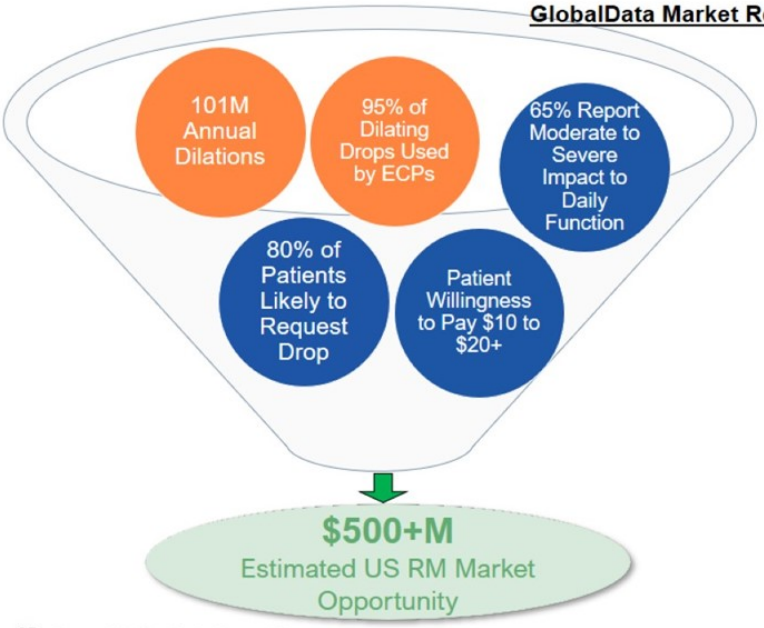
Reversal of Mydriasis (RM) Market Opportunity

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

GlobalData Market Research Findings



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

RM

Why 1990' Rev-Eyes is Not a Benchmark for Nyxol Future RM Sales

Nyxol's Broad Differentiation Addresses the Unmet Need for Reversal Drops in New Era

	Problems with Rev Eyes	Nyxol Differentiation
Efficacy	• 4 drops from a multiuse office bottle (added additional chair time)	• 1 to 2 drops for a rapid reversal from a single-unit vial

Safety	• Significant Side-effects
	  • Burning and stinging sensation
	  • Ptosis
	  • 'beefy red eyes'
	• Nicknamed "Red-Eyes"
		• No burning and stinging sensation
		• No ptosis
		• 94% of AEs were mild

Stability	• Not an acceptable commercial formulation • Burden of preparation given requirement to mix at physician office • Product stable for only 21 days	• A hassle-free, room temperature shelf-stable, sterile, preservative-free, single-unit vial
Commercialization	• Limited marketing effort • Years of being on-and-off the market given multiple pharma owners hindered uptake	• Experienced team committed to commercial success in RM • Expected growth in dilations due to an aging population and digital dependence

Rev-Eye label; Nyxol clinical trials

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RM Market Opportunity and Commercialization

Presented by: Bindu Manne

Bindu Manne
Head of
Commercialization
Ocuphire Pharma

- 16 years of experience primarily in product launches (12+) across all ophthalmic specialists
- Dynamic experience ranging from sales, market development, professional and medical affairs
- **O**phthalmic **W**orld **L**eader: Rising Star Award Recipient
- Non-Profit Board Member: Holland Foundation For Sight Restoration and Ophthalmic World Leaders

Perspective from Practice Administrators on Reversing Dilations

Leading Practice Administrators Confirm the 'Market Need,' and Value to Patient

- Anterior Segment Practice in Southeast
  - *"We've explored and offered several options over the years to reverse mydriasis – both as a tool to elevate the patient experience and to reduce liability when a patient with poor accommodation walks out of my practice. We've used pharmacologic agents to reverse the effects of dilation in the past, but those products had significant limitations, and I would welcome a new option indicated for RM in my practice."* – Certified Ophthalmic Executive and CEO

- Multi-Specialty Practice, Midwest
  - *"We call our patients guests so anything to enhance their experience is valuable for our practice. Pupil dilation is a perceived inconvenience – especially for the working-age population. They grab up our evening appointments typically, so they don't have to go back to work while dilated. Having an option to reverse dilation is something we and our guests would enjoy."* – Certified Ophthalmic Executive and CEO

- Leading Academic Eye Center
  - *"Patients have anxiety over dilation and if we could reduce that fear, help them regain accommodation faster, I would like to consider that option across all specialties."* – Head of Operations, Certified

Willingness to Implement:

~ We would be comfortable passing this cost to the patient as a premium to resume visual function faster.

~ Patients would be willing to pay for this benefit.

Pre-Commercial Activities in 2022

Activities Underway to Support Capital-Efficient Nyxol RM Commercial Launch

Market Development

Engage leading Key Opinion Leaders and Professional Societies to establish our commitment to refractive and retinal disorders

Physician Targeting

Broad HCP opportunity with focus on early adopters to capture post-market data and patient experience

Eye Care Practitioners in U.S.	
Total Ophthalmologists	18,000
Total Optometrists	46,000
Total Retina Specialists	3,000

Patient Journey

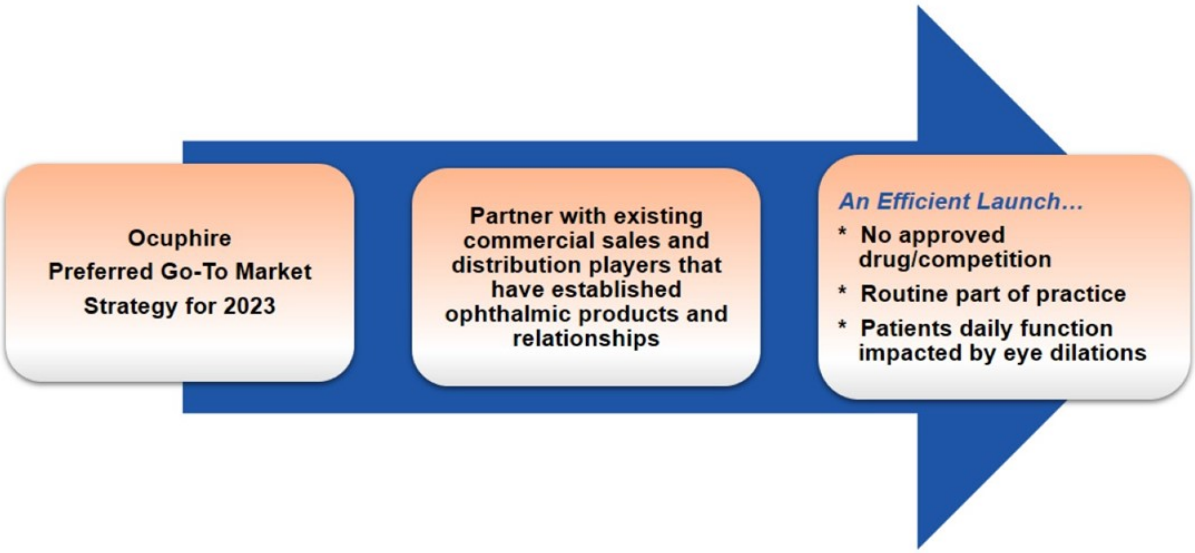
Establish Ocuphire as a patient-centric company and leader in improving everyday vision through education to empower purchasing decisions

Brand Awareness Across Eye Care Professionals

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

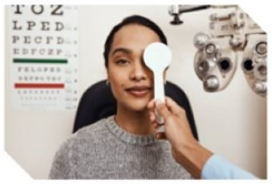
Go-To-Market Strategy for 2023

Nyxol as RM Allows Efficient Pharmaceutical Launch Across Eye Care Practices



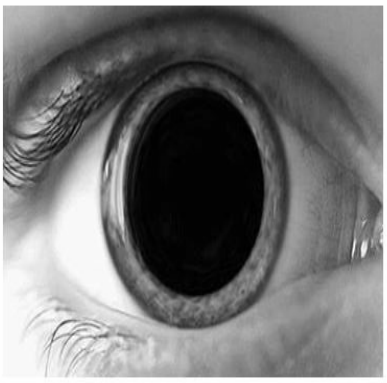
Practice Implementation Models

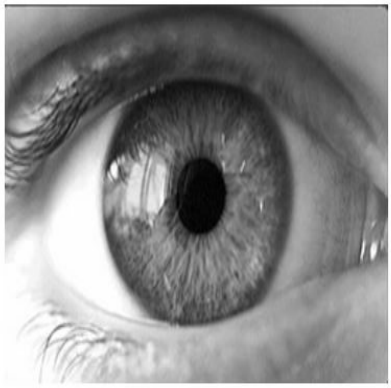
Positive Feedback from Physicians on Integration of a Reversal Agent into Practice

Optometry	Ophthalmology	Retina
		

- Adoption into practice requires no additional staff or patient training
- Practices across all specialties expressed the positive impact on patient experience and adherence to dilated exams
- Ophthalmology and Optometry practices would pass a nominal fee into their routine refraction and include it in their surgical pricing
- Retina practices across academic centers favored offering to patients at no additional cost due to the volume of dilated exams and as a patient satisfaction service

Nyxol® for Reversal of Mydriasis (RM)





QUESTION & ANSWER

Ocuphire PHARMA

Summary of Nyxol Reversal of Mydriasis Program

	Nyxol, the first ophthalmic formulation of **phentolamine mesylate**, is a differentiated MOA uniquely suited for **reversal of pharmacologically-induced mydriasis**
	In MIRA-1 and MIRA-2, Nyxol met its primary endpoint of rapidly returning subjects as well as many key secondary endpoints
	Consistent with prior trials, Nyxol has demonstrated **favorable safety and tolerability with a MOA uniquely suited to avoid safety issues** associated with cholinergic drug (e.g. pilocarpine) reversal of dilations
	MIRA-3 Phase 3 and MIRA-4 Pediatric Safety trials are **currently enrolling** patients at 15 sites in the US **with data expected in early 2022**
	We anticipate the results of these trials will support an **NDA submission for Nyxol in late 2022**
	Nyxol has the potential to be the **ONLY commercially-available, FDA-approved Rx treatment to reverse pupil dilation** in a growing $500+M US Market

III. Nyxol Presbyopia Program

Jay Pepose, MD, PhD
UCLA School of Medicine

James Katz, MD
University of Illinois, College of Medicine

Pupil Modulation Eye Drops for Presbyopia

Presented by: Jay Pepose, MD, PhD

PeposeVision INSTITUTE

Jay Pepose, MD, PhD
UCLA School of Medicine

- Founder and Medical Director of Pepose Vision Institute
- Founder of Midwest Vision Research Foundation
- Recognized Thought Leader in Ophthalmology
- 40 Years of Experience as a Treating Physician and Widely Published Researcher

The Time for Presbyopia Drops

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

September 22, 2021 | 11 min read SAVE

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

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

Presbyopia PHYSICIAN

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

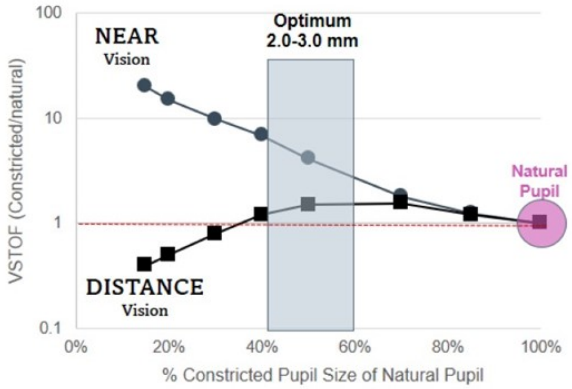
Presbyopia Treatment Market Size Projected to Rise Lucratively by 2026 end BioSpace

Sources: Academic review articles, journals, and publications

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 (CSRT), January 2022

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

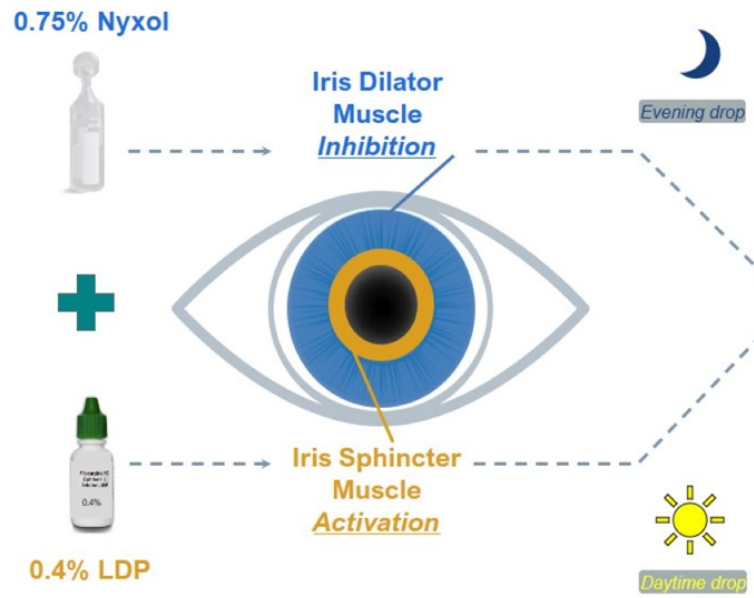
Ocuphire

Nyxol with LDP as Adjunctive Therapy in Presbyopia

Presented by: Jay Pepose, MD, PhD

Nyxol® with Low-Dose Pilocarpine (LDP) as Adjunct Therapy

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



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

Pin-hole target is 2 to 3 mm with contributions from each MOA

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

Source: 1) Nyxol® data from 9 completed trials; Pilocarpine Product label and Literature

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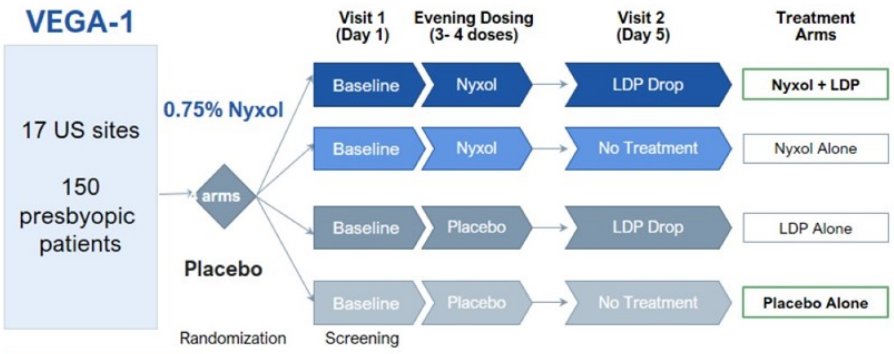
VEGA-1: Presbyopia Phase 2 Trial Design

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



Eligibility Criteria

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

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

Endpoints

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

Secondary:

- % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours in photopic lighting comparing Nyxol + LDP vs placebo, Nyxol alone, and LDP alone
- % of subjects with ≥ 3 lines of near vision gain with less than 5 letters of distance loss
- Pupil diameter at time points
- Safety and tolerability

Clinical trial NCT#04675151. DCNVA = distance-corrected near visual acuity . BCDVA = best corrected distance visual acuity; *3-4 evenings; VEGA-1 Study Design

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VEGA-1: Demographics and Baseline Characteristics

Treatment and Placebo Arms were Balanced in the VEGA-1 Phase 2 Clinical Trial

	Placebo Alone N=43	Nyxol Alone N=30	LDP Alone N=31	Nyxol+LDP Combo 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 (%) **Female** n (%)	15 (35%) 28 (65%)	7 (23%) 23 (77%)	13 (42%) 18 (58%)	5 (12%) 38 (88%)	40 (27%) 107 (73%)
Race: White n (%) **Other*** n (%)	37 (86%) 6 (14%)	26 (87%) 1 (3%)	28 (90%) 3 (10%)	40 (93%) 3 (7%)	131 (89%) 15 (11%)
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%)
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

Source: VEGA-1 TLR Table 14.1.2.2 Demographics and Baseline Characteristics (PP Population). Snellen Conversion Chart.

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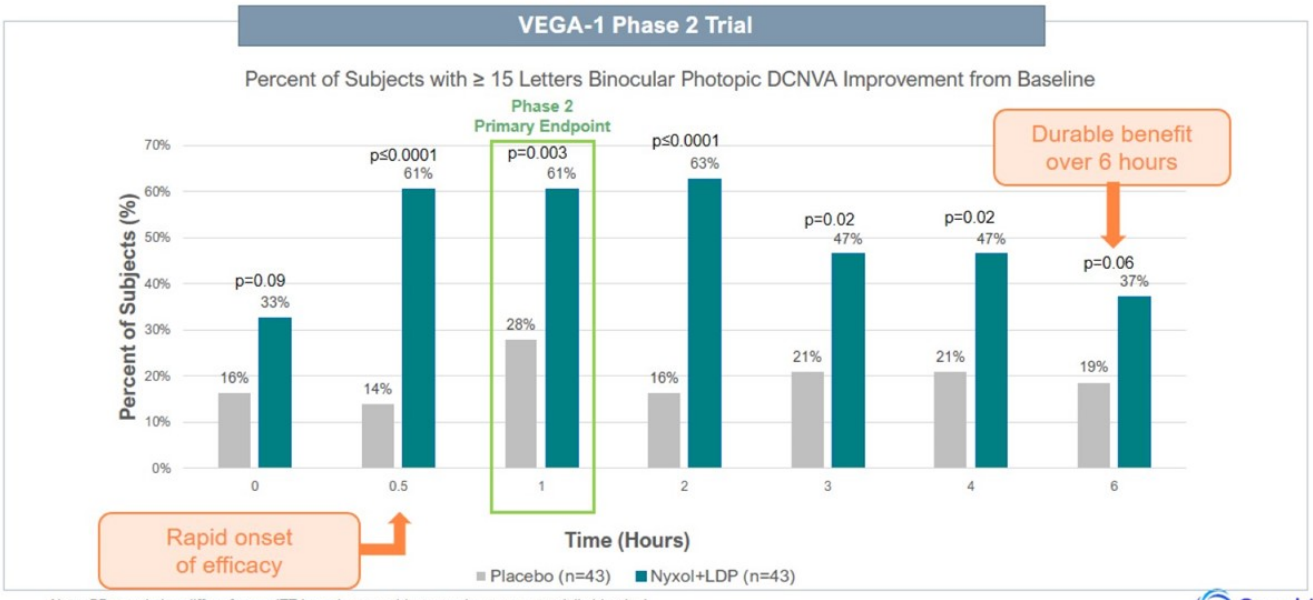
VEGA-1: Nyxol+LDP Met Primary & Secondary Endpoints

61% Patients with Nyxol+LDP had ≥ 15 Letter Near Gain with Fast Onset & Durable Responses



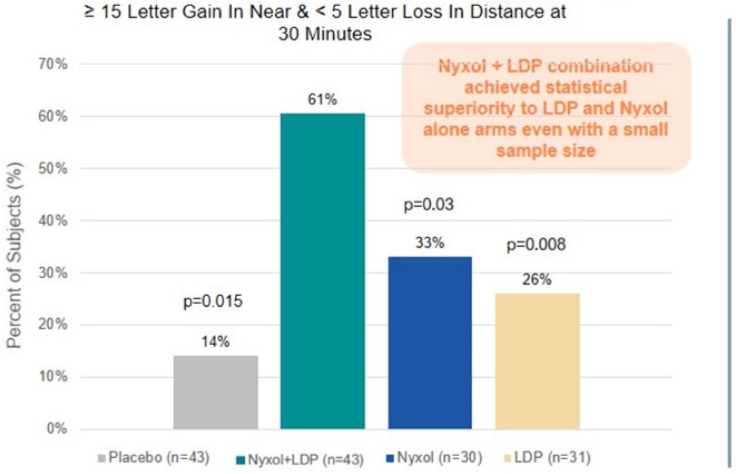
Note: PP population differs from mITT by only one subject; results were essentially identical.

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

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

Pre-Specified Endpoints Demonstrate Superiority of Combo vs. Components & ≥10 Letter Near Gain

VEGA-1 Phase 2 Trial



Nyxol + LDP combination achieved statistical superiority to LDP and Nyxol alone arms even with a small sample size

77%

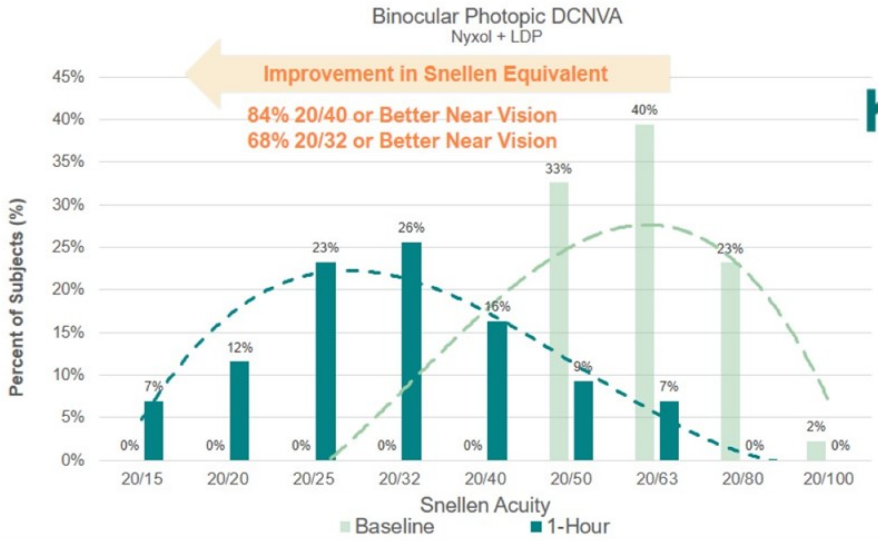
of subjects achieved ≥ 10 letter improvement in DCNVA at 30 minutes (p=0.015 vs placebo) and similar trend at other timepoints

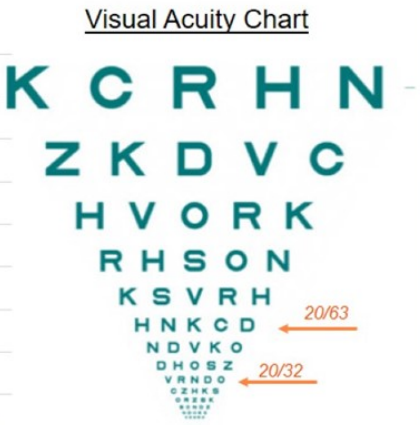
Source: VEGA-1 TLR Table 14.2.2.2 Percent of Subjects with >= 15 Letters of Improvement in Photopic DCNVA and < 5 Letters of Loss in Photopic Binocular BCDVA by Time Point (PP Population); Table 14.2.1.2 Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point (PP Population)

VEGA-1: Improvement in Functional Near Vision

Nyxol+LDP had a Rapid Improvement in Near Vision to 20/32 for many Patients

VEGA-1 Phase 2 Trial





84 Source: VEGA-1 TLR Table 14.2.24.1 Percent of Subjects with Photopic DCNVA by Time Point (PP Population)

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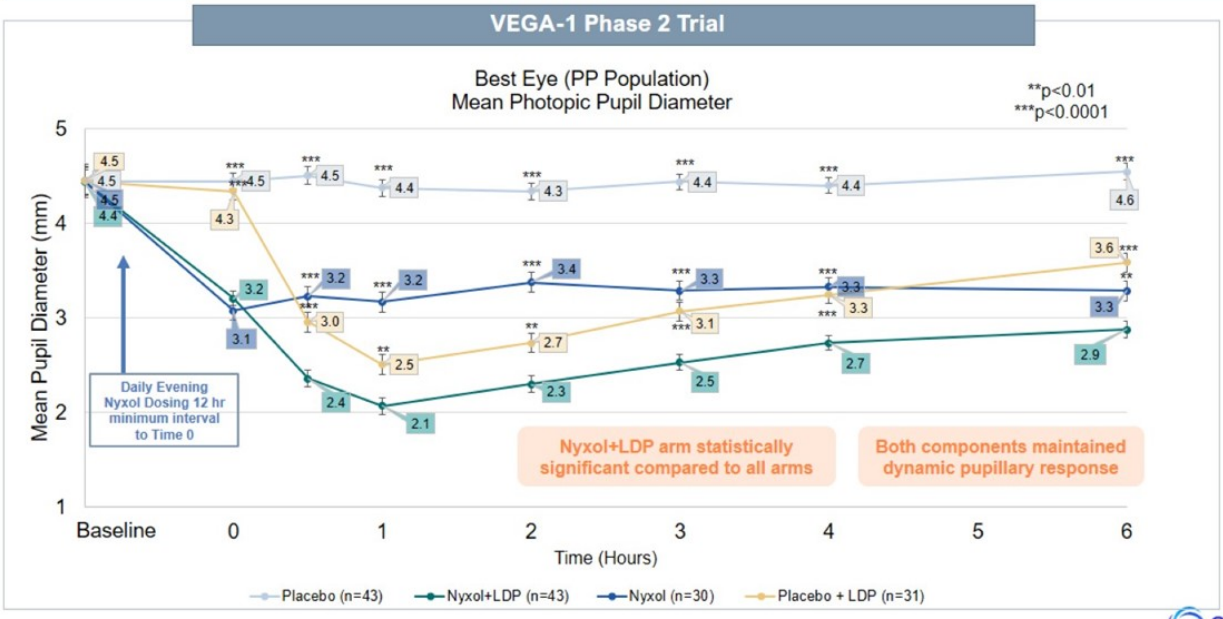
VEGA-1: Mean Pupil Diameter Over Time

Achieved Optimal Pupil Size in Nyxol+LDP (& Nyxol) Consistent with 3-line Near Vision Gain

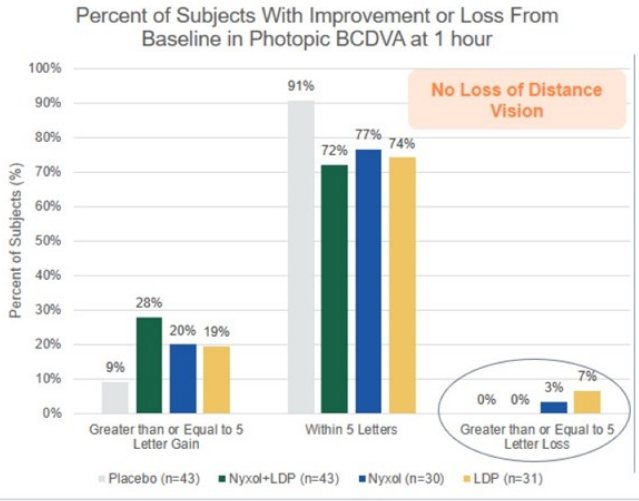


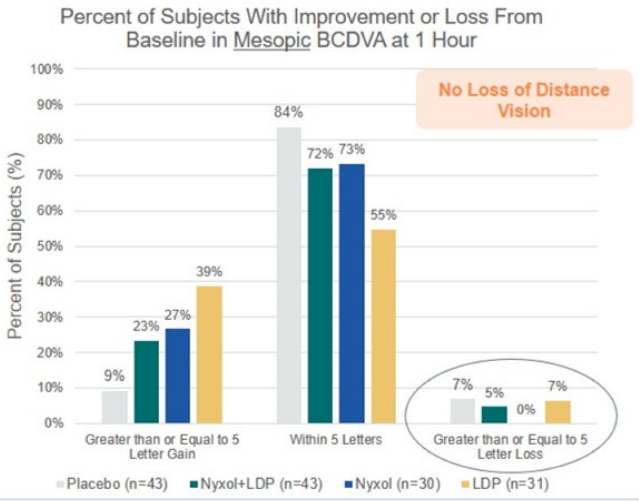
Source: VEGA-1 TLR Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)

VEGA-1: Photopic and Mesopic Distance Vision Effects

Nyxol and/or LDP Demonstrated No Loss of Distance Vision in Photopic and Mesopic Lighting

VEGA-1 Phase 2 Trial





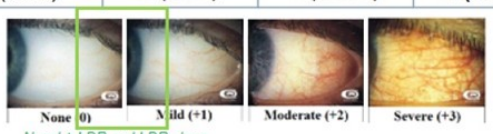
Source: VEGA-1 TLR Table 14.2.8.1 and 14.2.10.1 Percent of Subjects With Improvement or Loss From Baseline in Photopic and Mesopic BCDVA by Time Point (PP)

VEGA-1: Safety Findings Across All Arms

Nyxol+LDP Combination (& Nyxol Alone) was Well Tolerated with a Favorable Safety Profile

	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%)**

Conjunctival Hyperemia CCLRU Scale for Reference



Nyxol + LDP and LDP alone
Only transient 0.5 point mean increase

- No deaths, no serious AEs
- Almost all AEs were mild
- **0% headaches or brow aches reported for Nyxol+LDP arm; headaches not reported in Nyxol trials**
- **~5% mild, transient conjunctival hyperemia AEs in Nyxol+LDP arm**
- **Distance vision: 0% Nyxol + LDP arm had ≥ 5 letter distance loss in photopic lighting (5% in mesopic)**
- No change in IOP

Source: VEGA-1 TLR Table 14.3.1.1 Overall Summary of Treatment Emergent Adverse Events (TEAE) (Safety Population)
Table 14.3.1.3 Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term, and Severity (Safety Population)

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What's Important?

Nyxol+LDP has the Potential to be "Best in Class" Presbyopia Eyedrop

Efficacy Signal

Percent of subjects with ≥3-line improvement in near vision with less than 5 letters of distance loss in Nyxol+LDP combo compared to Nyxol alone and LDP alone as demonstrated in 2 well-controlled, multi-center clinical trials

Safety

No loss of distance (included in efficacy)
Maintain night distance vision
Well-tolerated

Broad Label Opportunity

For Vuity™, FDA did not limit the use of the product to clinical trial parameters such as:

- age
- lighting conditions (photopic or mesopic)
- monocular or binocular
- phakic status

Efficacy Signal

- Achieve "functional near vision" and intermediate vision
- Achieve optimal pupil size
- Durability
- Dynamic/responsive pupil

Safety

- No loss of distance vision
- No headaches or brow aches
- Reliable night distance vision
- No stinging or burning
- Minimal redness

Patient Experience

- Tunability - ability to customize treatment based on patient's lifestyle needs
- Favorable tolerability for continued use and Rx refills

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Nyxol Alone in Presbyopia

Presented by: James Katz, MD

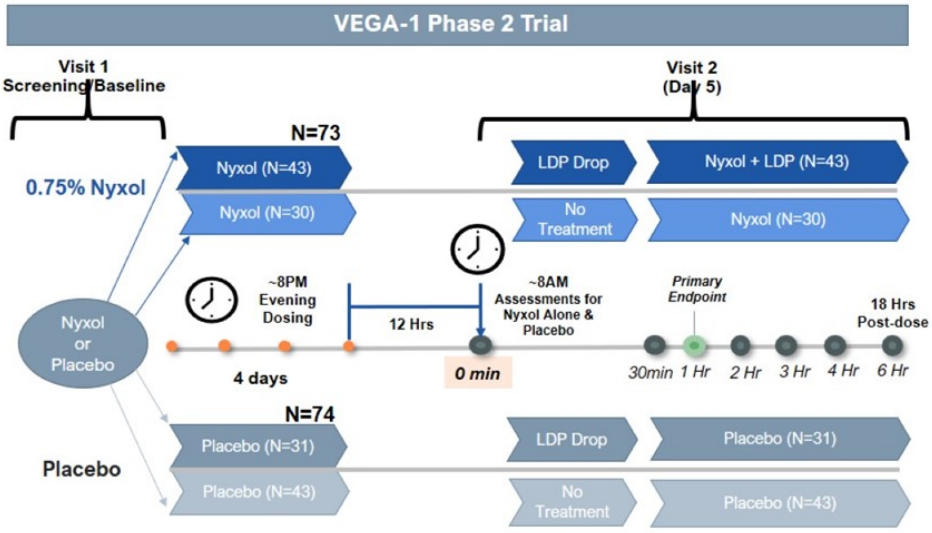
the Midwest Center for Sight

James Katz, MD
University of Illinois, College of Medicine

- President of the Midwest Center for Sight
- Board-certified Ophthalmologist with specialties in Cornea, Cataract, and Refractive Surgery
- Well-Published in Distinguished Ophthalmologic Journals With Over 50 Publications and Over 300 Presentations

VEGA-1 Study Design Assessed Nyxol Alone Efficacy

Nyxol as Single Drop vs. Placebo Met Pre-Specified Endpoints in the Trial



17 US sites

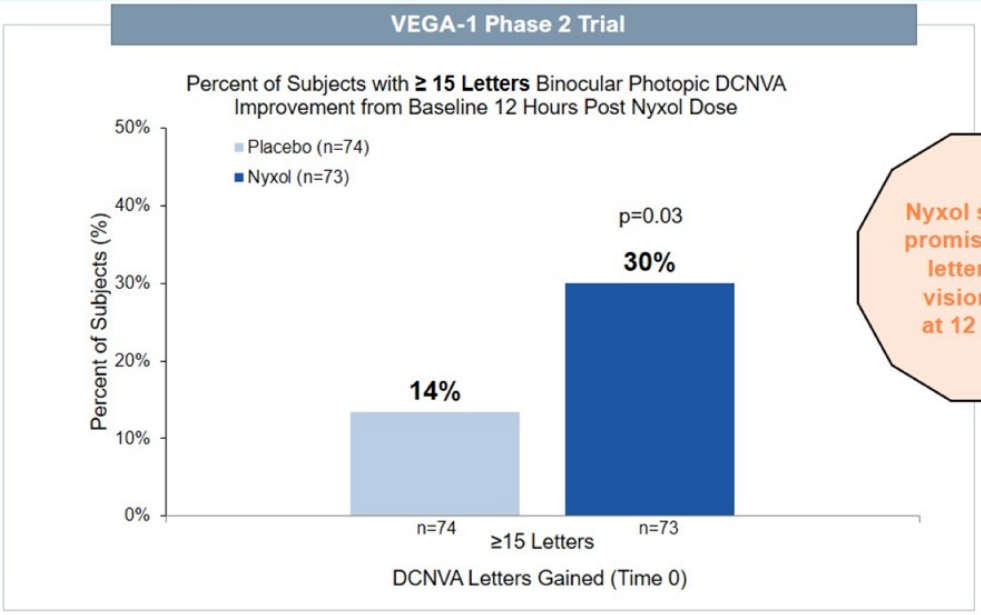
150 Presbyopic patients

Nyxol alone evaluated 12 hours post dosing

*3-4 daily evening doses and then visit 2 on Day 5
Source: VEGA-1 Study Design

VEGA-1: Nyxol Meets Planned P3 Efficacy Endpoint at 12 Hours

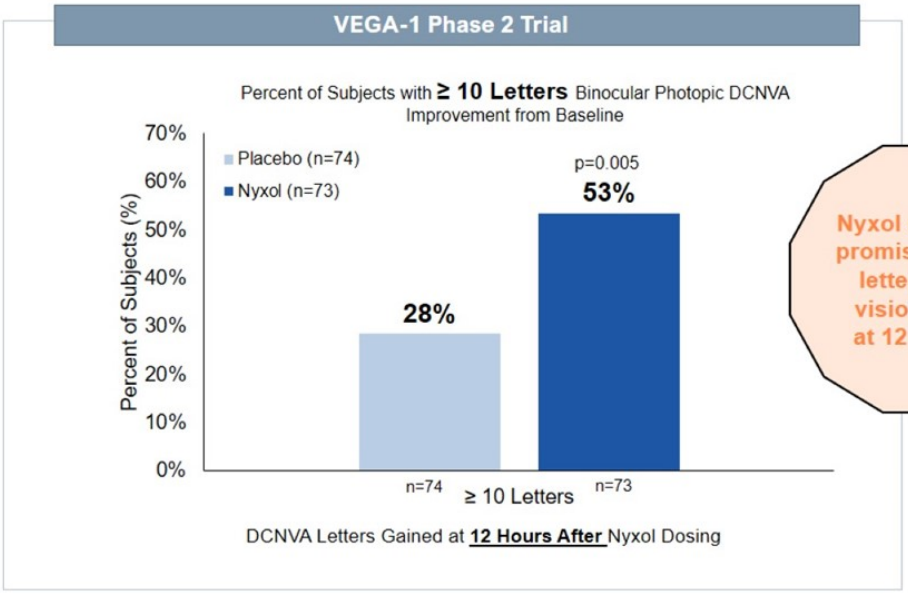
Nyxol as a Single Drop Provides a Statistical 3 Line or More Gain Compared to Placebo



Source: VEGA-1 TLR Table 14.2.1.7 Percent of Subjects with Improvement in Photopic DCNVA at 0 Minutes for Nyxol and Placebo Treated Subjects (PP Population)

VEGA-1: ≥10 Letter Gain in DCNVA with Nyxol at 12 Hours

Nyxol as a Single Drop Provides a Clinically Meaningful ≥10 Letter Gain Compared to Placebo

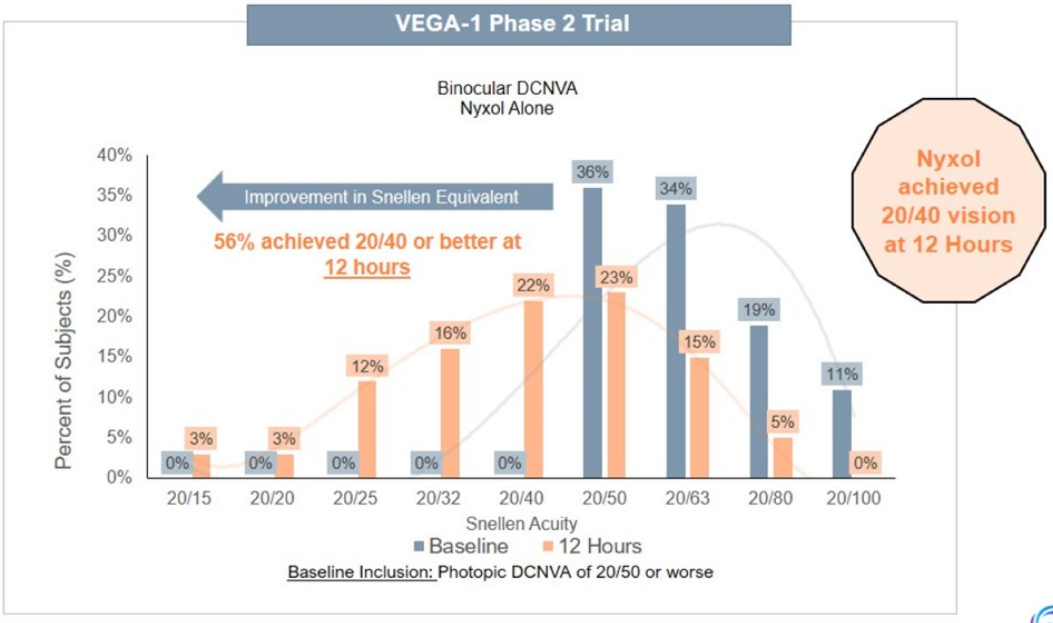


Nyxol showed promising ≥10 letter near vision gain at 12 hours

Source: VEGA-1 TLR Table 14.2.1.7 Percent of Subjects with Improvement in Photopic DCNVA at 0 Minutes for Nyxol and Placebo Treated Subjects (PP Population)

VEGA-1: Improvement in Functional Near Vision

Nyxol Single Drop Significantly Improves Functional Near Visual Acuity



Source: VEGA-1 TLR Table 14.2.24.1 Percent of Subjects with Photopic DCNVA by Time Point (PP Population)

VEGA-1: Functional Vision Durability

Single Drop of Nyxol has Durable Response for 18 Hours

18 hours post Nyxol consistent efficacy with 12 hours

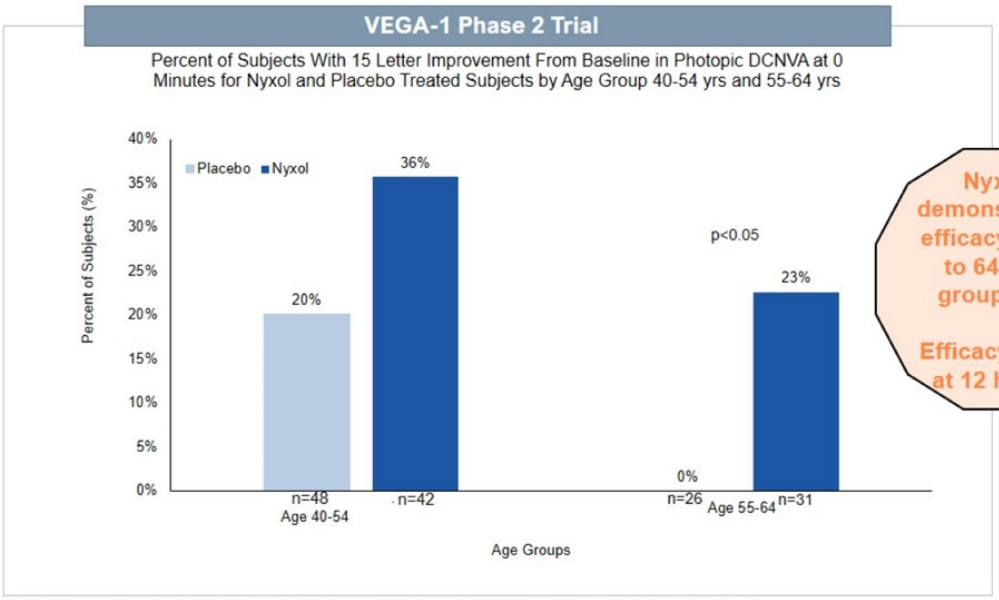
	Nyxol as a Single Drop		
	Time Point (Hrs post Nyxol dose)	% of Subjects	Statistics vs Placebo
Subjects achieving **3-line gain** in photopic, binocular DCNVA (N= 30)	12.5 18	33% 37%	p=0.07* p=0.11*
Subjects achieving **20/40 or better** in photopic, binocular DCNVA (N= 30)	18	60%	N/A (compared to baseline)

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

VEGA-1 TLR Table 14.2.1.2 Percent of Subjects with Photopic DCNVA by Time Point (PP Population) and Table 14.2.24.1 Percent of Subjects with Photopic DCNVA by Time Point (PP Population)

VEGA-1(Post-Hoc): Efficacy Across Presbyopia Ages

Nyxol Highest Efficacy in Young Presbyopes as Expected; Also Efficacy Seen in Older Presbyopes



Note: Trend toward statistical significance p=0.15 in age 40-54; larger sample size for all arms planned in Phase 3 program

Source: VEGA-1 TLR Table 14.2.1.7.1 & 14.2.1.7.2 Percent of Subjects with Improvement in Photopic DCNVA by Age Group (PP Population)

Presbyopia Drops: Ocuphire Next Steps and Competitive Landscape

Presented by: Jay Pepose, MD, PhD

Two Treatment Options for Spectrum of Presbyopic Patients

Two NDA Submissions Targeted in 2023: Nyxol Alone and Nyxol+LDP

Pursuing Product Labels for 1 Drop and 2 Drop Options for the Treatment of Presbyopia

Nyxol as a Single Agent for Presbyopia

Single Durable Drop

Nyxol with LDP as Adjunctive Therapy for Presbyopia

Two Drops Tunable Option

Initiating VEGA Phase 3 Program in Mid-2022 for Both Labels

Ocuphire

Potential 'Best in Class' Presbyopia Drop(s)

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

Product Attributes^	VUITY™	Ocuphire Nyxol	Ocuphire Nyxol+LDP
1) Efficacy (3 Line Gain in DCNVA - Primary Endpoint Responders)*	**26-31% (3 hours)**	**30% (12 hours)**	**~61% (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**

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

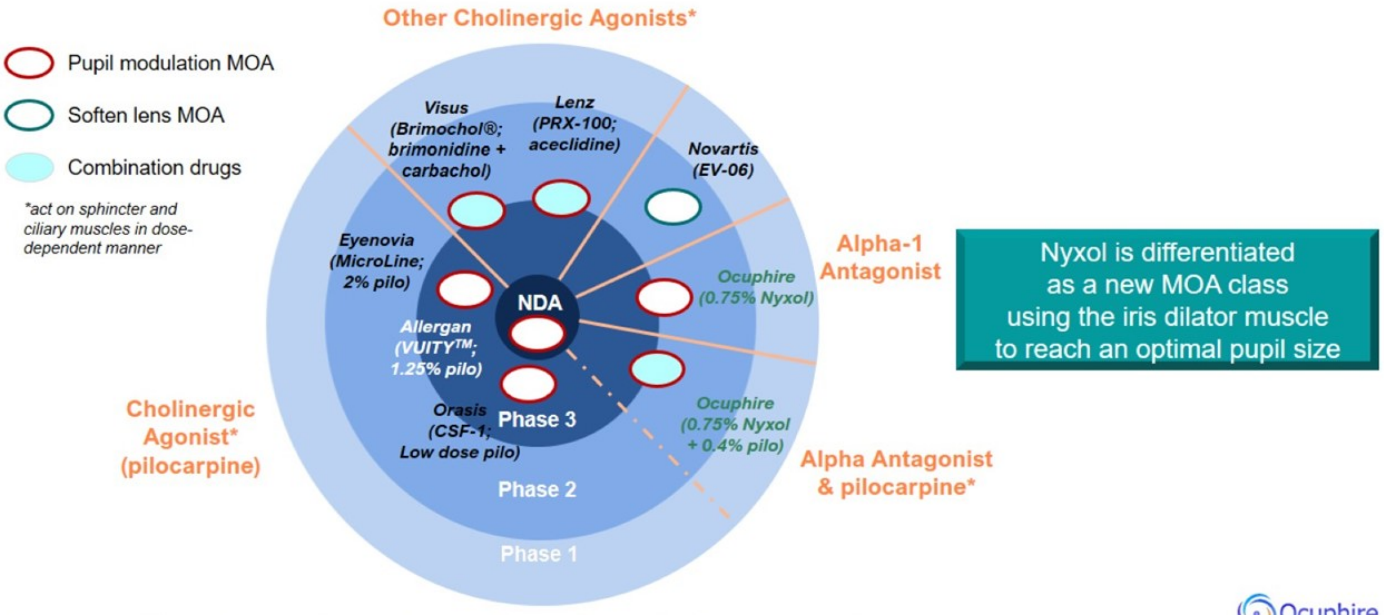
Nyxol's Potential Differentiated Solution

Placebo Adjusted Values for Vuity were 15-23% in Gemini1 & 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

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



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

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

Ocuphire

Large and Growing Presbyopia Market

Presented by: James Katz, MD

Presbyopia is a Burgeoning Opportunity

One of the Largest Disease Segments, Increasing Spend from Global Reading Glasses 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, but unable to see near and far at same time
- Aesthetics and inconvenience

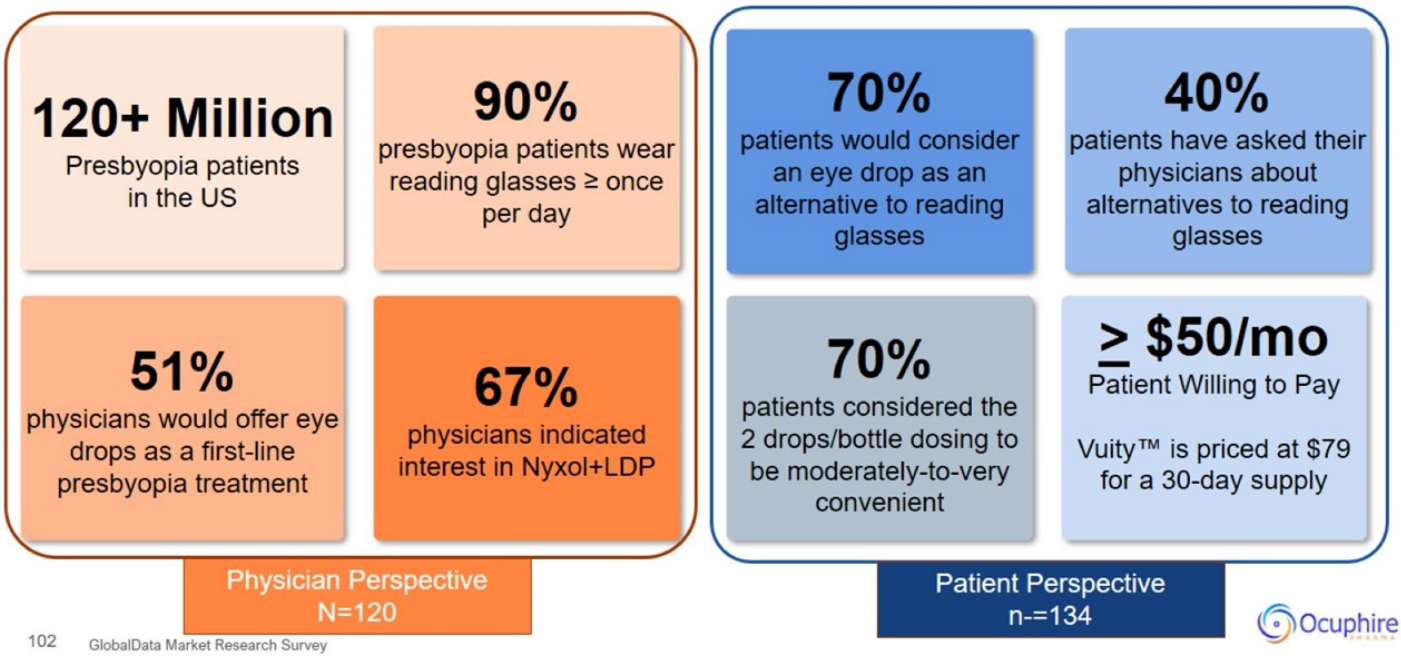
100%
of adults over the age of 40 years are at risk of developing presbyopia

Presbyopes (US)
~128 M

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

Key Findings from GlobalData Market Research on Presbyopia

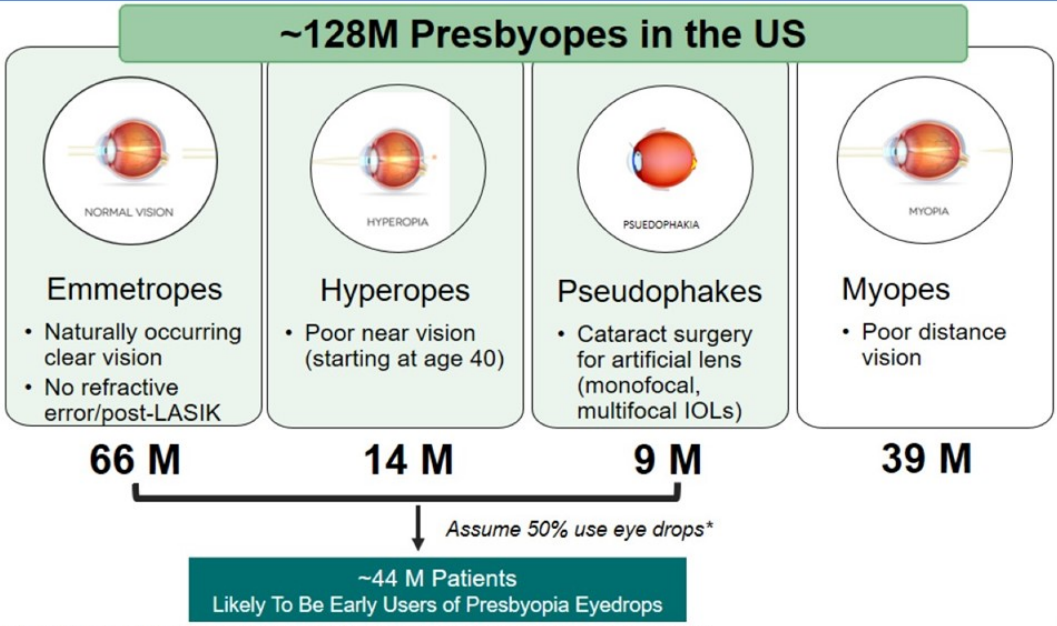
Insights Very Consistent with Other Competitors Market Research Surveys



GlobalData Market Research Survey

Presbyopia Market Segments

Tens of Millions of Likely Early Users → Emmetropes, Hyperopes, and Pseudophakes



Global Prevalence of Presbyopia, 2018, Fortune Business Insights Reading Glasses Forecast 2016-2027, NEI 2010 data. *GlobalData Market Research 2020
Vitale S. et. Al. JAMA Ophthalmology, 2008, Vision problems, US, Arch. Ophthal, 2014, Vision Monday.

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Vuity™ is the First FDA-Approved Eyedrop for Presbyopia

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

FDA Approval of Vuity™ positive for the presbyopia space

Opportunities for new entrants with differentiated product attributes in a newly established segment with physicians and patients/consumers

~44 M Patients Likely To Be Early Users of Presbyopia Eyedrops

3-6 refills per year assumed

Private Cash Pay (Vuity™ fill List Price)

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

~2 Billion Presbyopes Globally for Even Larger Market Potential

Global Prevalence of Presbyopia, 2018, Fortune Business Insights Reading Glasses Forecast 2016-2027, Cataract & Refractive Surgery Today, 2021, NEI 2010 data. Vitale S. et. Al. JAMA Ophthalmology, 2008, Vision problems, US, Arch. Ophthal, 2014, Vision Monday.

Ocuphire Pharma

Nyxol® for PRESBYOPIA

QUESTION & ANSWER

Summary of Nyxol and Nyxol+LDP Presbyopia Program

	**Nyxol as a single drop is differentiated as a new MOA class** working on the iris dilator muscles; **Nyxol with LDP as adjunct therapy uniquely offers pupil 'tunability'** depending on patient lifestyle
	In VEGA-1 trial: • Nyxol+LDP met its primary efficacy endpoint ≥ 15 letter near visual acuity gain. • **Nyxol as a single drop met efficacy endpoints at 12 hours and 18 hours**
	Consistent with prior trials across other indications, **Nyxol, dosed alone or with LDP, has demonstrated favorable safety and tolerability**
	**VEGA Phase 3 program** planned for Nyxol and Nyxol+LDP for the treatment of presbyopia **to initiate mid-2022**
	Potential NDA submissions for presbyopia in 2023 • **Nyxol as a single drop** • **Nyxol with LDP as adjunct therapy**
	Presbyopia drops projected to **be one of the largest $10+B new segments** in Ophthalmology

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Closing Remarks

Mina Sooch, CEO, Founder of Ocuphire Pharma

Ocuphire Management Team

Decades of Biotech and Drug Development Experience

Ocuphire's World-Class Medical Advisory Board

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

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UCLA School of Medicine

Refractive Specialist
Ed Holland, MD
Loyola University Chicago

elCON Medical
Refractive Specialist
Eliot Lazar, MD
Georgetown University

Retinal Specialist
Peter Kaiser, MD
Harvard Medical School

Refractive Specialist
James Katz, MD
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Refractive Specialist
Y. Ralph Chu, MD
Northwestern University

Retinal Specialist
David Lally, MD
Vanderbilt University

Retinal Specialist
David Brown, MD
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Refractive Specialist
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Refractive Specialist
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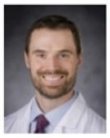
University of Texas



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Optometry
Douglas Devries, OD
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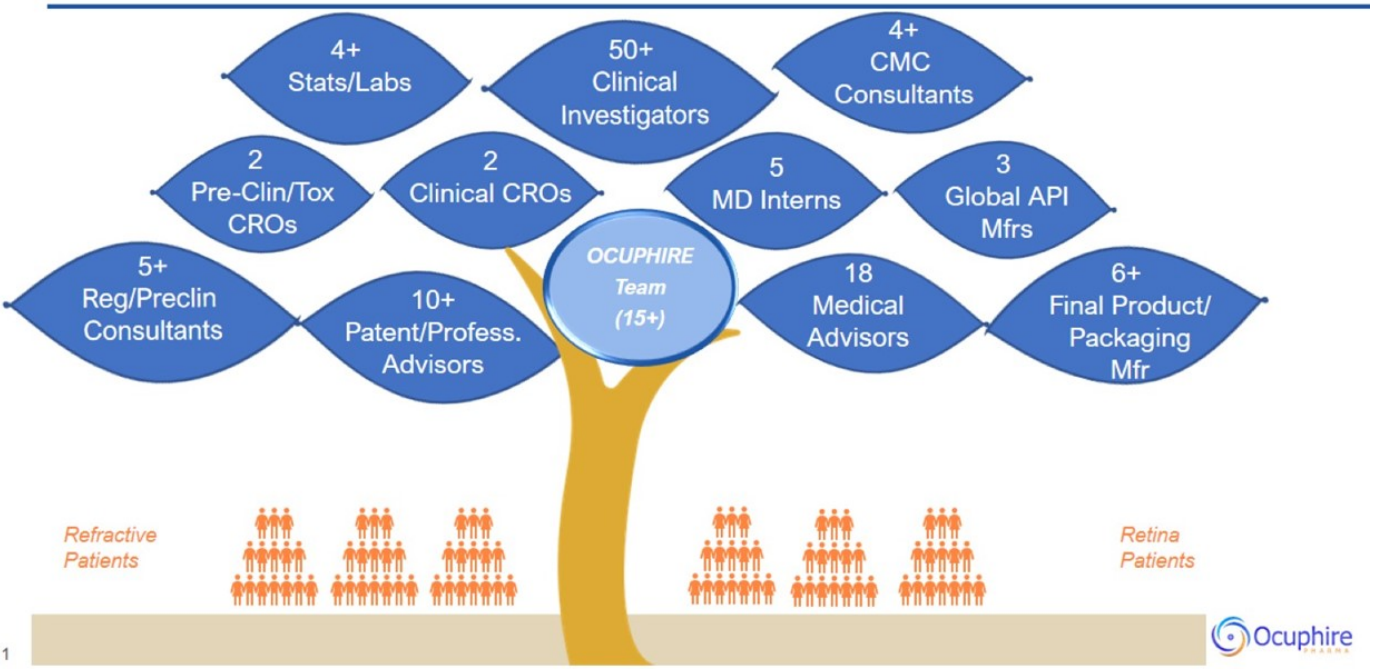
USF MUMA COLLEGE OF BUSINESS
Théa let's open our eyes
Shire
BAUSCH+LOMB

Ocuphire PHARMA

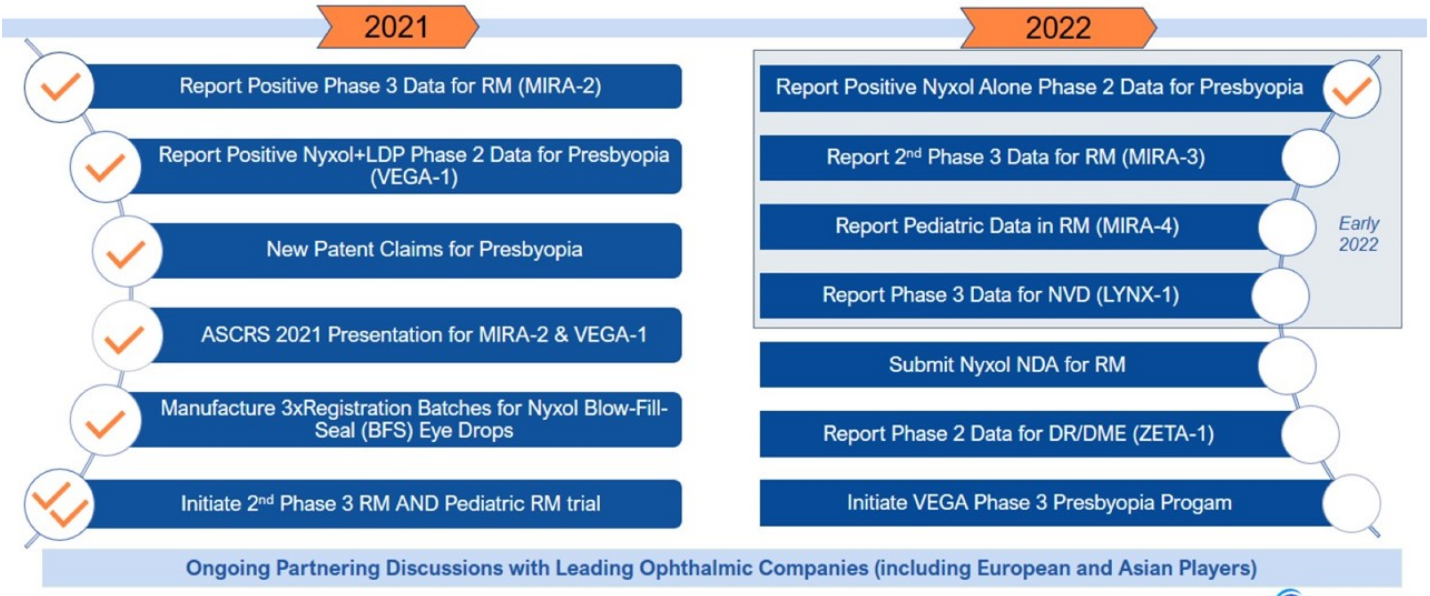
Thanks To Our Network of Partners

A Strong Foundation has been Built to Efficiently Grow and Deliver Our Vision for Patients…



Track Record of Achieving Milestones ➔ Exciting 2022 News Cadence

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



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Overall Highlights from Ocuphire Investor R&D Day

Nyxol®

Nyxol® eye drops, as a platform, is uniquely positioned to address growing markets in refractive disorders

Nyxol, if approved in 2023, would be the only Rx drop for reversing dilations and positively impact the patient experience in an eye care practice

Nyxol represents a novel class with a differentiated MOA and potential as a convenient single evening drop with efficacy at 12 hours (and 18 hours) in the large presbyopia market

Ocuphire plans to pursue both Nyxol as a single agent and with low dose pilocarpine as adjunctive therapy to treat a breadth of presbyopia patient types ➔ *more details to follow*

APX3330

The well-controlled, multi-center Phase 2b ZETA-1 for APX3330 is ~70% enrolled

APX3330 new interim masked safety data support favorable safety profile as a potential oral treatment for diabetics with DR/DME

APX3330 oral with dual MOA targeting VEGF and inflammation may be well-suited to reduce treatment burden and/or improve outcomes adjunctive to traditional anti-VEGF intravitreal injections across retinal diseases

Ocuphire

Ocuphire PHARMA

Restore Vision & Clarity

Thank You for Joining Us

Click Here for the Recorded Event

Ocuphire Pharma Investor R&D Day

January 31, 2022