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): August 12, 2021

Ocuphire Pharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-34079**	**11-3516358**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

37000 Grand River Avenue, Suite 120 Farmington Hills, MI	**48335**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(248) 681-9815**

N/A

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

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

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

Item 7.01 Regulation FD Disclosure.

On August 12, 2021, the Company posted an updated corporate presentation to its website at https://ir.ocuphire.com/presentations, which the Company may use from time to time in communications or conferences. A copy of the corporate presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K (this "Report").

The information in this Report, including Exhibit 99.2 hereto, is furnished pursuant to Item 7.01 and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing. The Company's submission of this Report shall not be deemed an admission as to the materiality of any information required to be disclosed solely to satisfy the requirements of Regulation FD.

This Report and Exhibits 99.1 and 99.2 hereto contain forward-looking statements within the meaning of the federal securities laws. These forward-looking statements are based on current expectations and are not guarantees of future performance. Further, the forward-looking statements are subject to the limitations listed in Exhibits 99.1 and 99.2 and in the other reports of the Company filed with the Securities and Exchange Commission, including that actual events or results may differ materially from those in the forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Press Release, dated August 12, 2021
99.2	Corporate Presentation, dated August 12, 2021

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

OCUPHIRE PHARMA, INC.

By: /s/ Mina Sooch
Mina Sooch
Chief Executive Officer

Date: August 12, 2021

Exhibit 99.1

Ocuphire Announces Financial Results for the Second Quarter 2021 and Provides Corporate Update

Continued Momentum in Nyxol® Programs with Announcement of Positive Top-Line Results from VEGA-1 Phase 2 Trial in Presbyopia

Nyxol plus Low-Dose Pilocarpine Phase 2 Trial Results Show Potential for Best-in-Class Presbyopia Drug Profile in Data Presentations at 2021 ASCRS Meeting

$24M Cash Balance at Quarter-End Provides Runway Into Late 2022 Allowing Planned NDA Submission for Nyxol in Reversal of Mydriasis Indication

FARMINGTON HILLS, Mich., August 12, 2021 - Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing therapies for the treatment of refractive and retinal eye disorders, today announced financial results for the second quarter of 2021 and provided a corporate update.

“The second quarter of 2021 proved to be highly productive for Ocuphire, with continued success in clinical trials, key pivotal data presentations featured at major medical meetings across both Nyxol and APX3330, and additional IP protection granted for our lead drug candidate Nyxol,” said Mina Sooch, MBA, President and CEO of Ocuphire Pharma.

“Following our first quarter announcement of positive MIRA-2 Phase 3 results of Nyxol for the treatment of reversal of mydriasis (RM), we also announced positive top-line results from our VEGA-1 Phase 2 study, which evaluated Nyxol in combination with low-dose pilocarpine (LDP) for the treatment of presbyopia, the gradual loss of your eyes' ability to focus on nearby objects. In our view, RM and presbyopia both represent attractive and large US and global market opportunities, with each indication having a significant unmet medical need with very few if any pharmaceutical treatment options. Following the recent ASCRS meeting, it is also clear that global pharmaceutical and consumer healthcare companies are aggressively pursuing innovative new medicines, further validating the significant commercial potential for the large presbyopia market. Based upon the success of our VEGA-1 trial, we are highly confident that Nyxol in combination with LDP presents a potentially best-in-class therapeutic solution that can address the needs of the presbyopia patient population.”

“With our balance sheet recently strengthened in the second quarter combined with our capital efficient operations, Ocuphire is well positioned to deliver additional late-stage clinical milestones in 2022 for Nyxol and APX3330 while continuing our global business development efforts.”

Key Anticipated Future Milestones

- **Reversal of Mydriasis (RM):** Initiate second Phase 3 (MIRA-3) registration trial and a small pediatric trial (MIRA-4) in the second half of 2021 investigating Nyxol with results expected in early 2022; Planning to file NDA submission with FDA for Nyxol in RM indication in late 2022
- **Presbyopia:** Initiate Phase 3 program (VEGA-2/3) in first half of 2022 investigating Nyxol and LDP
- **Night Vision Disturbances:** Completion of enrollment expected by year-end 2021 and top-line data expected in early 2022 from Phase 3 (LYNX-1) registration trial investigating Nyxol
- **Diabetic Retinopathy and Diabetic Macular Edema:** Completion of enrollment in Phase 2 (ZETA-1) trial investigating APX3330 and top-line data expected in 2022

Second Quarter and Recent Business Highlights

Clinical Development

- In June, the Company announced successful results from the VEGA-1 Phase 2 trial of Nyxol plus low-dose pilocarpine (LDP) for the treatment of presbyopia; the trial met its primary endpoint of 3 lines of near vision improvement and multiple key secondary endpoints such as fast onset of action and durability with statistical significance and a favorable safety profile (including no headaches)
- In April, the Company initiated the ZETA-1 Phase 2 clinical trial to evaluate oral APX3330 in non-proliferative diabetic retinopathy (NPDR) and mild proliferative diabetic retinopathy (mild PDR)

Presentations and Publications

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

- In July at the 2021 American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting, Dr. Jay S. Pepose, Medical Advisor and Board Director, presented two papers featuring the positive results Phase 2 Presbyopia (VEGA-1) and Phase 3 Reversal of Mydriasis (MIRA-2)

- In July, Mina Sooch, CEO, participated in the presbyopia drug therapy panel at the Eyecelerator held on July 22nd and in the Eye on Innovation panel at the Virtual Salon Series held on July 28th

- In late May, Ocuphire hosted a Key Opinion Leader Event on Nyxol as a potential new treatment option for reversing pharmacologically induced mydriasis, highlighting recent positive Phase 3 results from the MIRA-2 Phase 3 registrational study

- In May at the 2021 Association for Research in Vision and Ophthalmology (ARVO) Virtual Annual Meeting, Ocuphire presented data for APX3330 on pre-clinical ocular data and predictive human retina and plasma model data

Corporate

- Announced closing of a $15 million registered direct offering and just over $4 million from ATM, extending cash runway into late 2022

- Appointed Jay S. Pepose, M.D., Ph.D. to the Company's Board of Directors

- Received two new U.S. patent grants covering Nyxol® including Nyxol plus LDP claims for the treatment of presbyopia through 2039

- Entered into a license agreement granting Processa Pharmaceuticals (Nasdaq: PCSA) an exclusive license to develop, manufacture and commercialize globally RX-3117 (Rexahn legacy oncology intellectual property), excluding China, Hong Kong, Macau, Republic of Singapore and Taiwan (already licensed to BioSense Global LLC ("BioSense"))

- Ocuphire (Nasdaq: OCUP) added to the Russell Microcap® Index

Second Quarter and Year to Date 2021 Financial Highlights

As of June 30, 2021, the Company had cash and cash equivalents of approximately $24.2 million. Net cash used in operating activities for the three and six months ended June 30, 2021, was $4.3 million and $10.1 million, respectively.

Collaborations revenue was $0.1 million for the three and six months ended June 30, 2021. Revenue during the periods was derived from the license agreement with BioSense related to certain technology transfers. There was no collaborations revenue recognized during the comparable prior year periods.

General and administrative expenses for the three and six months ended June 30, 2021, were $3.4 million and $5.1 million, respectively, compared to $0.6 million and $0.9 million, respectively, for the three and six months ended June 30, 2020. The increases from the comparable periods in 2020 were attributable to increased costs primarily in administrative employee headcount, stock-based compensation, insurance, legal and settlement costs, and costs associated with operating as a public company subsequent to the reverse merger.

Research and development expenses for the three and six months ended June 30, 2021, were $3.8 million and $7.3 million, respectively, compared to $0.7 million and $0.9 million, respectively, for the three and six months ended June 30, 2020. The increases from the comparable periods in 2020 were primarily attributable to four new clinical trials and manufacturing activities for Nyxol and APX3330 as well as regulatory, preclinical, and other development activities.

There were no acquired in-process research and development expenses in the current six-month period. In the prior year in connection with the sublicense agreement with Apexian for the continued research, development and potential commercialization of APX3330, the Company recorded acquired in-process research and development expenses of $2.1 million during the six-month period ended June 30, 2020.

The total loss from operations for the three and six months ended June 30, 2021 was $7.1 million and $12.3 million, respectively, compared to $1.3 million and $4.0 million for the three and six months ended June 30, 2020, respectively. This included non-cash stock-based compensation expense of $0.5 million and $1.0 million during the three and six months ended June 30, 2021, respectively, and $0.3 million and $0.4 million during the three and six months ended June 30, 2020, respectively.

For further details on Ocuphire's financial results, including results for the three and six month periods ended June 30, 2021 refer to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, to be filed with the Securities and Exchange Commission.

About Ocuphire Pharma

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

Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning Nyxol plus LDP's potential to be a 'best-in-class' presbyopia treatment option, the US and global market and commercial potential of Nyxol alone or in combination with LDP, the expected timing of our future clinical trials in RM, NVD, presbyopia, and DR/DME, and the extent of the Company's cash runway. These forward-looking statements are based upon Ocuphire's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) the success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; (ii) regulatory requirements or developments; (iii) changes to clinical trial designs and regulatory pathways; (iv) changes in capital resource requirements; (v) risks related to the inability of Ocuphire to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vi) legislative, regulatory, political and economic developments, (vii) changes in market opportunities, (viii) the effects of COVID-19 on clinical programs and business operations, (ix) the success and timing of commercialization of any of Ocuphire's product candidates and (x) the maintenance of Ocuphire's intellectual property rights. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by Ocuphire from time to time with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Ocuphire undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Ocuphire Contacts

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LifeSci Advisors
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Ocuphire Pharma, Inc.
Condensed Consolidated Balance Sheets
(in thousands, except share amounts and par value)

	As of	
	Jun 30, 2021	**Dec 31, 2020**
	(unaudited)	
Assets		
Current assets:		
Cash and cash equivalents	$ 24,234	$ 16,399
Collaborations receivable	50	—
Prepaids and other assets	956	1,269
Total current assets	25,240	17,668
Property and equipment, net	12	14
Total assets	$ 25,252	$ 17,682
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,496	$ 1,214
Accrued expenses	1,203	1,971
Total current liabilities	2,699	3,185
Warrant liabilities	—	27,964
Total liabilities	2,699	31,149
Commitments and contingencies		
Stockholders' equity (deficit):		
Preferred stock, par value $0.0001; 10,000,000 shares authorized as of June 30, 2021 and December 31, 2020; no shares issued and outstanding at June 30, 2021 and December 31, 2020.	—	—
Common stock, par value $0.0001; 75,000,000 shares authorized as of June 30, 2021 and December 31, 2020; 16,891,855 and 10,882,495 shares issued and outstanding at June 30, 2021 and December 31, 2020, respectively.	2	1
Additional paid-in-capital	101,376	19,207
Accumulated deficit	(78,825)	(32,675)
Total stockholders' equity (deficit)	22,553	(13,467)
Total liabilities and stockholders' equity	$ 25,252	$ 17,682

Ocuphire Pharma, Inc.
Condensed Consolidated Statements of Comprehensive Loss
(in thousands, except share and per share amounts)
(unaudited)

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2021	2020	2021	2020
Collaborations revenue	$ 100	$ —	$ 100	$ —
Operating expenses:				
General and administrative	3,408	551	5,112	942
Research and development	3,829	711	7,311	929
Acquired in-process research and development	—	—	—	2,126
Total operating expenses	7,237	1,262	12,423	3,997
Loss from operations	(7,137)	(1,262)	(12,323)	(3,997)
Interest expense	—	(689)	—	(1,243)
Fair value change of warrant liability and premium conversion derivatives	—	(919)	(33,829)	(721)
Gain on note extinguishment	—	1,260	—	1,260
Other income	1	6	2	9
Loss before income taxes	(7,136)	(1,604)	(46,150)	(4,692)
Benefit (provision) for income taxes	—	—	—	—
Net loss	(7,136)	(1,604)	(46,150)	(4,692)
Other comprehensive loss, net of tax	—	—	—	—
Comprehensive loss	$ (7,136)	$ (1,604)	$ (46,150)	$ (4,692)
Net loss per share:				
Basic and diluted	$ (0.52)	$ ($0.43)	$ (3.76)	$ (1.29)
Number of shares used in per share calculations:				
Basic and diluted	13,608,596	3,743,907	12,273,541	3,645,948

Exhibit 99.2

Ocuphire PHARMA

Restore Vision & Clarity

Ocuphire Corporate Presentation

Mina Sooch CEO

August 12, 2021

Disclosures and Forward Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning Ocuphire Pharma, Inc.'s ("Ocuphire" or the "Company") product candidates and future milestones, including the potential for Nyxol to be a "best in class" presbyopia drop. These forward-looking statements are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) timing or ability for the company to achieve its targeted milestones; (ii) the success and timing of regulatory submissions and pre-clinical and clinical trials; (iii) regulatory requirements or developments; (iv) changes to clinical trial designs and regulatory pathways; (v) changes in capital resource requirements; (vi) risks related to the inability of the Company to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vii) legislative, regulatory, political and economic developments, and (viii) the effects of COVID-19 on clinical programs and business operations. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by the Company from time to time with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

The Company makes no representation or warranty, express or implied, as to the accuracy or completeness of the information contained in or incorporated by reference into this presentation. Nothing contained in or incorporated by reference into this presentation is, or shall be relied upon as, a promise or representation by the Company as to the past or future. The Company assumes no responsibility for the accuracy or completeness of any such information. This presentation may not be reproduced or provided to any other person (other than your advisor) without our prior written consent. By accepting delivery of this presentation, you agree to the foregoing and agree to return this presentation and any documents related thereto and any copies thereof to us or to destroy the same if you do not make an investment in any securities. The information contain within this presentation shall not, except as hereinafter provided, without the prior written consent of the Company, be disclosed by you or your representatives in any manner whatsoever, in whole or in part, and shall not be used by you or your representatives other than for the purpose of evaluating the transaction described herein. By accepting delivery of this presentation you further acknowledge and agree aware of the restrictions imposed by the United States securities laws on the purchase or sale of securities by any person who has received material, nonpublic information from the issuer of the securities or any affiliate thereof and on the communication of such information to any other person when it is reasonably foreseeable that such other person is likely to purchase or sell such securities in reliance on such information for so long as the information remains material and non-public. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market shares and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

Ocuphire Opportunity

A Late-Stage Clinical Ophthalmic Biotech (Nasdaq Symbol: OCUP)

Late Clinical Stage Company Targeting Large, Unmet Ophthalmic Markets	• Nyxol eye drops target multiple chronic and acute front of the eye indications addressing large markets: Dim Light / Night Vision Disturbances (NVD), Reversal of Mydriasis (RM), & Presbyopia (P) • APX3330 tablets target chronic back of the eye indications: Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME), a leading cause of blindness in diabetic patients
Significant Clinical Data and Regulatory Precedents	• Nyxol and APX3330 achieved promising clinical data over multiple Phase 1, 2, and 3 trials ✓ Nyxol with > 330 patients treated across 9 trials ✓ APX3330 with > 340 patients treated across 11 trials • FDA End of Phase 2 meeting guidance for Nyxol (all indications) in May 2020
Significant IP Portfolio and Small Molecule CMC Advantages	• US and global issued patents thru 2034 for both assets; new 2039 Nyxol patent issued for presbyopia • Stable, small-molecule drugs ✓ Nyxol = single-use, preservative-free eye drop ✓ APX3330 = oral pill
Multiple Near-Term Data Catalysts with Capital Efficient Plan	• **Initiated 4 late-stage trials (2 Phase 3, 2 Phase 2) with readouts expected in 2021-2022** ✓ **Reported positive P3 data in RM in 1Q21 with Nyxol NDA submission targeted late 2022** ✓ **Reported positive P2 data in Presbyopia in 2Q21 with plans to advance to P3 in 2022** • Recent $15M offering combined with cash on hand sufficient to run operations into late 2022 • Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and Encode Ideas

Ocuphire PHARMA

Ocuphire Management Team

Decades of Biotech and Drug Development Experience

Mina Sooch, MBA
President & CEO and Founder

HARVARD BUSINESS SCHOOL
Gemphire Therapeutics
Apjohn Ventures
MONITOR
ProNAi

Charlie Hoffmann, MBA
VP Corporate Development and Operations

Tuck School of Business at Dartmouth
Ocularis Pharma
Prudential
SynDevRx
Goldman Sachs

Amy Rabourn, CPA
VP Finance

MICHIGAN ROSS
Gemphire Therapeutics
Pfizer
NeuroBo PHARMACEUTICALS
pwc

Ronil Patel, MS
Senior Director BD and Market Strategy

FLORIDA TECH
BETALIO
RevitaLid
POINTGUARD
OCULOS Integrated Insight

Mitch Brigell, PhD
Head Clinical Development and Strategy

KANSAS STATE UNIVERSITY
aerpio
Pfizer
NOVARTIS

Daniela Oniciu, PhD
Head CMC and Global Clinical Supply

UF UNIVERSITY of FLORIDA
Gemphire Therapeutics
ESPERION
Cerenis THERAPEUTICS
Pfizer

Drey Coleman
Head Clinical Operations

UCF
SIRION Therapeutics
OCULOS Integrated Insight

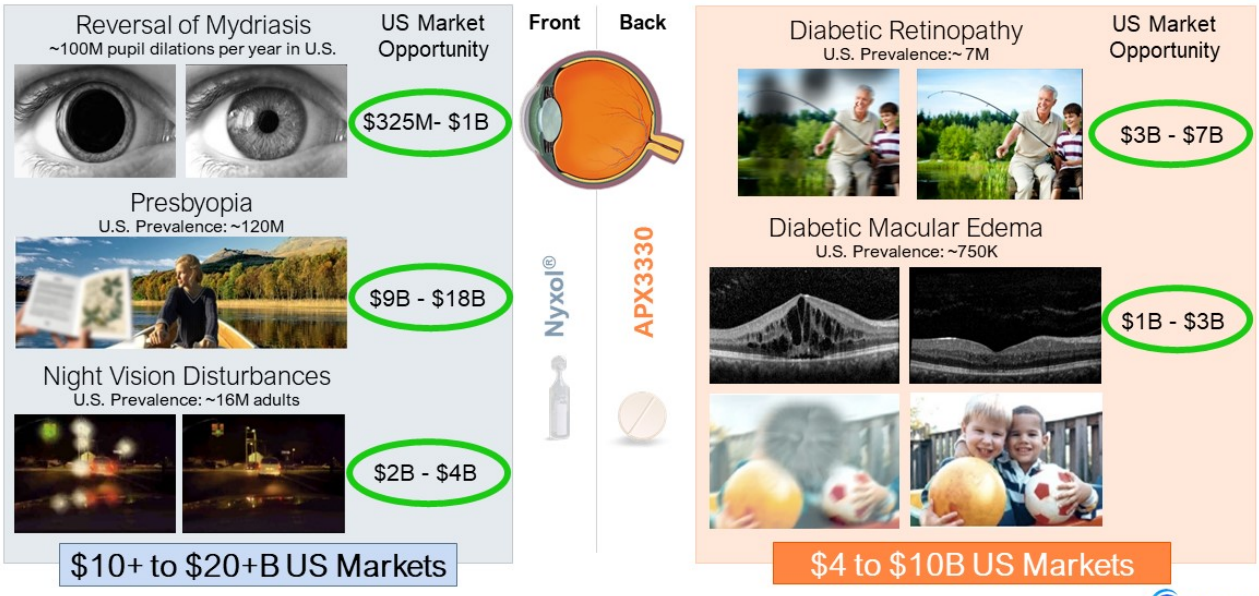
Chris Ernst
Quality Assurance Lead

NORTHERN KENTUCKY UNIVERSITY
aerpio
Akebia THERAPEUTICS
MEDPACE

Ocuphire PHARMA

Large Unmet Opportunities for the Aging Eye

Developing Drugs to Treat Front & Back of the Eye Diseases



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

Ocuphire PHARMA

Ocuphire Pipeline & Upcoming Milestones

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

	Product Candidate	Indication	Development Stage				Anticipated Milestones
			Pre-clinical	Phase 1	Phase 2	Phase 3	
Ocuphire-Focused Development	0.75% Nyxol® Eye Drop	Reversal of Mydriasis (RM)				Positive Data Readout	Initiated Phase 3 MIRA-2 trial 4Q20; Topline data reported in 1Q21 (n=185) Initiate Phase 3 MIRA-3 trial 2H21; Data expected in early 2022 (n=330) Initiate Pediatric trial 2H21; Data expected in early 2022 (n=20)
	0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops	Presbyopia (P)			Positive Data Readout		Initiated Phase 2 VEGA-1 trial 1Q21; Topline data reported in 2Q21 (n=150) Initiate Phase 3 program in 1H22
	0.75% Nyxol® Eye Drop	Dim Light or Night Vision Disturbances (NVD)				Recruiting	Initiated Phase 3 LYNX-1 trial 4Q20; Data expected in early 2022 (n=160)
	APX3330 Oral Pill	Diabetic Retinopathy (DR)/ Macular Edema (DME)			Recruiting		Initiated Phase 2 ZETA-1 trial Apr21; Data expected in 2022 (n=100)
Partnering-Focused Development	APX2009 Intravitreal	DME, Wet Age-Related Macular Degeneration (wAMD)					Next steps: IND enabling studies (with partner funding)

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

Extensive Development on Both Drug Candidates

Well-Controlled Phase 1, 2, and 3 Clinical Programs with MIRA-2 Data Leading the NDA Path

Nyxol

9
Phase 1, Phase 2, and Phase 3 Trials

> 330
Subjects Dosed

Exposure in Humans
28
Days

Patents to
2034+

Studied in multiple ocular refractive indications

505(b)(2) Development Pathway

APX3330

11
Phase 1 & Phase 2 Trials

>340
Subjects Dosed

Exposure in Humans
365
Days

Patents to
2034+

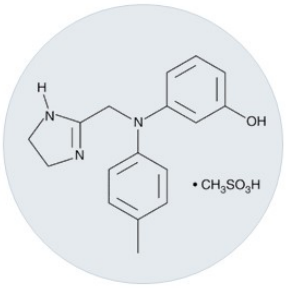
Studied in inflammation/hepatitis & cancer patients

NCE Development Pathway

Ocuphire PHARMA

Nyxol®

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



Phentolamine Mesylate

Nyxol History & MOA

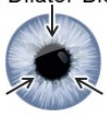
Rationale for Differentiated Product Profile & 505(b)(2) Path

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

Phentolamine Mesylate

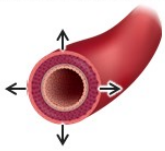
Reduces Pupil Size

α1: Iris Dilator Blockade



Dilates Blood Vessels (Vasodilation)

α1: Smooth Muscle Blockade



Ocuphire Pharma

Nyxol Product Candidate Profile

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

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

Efficacy Data

Improving Vision

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

Safety Data

No Systemic Effects
No Changes in Blood Pressure
No Changes in Heart Rate

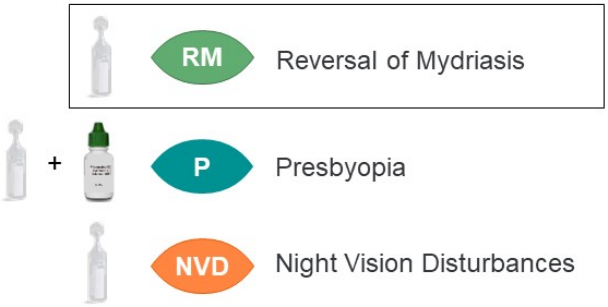
Tolerated Topical Effects
Mild / Transient / Reversible Eye Redness

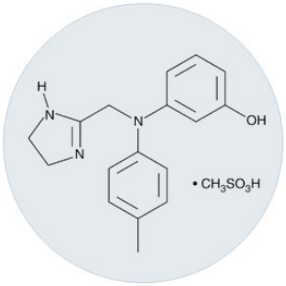
IOP Unchanged or Decreased
↓ Intraocular Pressure (IOP) at Normal Baseline

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

Ocuphire PHARMA

Nyxol®





Phentolamine Mesylate

RM

Reversal of Mydriasis (RM) – Acute Treatment

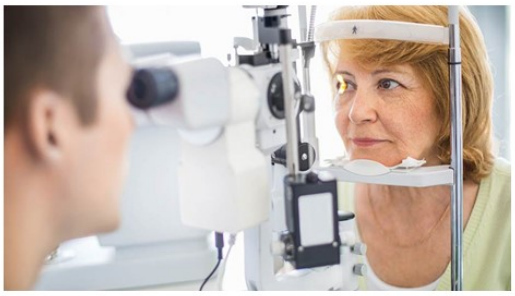
Annual Exams and Specialty Visits Involve Dilation to Monitor Eye Health

The Problem

- At many annual eye exams and specialty visits, pupils are pharmacologically dilated, impairing vision for 6-24 hours
- Dilated eyes:
  - heightened sensitivity to light
  - inability to focus
  - reading, working, and driving are difficult
  - halos and glare

> *"I have to stay indoors. They say it only lasts a few hours, but it lasts all day, and it is very annoying."*
>
> *RM Patient, Aged 51*

No Current Commercially Available Treatments



~100M eye exams / year in US

Source: GlobalData Market Research Report, 2020

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RM

Reversal of Mydriasis (RM) – Acute Treatment

Single Use Indication Leveraging a Precedent Approval Pathway

Nyxol's Potential Differentiated Solution

- **Regulatory Precedent** with Rev-Eyes (an alpha 1 blocker), approved by the FDA in 1990 but shortly thereafter discontinued (not for safety or efficacy reasons)
- **Clinical Effect** to potentially reduce pupil size and counteract the effect of mydriatic drugs (alpha agonists and cholinergic blockers) used to dilate the pupil
- **Convenient and Stable** eye drop given at the office that may allow vision to return to normal sooner
- **Tolerable** with a minimal side effect profile (unlike cholinergic agonists such as pilocarpine)

Before

After

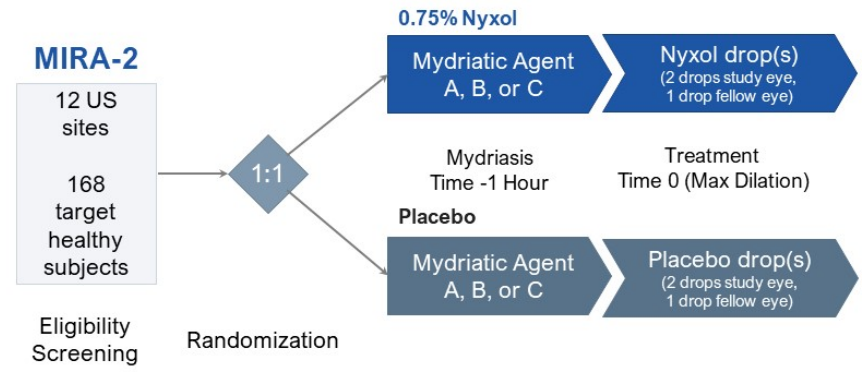
Seeking Treatment Findings	
Patients likely to request reversal of dilation[1]	80%
Eye care providers likely to use reversal drops[2]	70%

Source: 1.GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (4-7 on a scale of 1-7)
2.GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (6-10 on a scale of 0-10)

Ocuphire PHARMA

RM MIRA-2 Phase 3 Registration Design

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



Started and Completed Enrollment in 4Q20 – 185 Subjects

Topline Results Expected in 1Q21 → Reported in March 2021

Endpoints

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

Secondary:

- % of subjects returning to baseline at 30min, 1h, 2h, 3h, 4h, 6h, 24h (overall, by mydriatic agent, by iris color)
- Mean change in pupil diameter from mydriatic max at all timepoints (overall, by mydriatic agent, by iris color)
- Accommodation (Tropicamide/Paremyd)
- Safety and tolerability (redness)

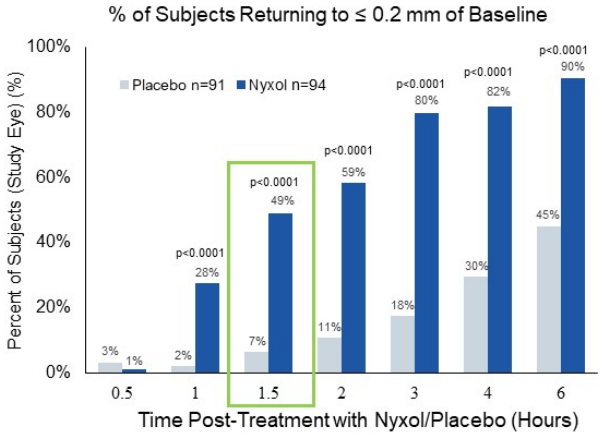
Mydriatic Agents 3:1:1 – 2.5% phenylephrine (alpha 1 agonist), 1% tropicamide (cholinergic blocker), Paremyd® (combination)

Primary Endpoint: % of Subjects Study Eye Returning to Baseline PD at 90 Min

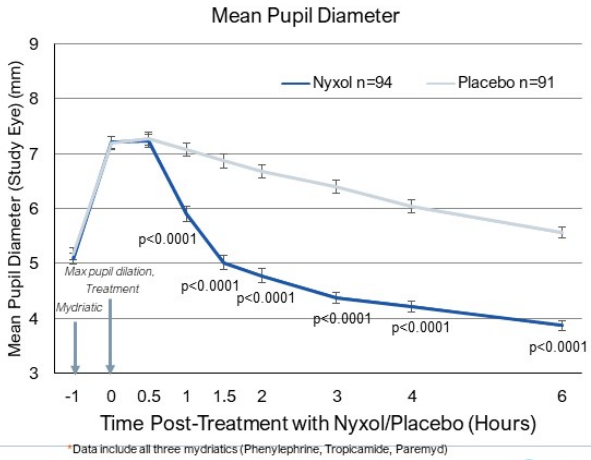
Nyxol Met the Primary & Secondary Endpoints at 90 Min; Additionally at 60 Min & All Subsequent Timepoints

MIRA-2 Phase 3 Trial

Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD)



Nyxol Reduced PD Faster Across All Mydriatic Agents*



*Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

15 Source: MIRA-2 Trial, mITT Population (same as Safety Population), *Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

Secondary Endpoint: Mean Pupil Diameter Over Time by Mydriatic Agent

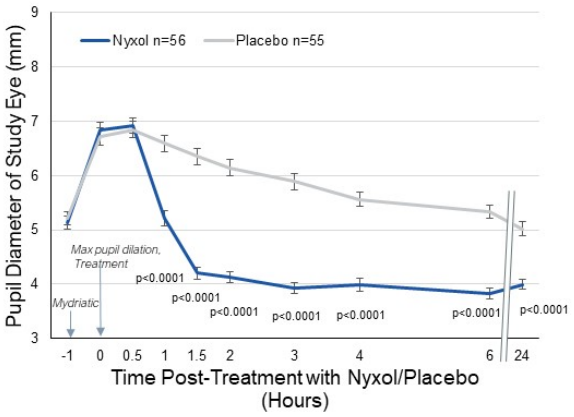
Nyxol Reduced Pupil Diameter With All Mydriatic Agents; More Rapidly with Phenylephrine as Expected

MIRA-2 Phase 3 Trial

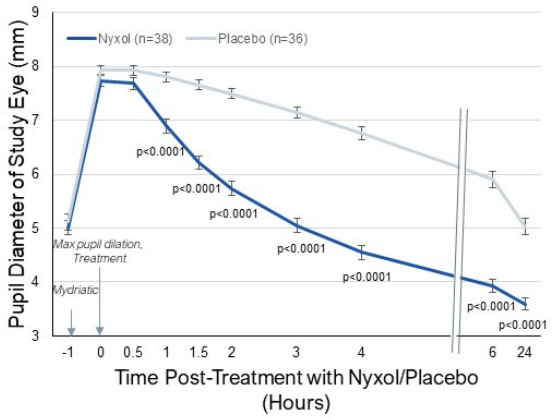
Nyxol More Rapidly Reduced PD in Subjects Across All 3 Mydriatic Agents

Mean Pupil Diameter

Phenylephrine



Tropicamide and Paremyd



Source: mITT Population, MIRA-2 Trial, Standard Error bars are shown.

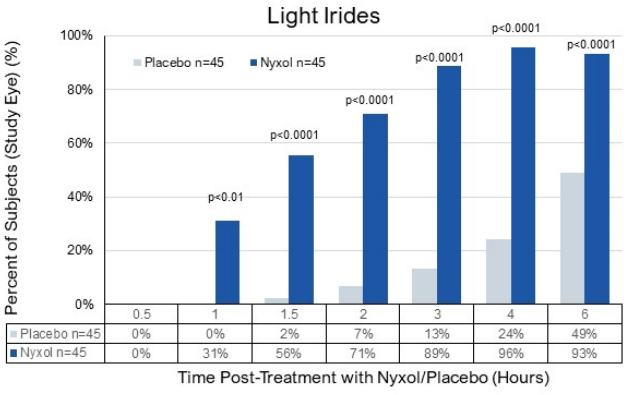
Secondary Endpoint: % of Subjects Returning to Baseline PD by Iris Color

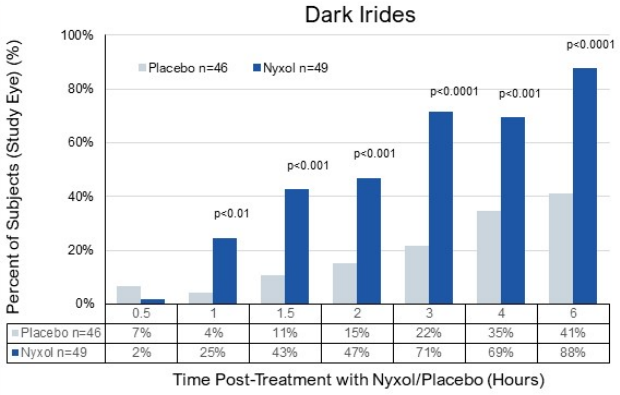
Evidence of Efficacy in Subjects with Either Light or Dark Irides, with a More Vigorous Response in Light Irides

MIRA-2 Phase 3 Trial

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

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



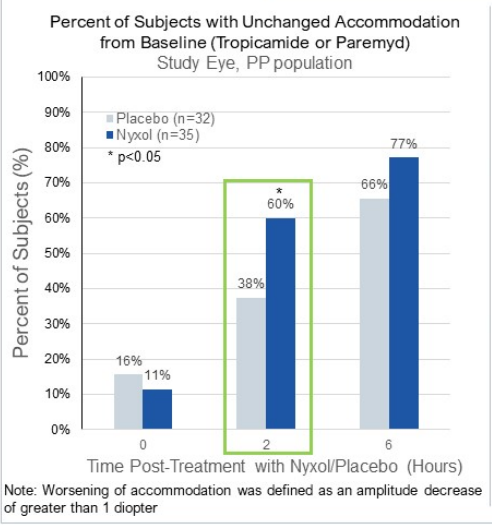


Source: MIRA-2 Trial mITT Population,, Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

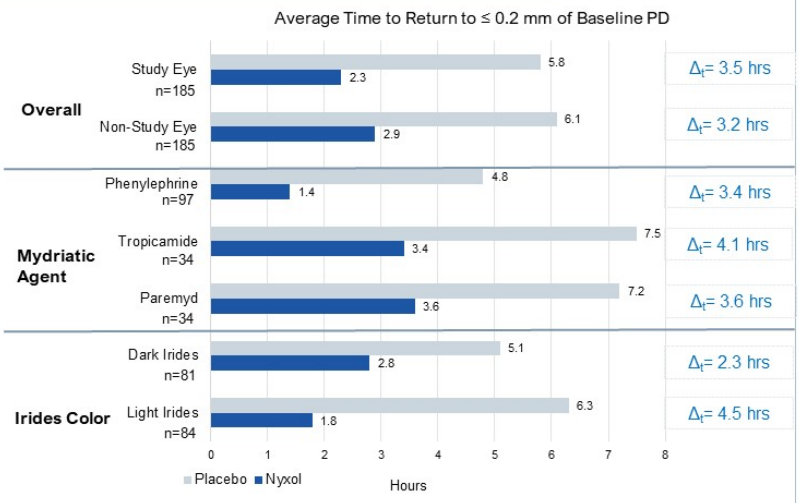
Secondary Endpoint: Accommodation And Time Savings

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

MIRA-2 Phase 3 Trial



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



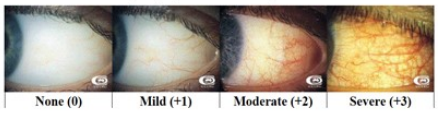
Source: MIRA-2 CSR table #14.2.3.2.1. PP population is the per protocol population.

RM

Summary of Positive MIRA-2 Phase 3 Results for Nyxol Eye Drops

Sustained Efficacy with a Favorable Safety Profile in Reversing Mydriasis with Nyxol

- **Met primary endpoint at 90 minutes with high statistical significance with 2 drops of Nyxol**
- **Met all key secondary endpoints with high statistical significance**
  - Efficacy for all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
  - Efficacy in both light and dark iris colors
  - Efficacy with only one Nyxol drop in non-study eye
- **Favorable safety profile**
  - No serious AEs, no drop-outs from AEs, no systemic AEs were observed in ≥ 5% of subjects
  - Mild, transient conjunctival hyperemia reported in the first hour and declined steadily thereafter. Baseline mean of 0.7, the mean hyperemia score increased by approximately 1.0 unit on CCLRU scale



Path to Registration

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

Submit NDA by Late 2022

Proposed Indication

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

mITT Population, MIRA-2 Trial

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RM

Reversal of Mydriasis (RM) Market Opportunity

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

100M+
General and specialty eye exams per year[1]

> 65% Patients
Report moderate to severe negative impact of dilated exams[1]

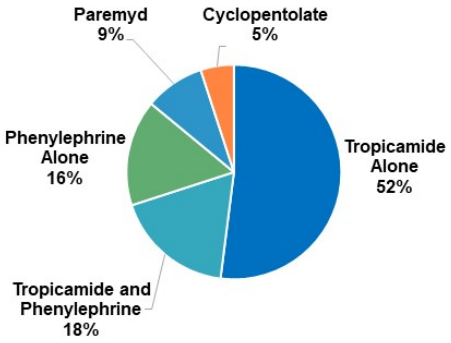
$5 - $20
Price range surveyed for cash pay per patient with room for physician markup[1]

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

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

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

Physician's Use of Mydriatic Agents[1]

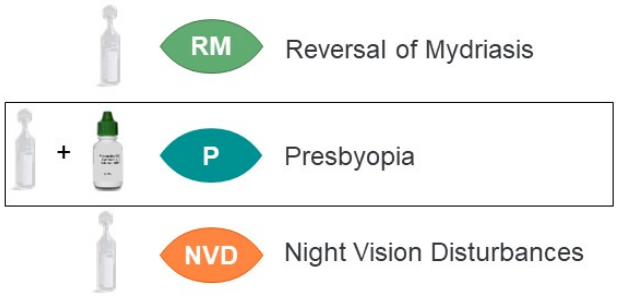


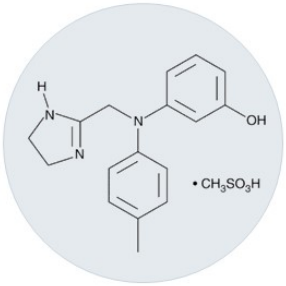
Use of phenylephrine, tropicamide, Paremyd®, or combinations of such comprise nearly 95% of dilating eye drops used by eyecare professionals.[1]

1. GlobalData market research report
2. Vision Care Market Grows 2.4 Percent in 12-Months Ending September 2019. Vision Monday, January 20, 2020.

Ocuphire PHARMA

Nyxol®





Phentolamine Mesylate

Presbyopia – Chronic Opportunity

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

The Problem

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

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

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

No Currently Approved Drug Therapies

~$9-$18B Market Opportunity

Market Assumptions:

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

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Source: GlobalData Market Research Report, 2020

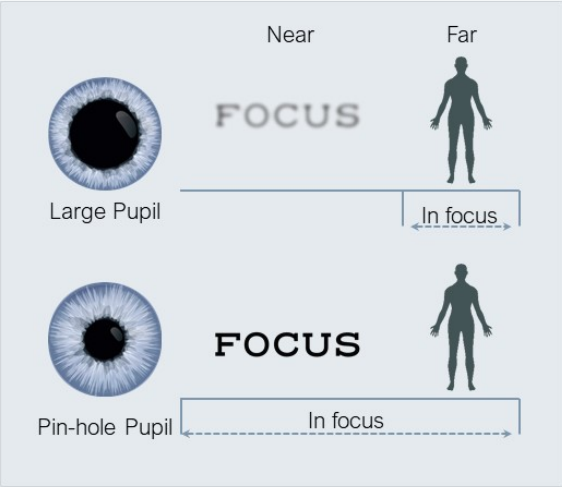
Presbyopia – Chronic Opportunity

Pupil Modulation Eye Drops May Replace Reading Glasses

Nyxol's Potential Differentiated Solution

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

> *"This would just become part of my daily routine for my eyes to be able to see things up close. How convenient is that?"*
>
> *Presbyopic Patient, age 49*

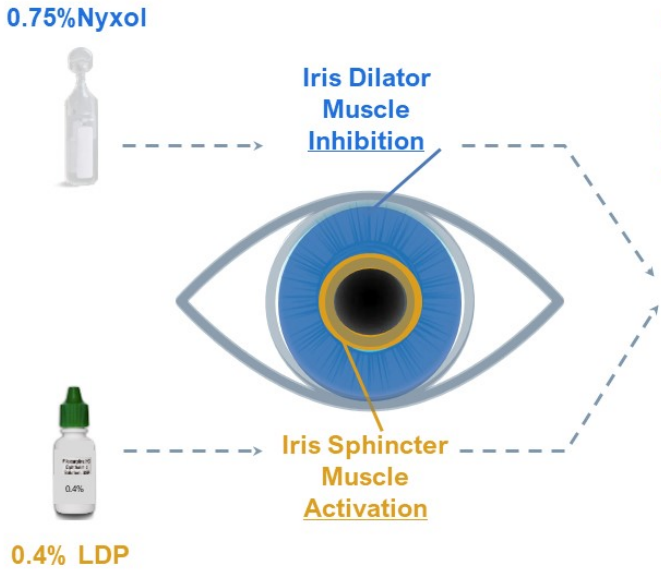


Retinaeyedoctor.com, GlobalData Market Research Report, 2020

Ocuphire Pharma

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

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



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

1.5 to 2.5 mm PD reduction moves toward the 'pin-hole' (2.0 to 2.5 mm, up to 3 mm)

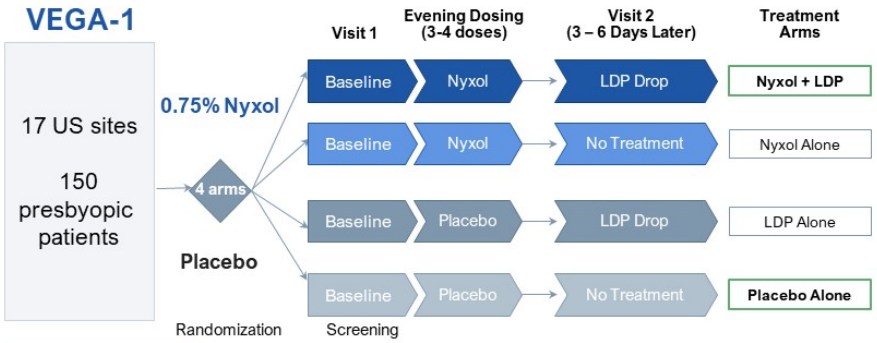
- Pilocarpine (cholinergic agonist) approved decades ago
- Known MOA on sphincter muscle with potent miotic effects at approved doses (1%, 2%, 4%)
- Chronic daily dosing of LDP, a more moderate miotic
- Low concentration avoids known tolerability issues:
  - headache and browache
  - redness
  - accommodative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

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

Ocuphire PHARMA

Presbyopia VEGA-1 Phase 2 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 and mesopic lighting comparing Nyxol + LDP vs placebo, Nyxol alone, and LDP alone
- No loss of distance vision
- Pupil diameter at time points
- Safety and tolerability (redness)

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

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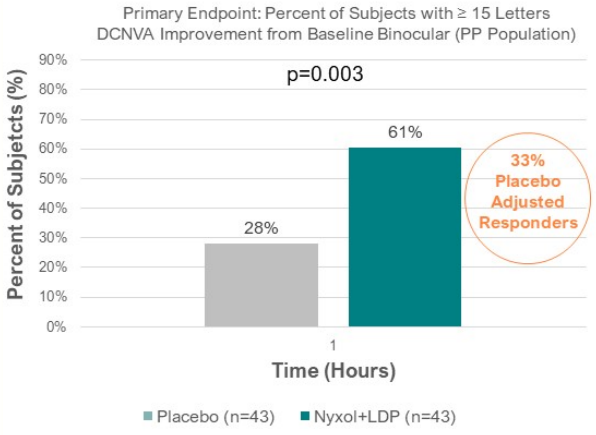
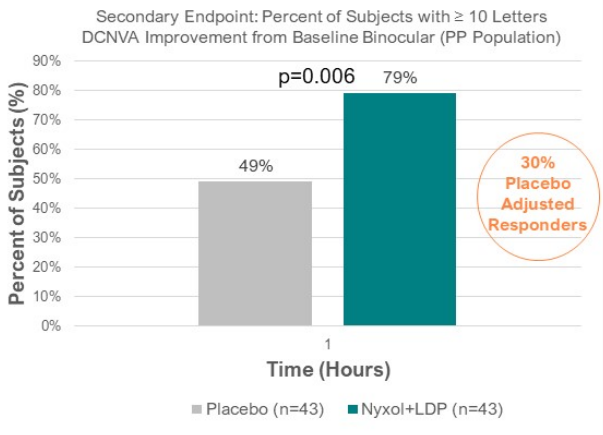
Primary Endpoint: % of Subjects ≥ 15 Letter Gain in Photopic DCNVA at 1 Hour

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

VEGA-1 Phase 2 Trial





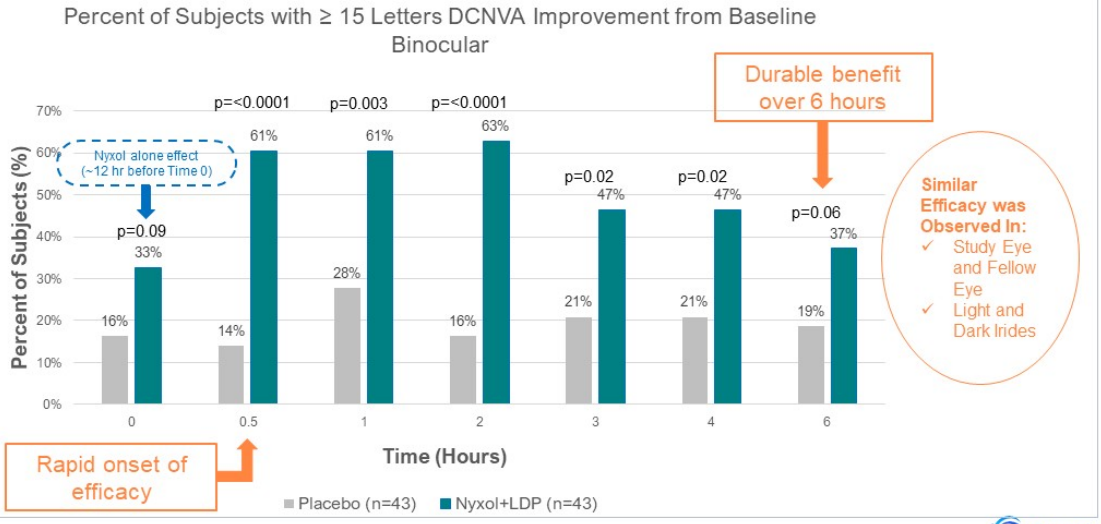
Note: PP population differs from mITT by only one subject; results were essentially identical.

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

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

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

VEGA-1 Phase 2 Trial



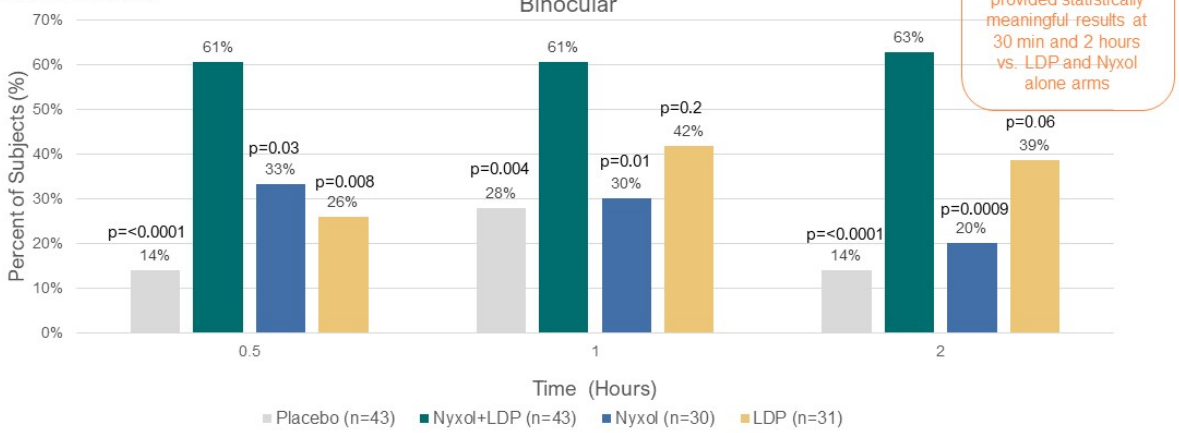
Source: VEGA-1 TLR Table 14.2.1.2 Percent of Subjects with Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters is 3 lines.

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

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

VEGA-1 Phase 2 Trial

Statistics Compared to Nyxol+LDP arm
Powered for comparison to placebo whereas comparison to component arms were designed to inform the Phase 3 sample size



Even with a small sample size, combination arm provided statistically meaningful results at 30 min and 2 hours vs. LDP and Nyxol alone arms

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)

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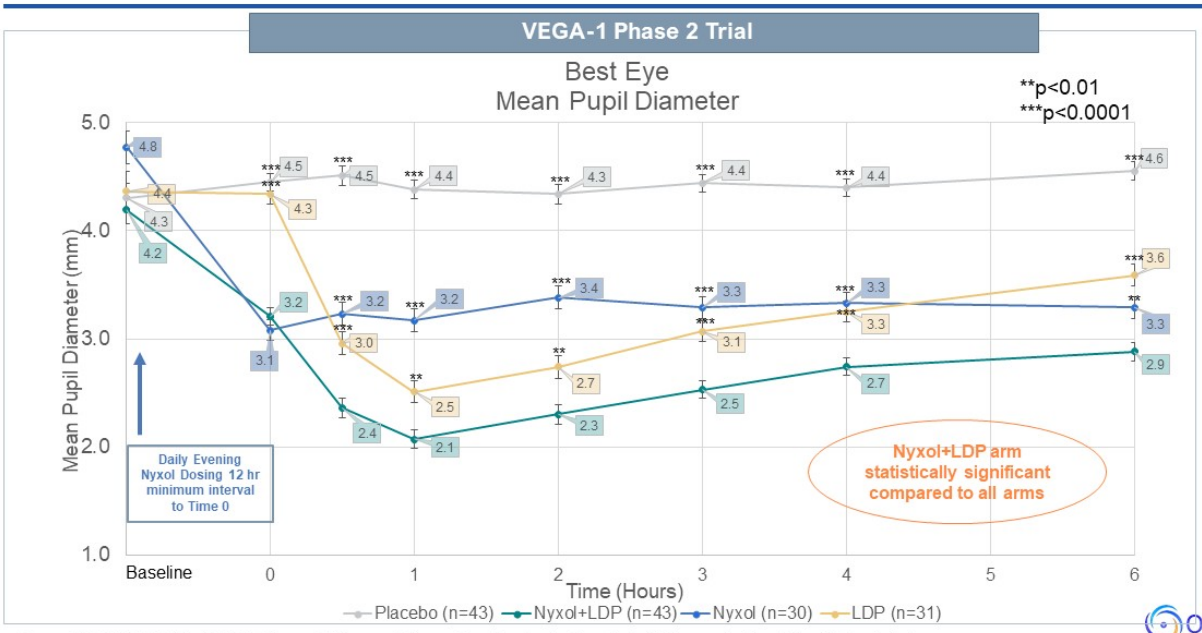
Secondary Endpoint: Mean Pupil Diameter Over Time

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



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

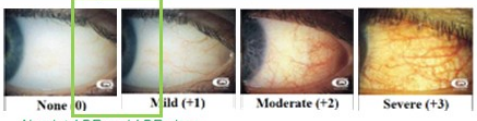
Secondary Endpoint: Safety Findings

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

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

- No deaths, no serious AEs
- Almost all AEs were mild
- **0% headaches or brow aches reported for Nyxol+LDP arm**
- **≤ 5% mild, transient conjunctival hyperemia AEs in Nyxol+LDP arm**
- **Distance vision: 100% Nyxol + LDP arm had ≤ 5 letter distance loss in photopic lighting (95% in mesopic)**
- No change in IOP

Conjunctival Hyperemia CCLRU Scale for Reference



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

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)

Potential 'Best in Class' Presbyopia Drop

Nyxol+LDP Combination Outperforms Market Leader in Efficacy, Safety, Durability and Onset

Product Attributes*	Nyxol+LDP compared to market leader
Efficacy (all time-points)	✓+
Safety: Maintain Distance Vision (especially at night)	✓+
Safety: Tolerability (no headaches)	✓+
Durability (at least 6 hours)	✓+
Fast Onset (within 30 mins)	✓+
Convenience (daily drops)	✓
Tunable Pupil Modulation	✓+

Gemini I Phase 3: AGN-190584 Provides Rapid Improvement of Distance Corrected Near Vision That Is Maintained in Participants with Presbyopia- ASCRS 2021 Presentation

Gemini I Phase 3: Safety and Efficacy of AGN-190584 in Participants with Presbyopia- ASCRS Abstract# 74336

Phase 2 Clinical Trial To Evaluate The Efficacy of Phentolamine Ophthalmic Solution And Low-Dose Pilocarpine For The Treatment of Presbyopia- ASCRS Abstract# 76645

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

✓+- Indicates better compared to market leader

✓- Indicates comparable to market leader

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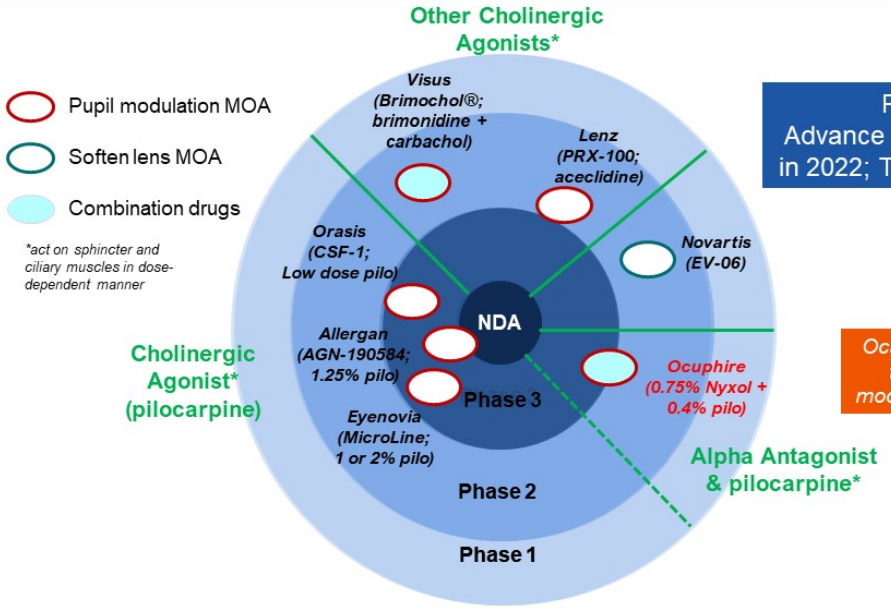
Presbyopia Eye Drops Competitive Landscape

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



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

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

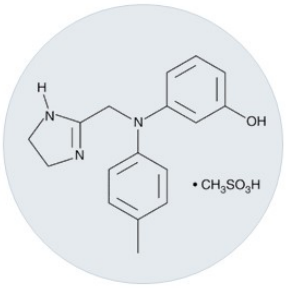
Corporate Websites, Grzybowski, A, Markeviciute A, Zemaitiene R. A Review of Pharmacological Presbyopia Treatment. 2020

Nyxol®

RM Reversal of Mydriasis

P Presbyopia

NVD Night Vision Disturbances



Phentolamine Mesylate

NVD

Night Vision Disturbances (NVD) – Chronic Opportunity

Imperfections in the Eye Affect Night Vision in Millions

The Problem

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

> *"I'm no longer comfortable driving at night, especially with my son in the car. I have a hard time playing beach volleyball in the evenings due to the bright lights at the courts."*
>
> *Post-LASIK, aged 42*

No Currently Approved Therapies

Moderate-to-Severe NVDs	US Patients
Night Myopia	10.8M
Cortical Cataracts	4.1M
Post-LASIK	500k
Post-IOL Implant	300k
Total	**~16M**

Source: GlobalData Market Research Report, 2020

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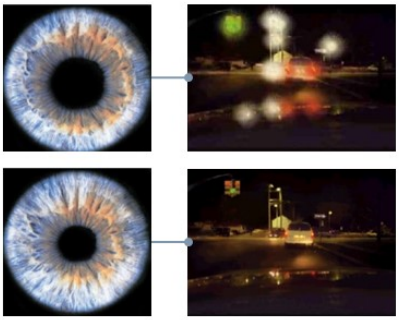
NVD

Night Vision Disturbances (NVD) – Chronic Opportunity

Peripheral Optical Imperfections Allowing Pupil Modulation as a Solution

Nyxol's Potential Differentiated Solution

- **Moderate Decrease in Pupil Size** for scattered light gets blocked by the iris
- **Clinical Effect** to potentially improve low contrast night vision as seen in trials
- **Tolerable** with a minimal side effect profile
- **Convenient and Durable** with chronic once-daily evening dose



Before

After

> *"Once there is a drug and a category, that's when they start looking for the disease."*
>
> *Physician KOL*

Seeking Treatment Findings	
Patients willing to try a new eye drop treatment	67%
Patients avoiding driving at night	25%

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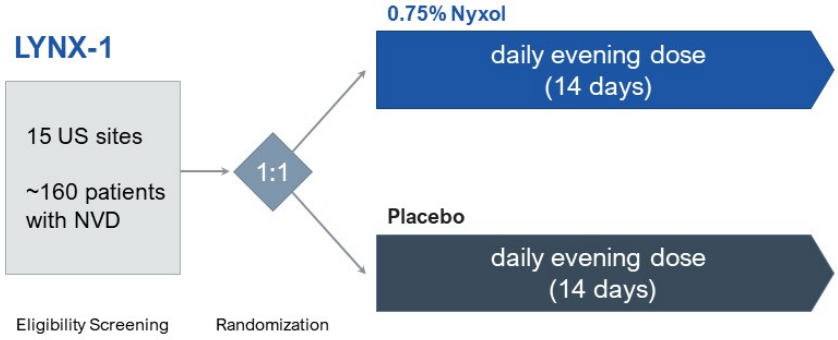
NVD LYNX-1 Phase 3 Registration Design

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



Phase 3 Initiated in Late 4Q20

Top Line Expected Early 2022

Endpoints

Primary: % of subjects with ≥ 3 lines of improvement in mesopic low contrast best-corrected distance visual acuity (Day 8)

Secondary (Days 8 & 15):

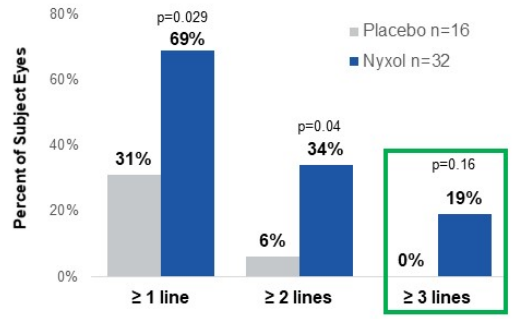
- Pupil diameter
- Visual acuity measures (distance and near)
- Safety and tolerability (redness)

Nyxol Demonstrated Clinical Effect in NVD

Key Endpoints Observed in Multiple Phase 2 Trials

NYX-SNV Phase 2 Trial

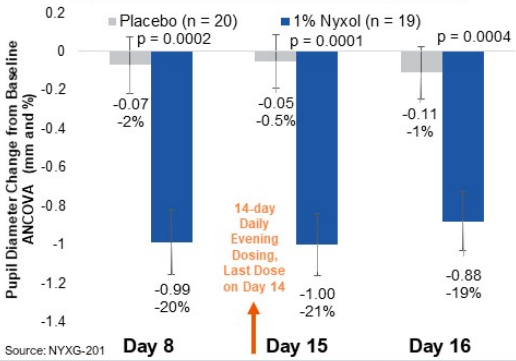
Improved Low Contrast Distance Visual Acuity*



Source NYX-SNV

ORION-1 Phase 2 Trial

Durable > 24-hour Pupil Modulation Effect

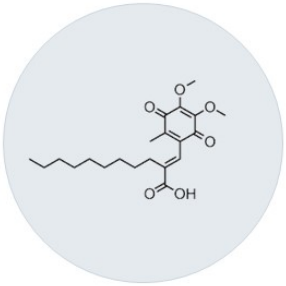


Source: NYXG-201

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

APX3330

- **DR** Diabetic Retinopathy
- **DME** Diabetic Macular Edema
- **wAMD** Wet Age-Related Macular Degeneration



APX3330

Diabetic Retinopathy & Macular Edema

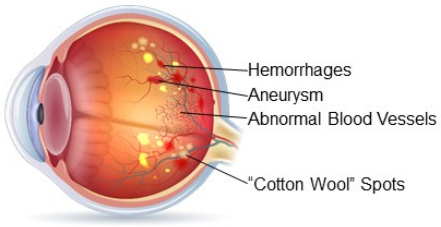
Non-Injectable Alternative Therapies are Needed for Earlier Stages of Disease

The Problem

- Diabetic retinopathy (DR) and diabetic macular edema (DME) are a leading cause of vision loss worldwide, especially in working age adults in developed countries
- Diabetes damages small blood vessels within the eye causing leakage, oxygen starvation, and abnormal vessel growth, which can obstruct vision
- DR patients are not commonly treated with approved injectable anti-VEGF drugs given earlier stage of retinal disease and many are asymptomatic
- DR progresses in steps and may result in vision loss if left untreated
- Current treatment for DME: 25% non-responders and 50% partial responders to anti-VEGF drugs

Injectable Anti-VEGF Approved Therapies Not Commonly Used for NPDR

Diabetic Eye



Diabetic Eye Opportunity	
DR	~7.7M Patients
DME	~750K Patients

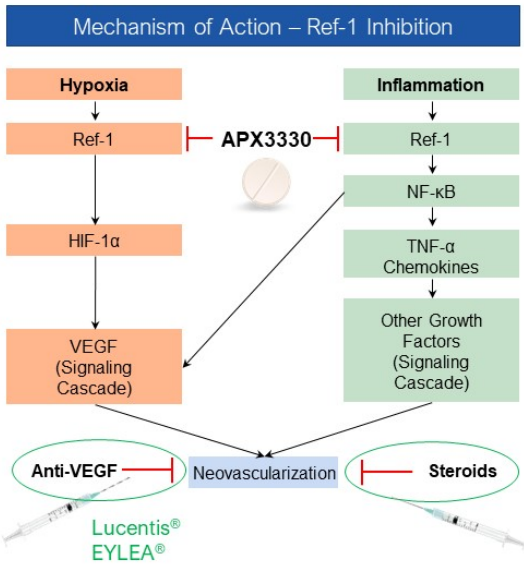
Sources: Global Market Insights Report 2019-2025, Market Watch 2019 Report, Gene.com Retinal Diseases Fact Sheet

DR
DME

APX3330 History and Ref-1 Inhibition Mechanism

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

- APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of Ref-1
- Ref-1 (reduction-oxidation effector factor-1) is a novel target discovered and characterized by Dr. Mark R. Kelley at Indiana University School of Medicine
- 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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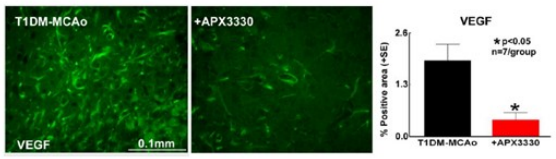
DR
DME

APX3330 Down-Regulates VEGF Protein and Anti-Inflammatory Cytokines

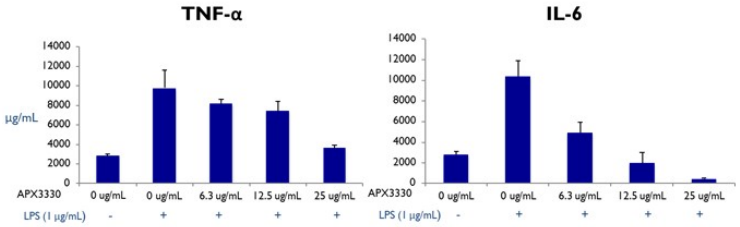
In Vivo and In Vitro Evidence of APX Dual Pathway Mechanism of Action

APX3330 Reduces VEGF Protein in the Brain of Preclinical Models



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

APX3330 Reduces Pro-inflammatory Cytokines in Murine Cell Lines Involved in Macular Degeneration



- In vitro APX3330 suppresses pro-inflammatory cytokines in LPS stimulated murine macrophage cell lines **known to be involved in macular degeneration:**
  - TNF-α is a potent cytokine that enhances secretion of VEGF-A and VEGF-B by human choroidal fibroblast cells. J Cell Physiol. 2011
  - Genetic ablation of IL-6 led to significant suppression of AMD (murine CNV model). Am J Pathol. 2007

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

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DR
DME

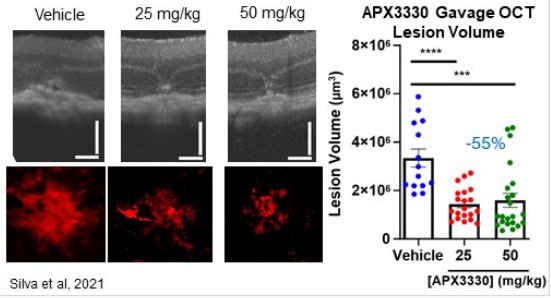
APX3330 Generally Well Tolerated with Clinical Signals

Observations from Pre-Clinical Studies and 11 Clinical Trials of APX3330

L-CNV Mouse Retina Model

APX3330 Reduces Neovascularization Similar to Eylea in Preclinical Models

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

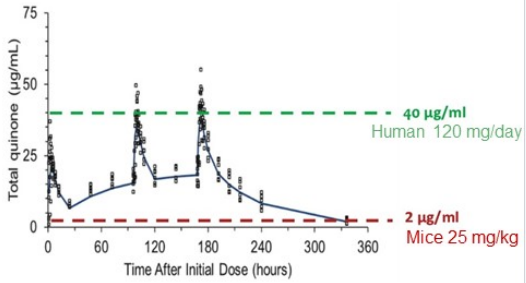


Silva et al, 2021

Phase 1 Clinical Trials

Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels

Human Pharmacokinetics of APX3330 at 120 mg/day



Source: Unpublished Data

300 mg BID (600 mg/day total) dosing strategy for APX3330 is predicted to reach retinal AUC concentrations of 15.4 µg/mL; Significant APX3330 reaches human retina, folds greater than mice who were given APX3330 25 mg/kg (actual 2hr conc. in retina 0.1 µg/mL)[1]

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

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APX3330 Product Candidate Profile

DR
DME

First-in-Class Ref-1 Inhibitor Phase 2 Ready for Retina Diabetic Indications

APX3330: 600mg Oral Dose

Expected Efficacy Data

Improving Eye Health in Diabetics
↓ Inflammation
↓ Hypoxia Signaling
↓ Abnormal Angiogenesis

Enhance Compliance & Exposure
Oral pill may reduce the burden of frequent anti-VEGF injections

Safety Data

Few Systemic Adverse Effects
- ~1% Mild Gastrointestinal (diarrhea)
- ~1% Mild Skin Rash (reversible)
- Lack of Significant Acute Neurologic, Cardiovascular, Liver, or Pulmonary toxicity

No Topical Effects
- No observed ocular AEs

Twice a day dosing of APX3330 being developed to provide steady state effectiveness with a tolerable chronic safety profile

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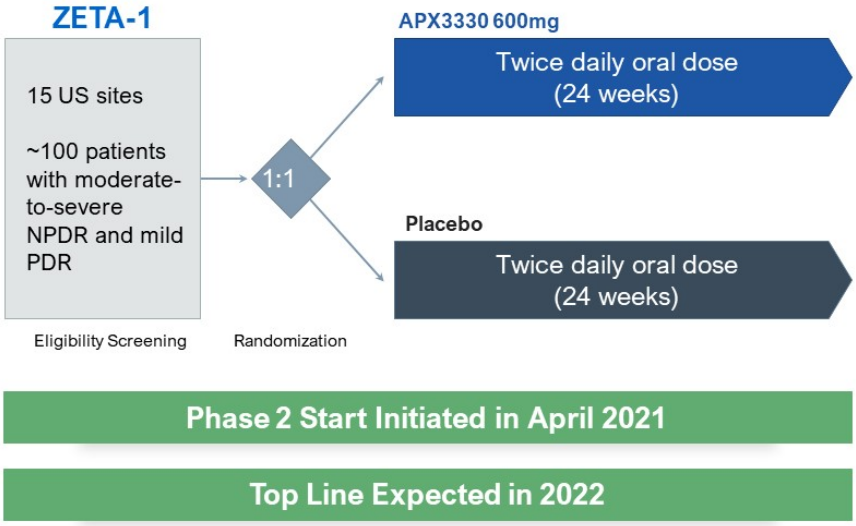
DR/DME ZETA-1 Phase 2 Design

Ongoing, Randomized, Double-Masked, Placebo-Controlled 24-Week Trial (Similar to Eylea P3 for Approval)



Phase 2 Start Initiated in April 2021

Top Line Expected in 2022

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)
- 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)

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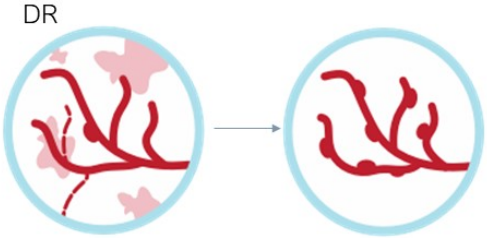
Diabetic Retinopathy & Macular Edema

APX3330 to Treat Patients Before Vision Loss Occurs

APX3330's Potential Differentiated Solution

- **Potential First Oral Therapy** to be used as an earlier intervention for the diabetic eye before vision symptoms appear or as add-on therapy to current anti-VEGF treatment
- **Proven Novel Mechanism** that may decrease both inflammation and VEGF activity
- **Convenient** option for patients to potentially alleviate the burden of injections and increase compliance
- **Tolerable** as seen in 11 completed Phase 1 and Phase 2 clinical trials

DR



DME

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Boards and Milestones

Prestigious Ocular Medical Advisory Board

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

eICON Medical

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Georgetown University

LasikPlus

Gerald Horn, MD
University of Illinois
Co-Founder Ocularis/Nyxol
Past MAB Member

Indiana University Melvin and Bren Simon Cancer Center

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

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OCLI

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Richard Messmann, MD
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CMO Apexian/APX3330

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arcscan

Jack Holladay, MD
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Minnesota Eye Consultants

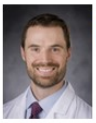
Thomas Samuelson, MD
University of Minnesota

PharmaLogic

Gary Novak, PhD
UC Davis

Cleveland Clinic
Cole Eye Institute

Peter Kaiser, MD
Harvard Medical School



Duke Eye Center

Michael Allingham, MD, PhD
University of North Carolina

Retina-Vitreous Associates Medical Group

David Boyer, MD
Chicago Medical School

Ophthalmic Consultants of Boston
Excellence in Eye Care

Jeffrey Heier, MD
Boston University

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Théa let's open our eyes
Shire
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2021 to 2022 Ocuphire Cadence of Milestones

Multiple Data Catalysts On Path To NDA(s)

2020

- ✓ Completion of APX3330 License
- ✓ ARVO 2020 Presentation for MIRA-1 & ORION-1
- ✓ FDA EOP2 Meeting May 2020
- ✓ Completion of Transaction (Nasdaq: OCUP) and concurrent $20M financing
- ✓ Initiate Phase 3 RM Trial
- ✓ Initiate Phase 3 NVD Trial
- ✓ Complete Nyxol Market Research
- ✓ Journal Publications

1H 2021

- ✓ Enrollment of Phase 3 RM Trial
- ✓ Initiate Phase 2 Presbyopia Trial
- ✓ **Report Positive Phase 3 Data for RM**
- ✓ Initiate Phase 2 DR/DME Trial
- ✓ Enrollment of Phase 2 Presbyopia Trial
- ✓ New Patent Claims
- ✓ Closed $15M registered direct offering
- ✓ **Report Positive Phase 2 Data for Presbyopia**

2H 2021

- ❑ ASCRS 2021 Presentation for MIRA-2 & VEGA-1
- ❑ **Initiate 2nd P3 RM and Pediatric RM trial for NDA**
- ❑ Enrollment of Phase 3 NVD Trial
- ❑ Enrollment of Phase 2 DR/DME Trial
- ❑ Industry Conferences & Publications
- ❑ Manufacture 3xRegistration Batches for Nyxol Blow-Fill-Seal (BFS) Eye Drops
- ❑ Complete 6-month Rabbit Tox Study

2022*

- ❑ **Report Phase 3 Data for NVD**
- ❑ **Report 2nd Ph3 RM Trial**
- ❑ **Report Pediatric RM trial**
- ❑ Initiate 2 Phase 3 Presbyopia Trials
- ❑ **Report Phase 2 Data for DR/DME**
- ❑ Initiate Chronic Ph3 Safety Trial (Nyxol /LDP)
- ❑ Complete 1 year CMC stability on 3xreg batches
- ❑ **Submit Nyxol NDA filing for RM in late 2022**
- ❑ Manufacture Commercial Batches of Nyxol Eye Drop

2023*

- ❑ Report Phase 3 Data for Presbyopia Trials
- ❑ Potential NDA for Nyxol in RM
- ❑ Potential Commercial Launch of Nyxol in US
- ❑ **Submit NDA filing for Nyxol for Presbyopia in 2023**

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

**Additional Studies for NVD and DR based on Data Readouts*

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OCUP – Market Snapshot

Sufficient Cash Runway Into Late 2022 and Substantial Trading Liquidity

Ticker	OCUP	
Price	$4.89	As of 8-10-21
Market Cap	$82 M	As of 8-10-21
Primary/FD Shares	16.9 M / 18.6 M	As of 6-30-21
Cash	$24.2 M	As of 6-30-21
Cash Runway	Into Late 2022	Guidance as of 6-30-21
Average Daily Volume	930,341	Month-to-date at 8-10-21
Short Interest	1.1%	As % of float; as of 7-31-21

Research Analyst Coverage on OCUP

James Molloy	Alliance Global Partners
John Newman	Canaccord Genuity
Kristen Kluska	Cantor Fitzgerald
Prakhar Agrawal	Jones Trading

Source: FactSet

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Restore Vision & Clarity

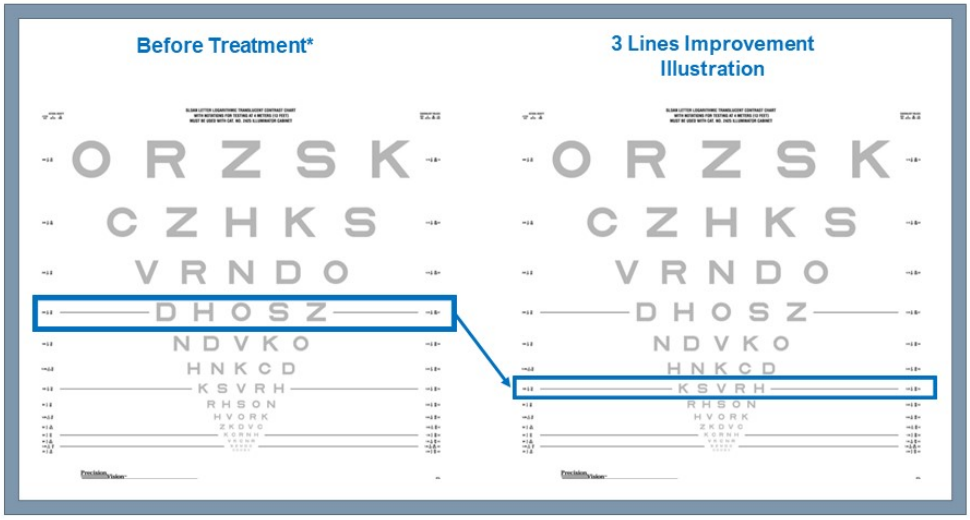
www.ocuphire.com
ir@ocuphire.com

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

FDA Accepted Endpoint for Contrast Sensitivity Assessment

Primary Endpoint of Nyxol LYNX-1 Trial

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



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

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

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

Primary Endpoint of APX3330 ZETA-1 Trial

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

Patients included in the ZETA-1 Trial

DRSS Score	1 (10)	2 (20)	3 (35)	4 (43)	5, 6 (47, 53)	7 – 13 (60, 61, 65, 71, 75, 85,90)
Description	DR Absent	Micro-aneurysm only	Mild NPDR	Moderate NPDR	Moderately Severe NPDR	PDR – Mild, Moderate, and Severe
Retinal Image						
	Healthy blood vessels with no bulges	Small bulges in blood vessel walls as well as other signs in the retina	More changes in the blood vessels in the retina and small spots of blood can become more visible	More blood vessels in larger areas of the retina show changes	Many of the blood vessels in the retina show visible changes	Increased growth of new, damaged blood vessels

A 13-point Scale Outlining the Various Stages of Diabetic Retinopathy