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 1, 2023**

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 and zip code)

248-957-9024
(Registrant's telephone number including area code)

(Registrant's 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:

☐ 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, par value $0.0001 per share	OCUP	The Nasdaq Stock Market LLC

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 August 1, 2023, 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 99.1 to this Report.

The information in this Report, including Exhibit 99.1 hereto, is furnished pursuant to Item 7.01 and shall not be deemed "filed" for purposes of Section 18 of the 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.

Exhibit 99.1 hereto contains 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 Exhibit 99.1 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	Corporate Presentation, dated August 1, 2023
104	Cover Page Interactive Data File (embedded within Inline XBRL document).

SIGNATURES

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

OCUPHIRE PHARMA, INC.

Date: August 1, 2023

By: /s/ Richard J. Rodgers
Richard J. Rodgers
Interim President and Chief Executive Officer

Exhibit 99.1

Ocuphire PHARMA

Restore Vision & Clarity

August 2023

Ocuphire Corporate Presentation

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 success and timing of planned regulatory filings and approvals, pre-commercial activities, commercialization strategy and timelines, business strategy, product labels, cash runway, scalability, future clinical trials in presbyopia (P), dim light/night vision disturbance (DLD) and diabetic retinopathy (DR) / diabetic macular edema (DME), including the potential for Nyxol to be a "best in class" presbyopia drop, and timing of planned future clinical trials for APX3330, APX2009 and APX2014, timing and occurrence of an End-of-Phase 2 meeting with the FDA, the potential of a Phase 3 registration path for APX3330, the success and timing of planned regulatory filings, business strategy, cash runway, scalability, the potential for APX3330 to be the most advanced and the first line of therapy for DR patients, and the potential market opportunity for the slowing of DR progression. These forward-looking statements are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) the success, costs, and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; (ii) regulatory requirements or developments; (iii) changes to clinical trial designs and regulatory pathways; (iv) changes in capital resource requirements; (v) risks related to the inability of Ocuphire to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; (vi) legislative, regulatory, political and economic developments, (vii) changes in market opportunities, (viii) risks that the partnership with Viatris may not facilitate the commercialization or market acceptance of Ocuphire's product candidates; (ix) the success and timing of commercialization of any of Ocuphire's product candidates, including the scalability of Ocuphire's product candidates and (x) the maintenance of Ocuphire's intellectual property rights. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by the Company from time to time with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

The Company makes no representation or warranty, express or implied, as to the accuracy or completeness of the information contained in or incorporated by reference into this presentation. Nothing contained in or incorporated by reference into this presentation is, or shall be relied upon as, a promise or representation by the Company as to the past or future. The Company assumes no responsibility for the accuracy or completeness of any such information. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market shares and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

Corporate Highlights

Late-Stage Clinical Candidates for Retinal Diseases Represent Multi-Billion Dollar Opportunity

APX3330: *Paradigm Changing, Non-invasive, Safe Oral Tablet for millions of NPDR patients that are currently left untreated*

- *Ref-1, a novel, dual target (angiogenesis and inflammation) for retinal diseases*
- *ZETA-1 Phase 2 demonstrated slowing progression of Diabetic Retinopathy (DR) with statistically significant efficacy on potential Phase 3 registration endpoint*

Nyxol: Eyedrops for refractive disorders

- Global License Agreement with Viatris to Fund all Development and Commercialization for Nyxol Indications:
  - *Reversal of Mydriasis (RM)*- PDUFA Date on September 28, 2023. Approval would trigger $10M milestone
  - *Presbyopia- currently in Phase 3*
  - *Dim Light Disturbances- currently in Phase 3*

Strong Financial Position to Advance APX3330

Ocuphire Pipeline

Product Candidate	Indication	Pre-clinical / Phase 1 / Phase 2 / Phase 3 / Regulatory Approval	Upcoming Milestones
APX3330 Oral Pill	Diabetic Retinopathy (DR)	EOP2 Meeting	❑ EOP2 Mtg Q4 2023
APX3330 Local Delivery	Retina		❑ Select retinal drug delivery technology
APX2009 and APX2014 Local Delivery	Retina		❑ Select retinal drug delivery technology
Nyxol® Eyedrops	Reversal of Mydriasis (RM)	Partnered with Viatris	❑ PDUFA Date Sep 28, 2023
	Presbyopia (P)		❑ VEGA-2 Phase 3 Topline Data Q4 2023
	Dim Light or Night Vision Disturbances (DLD)		❑ LYNX-2 2nd Phase 3 trial (n=150+)

Diabetic Retinopathy Market and Unmet Need

Diabetic Eye Disease is Common Cause of Blindness

Diabetes and Diabetic Retinopathy (DR)

Diabetes Mellitus is a group of diseases characterized by high blood glucose levels. Diabetes results from defects in the body's ability to produce and/or use insulin

Type 1 diabetes (T1D): The body produces very little or no insulin, which means that patients need daily insulin injections to maintain blood glucose levels

Type 2 diabetes (T2D): The most common form of diabetes - either the body does not produce enough insulin, or resists insulin

Diabetic retinopathy (DR) occurs when fluctuations or instability in blood glucose levels damages blood vessels in the retina

Two Types of DR

Non-Proliferative Diabetic Retinopathy (NPDR) – most common form of DR – early stages of edema and exudates, blurred central vision

Proliferative Diabetic Retinopathy (PDR) – later stage of DR, marked by abnormal blood vessels and scar tissue on retina

Diabetic Macular Edema (DME) can occur at any stage of DR

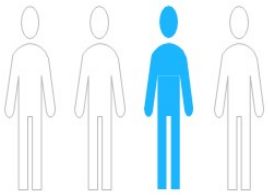
- https://webeye.ophth.uiowa.edu/eyeforum/tutorials/diabetic-retinopathy-med-students/Classification.htm
- https://www.mayoclinic.org/diseases-conditions/type-1-diabetes/symptoms-causes/syc-20353011
- https://www.mayoclinic.org/diseases-conditions/type-2-diabetes/symptoms-causes/syc-20351193

Diabetic Retinopathy At a Glance

Current Treatment Landscape Demonstrates Need for Non Invasive Therapies

There are ~8M adults in the U.S. with NPDR

The number of people with DR expected to increase more than 14M by 2050

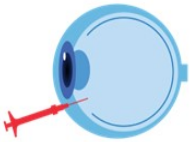


DR is the leading cause of blindness among working-age adults with the median age of onset at 45 – 50 years

Physicians have no non-invasive options for NPDR with current standard being wait-and-monitor

Prevention of Progression is favored by payors in chronic disease such as diabetes which is the leading cost driver

Majority of moderate to severe patients with DR are not treated with anti-VEGF due to injection burden and no benefit to visual acuity



- American Diabetes Association; International Diabetes Federation; Healthline; *Ocuphire internal analysis and assumptions;
- 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
- Patient survey adapted from Lions International Foundation and International Diabetes Foundation-Europe; Meltzer 2000
- Guidehouse Triangulation of Global Data, Market Scope and Investor Forecasts (2020) AMD = Age-Related Macular Degeneration; DME = Diabetic Macular Edema ; BRVO = Branch Retinal Vein Occlusion
- National Center for Chronic Disease Prevention & Health Promotion. Health & economic costs of chronic diseases.Atlanta (GA): Centers for Disease Control & Prevention, US Department of Health and Human Services; 2018
- Four-Year Visual Outcomes in a Randomized Trial of Intravitreous Aflibercept for Prevention of Vision Threatening Complications of Diabetic Retinopathy (Protocol W)." JAMA, February 7, 2023

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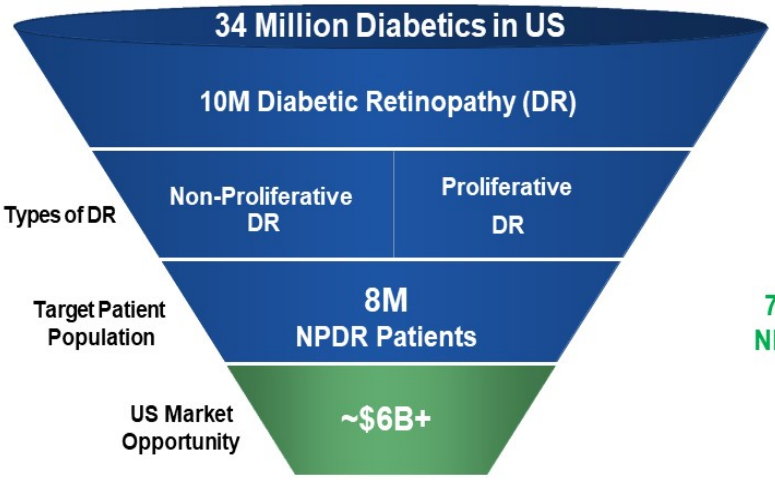
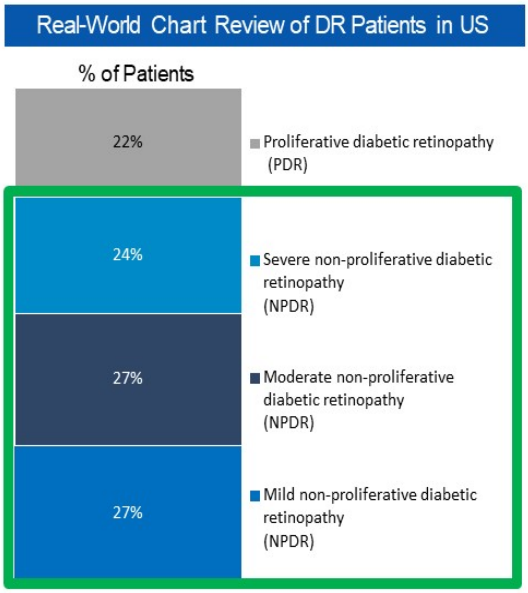
U.S Diabetic Retinopathy Market

Majority of the DR patients are NPDR Severity → Target Population for APX3330



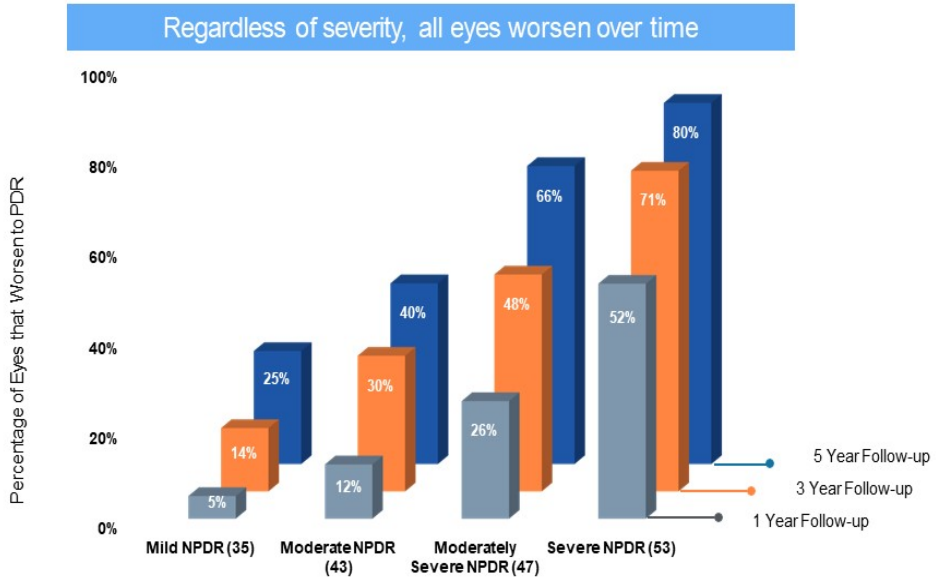
78% NPDR



- American Diabetes Association; International Diabetes Federation; Healthline; *Ocuphire internal analysis and assumptions; Spherix Global Insights
- Patient survey adapted from Lions International Foundation and International Diabetes Foundation-Europe; Meltzer 2000
- Estimates are provided by the National Eye Institute, FactSheet, Global Data, and Research and Markets. Estimated values are rounded.
- Estimated prevalence in the U.S.; DME- Diabetic Macular Edema; Age-related Macular Degeneration; Geographic Atrophy; Retinal Vein Occlusion

Progression Based on DR Severity

NPDR Patients are Rarely Treated with anti-VEGF Intravitreal Injections; Non-Invasive, Early Intervention is an Unmet Need

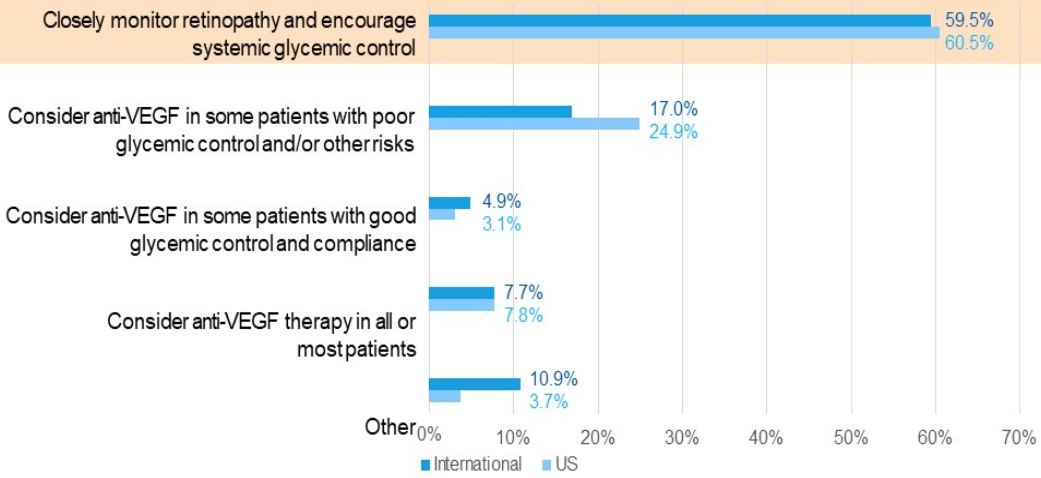


- Spherix Global Insights: DR Market DYNAMIX October 2022
- Early treatment diabetic retinopathy study research group. ophthalmology. 1991;98(5 suppl):823-33.
- Diabetes control and complications trial research group. N Engl J Med. 1993;329(14):997-86.
- Fathy C, Patel S, Sternberg P Jr, Kohanim S. Disparities in adherence to screening guidelines for diabetic retinopathy in the United States: a comprehensive review and guide for future directions. *Semin Ophthalmol.* 2016;31(4):364–377. doi:10.3109/08820538.2016.1154170

ASRS PAT Survey: Majority of Physicians Use a "Wait and Monitor" Approach for DR

NPDR Patients Are Not Treated Proactively and Anti-VEGF Use is Limited

How do physicians treat patients with severe NPDR without DME?



Diabetic Retinopathy Treatment Landscape

Landscape of Non-Invasive Therapies for Diabetic Retinopathy

Ocuphire's APX3330 is the Most Advanced and The Only Dual Mechanism Oral Drug Candidate

Company	Drug	Target/MOA	Indication	Route of Administration	Phase 1	Phase 2	Phase 3	Primary Endpoint/ Secondary Endpoints
Ocuphire	APX3330	Ref-1 inhibitor (Anti-VEGF and Anti-inflammatory)	DR	Oral	✓	✓ 2022		2020: 2-step DRSS @wk24
Roche	RG7774	CB2 receptor (cannabinoid)	DR	Oral	✓	○		2020: 2-step DRSS @wk36
Bayer	BAY1101042	Guanylate Cyclase activator	DR	Oral	✓	○		2021: 2-step DRSS @wk24
Valo	OPL-0401	ROCK 1/2 inhibitor	DR	Oral	✓	○		2021: 2-step DRSS @wk24
OcuTerra Therapeutics	OTT166	Integrin inhibitor	DR	Eyedrop	✓	○		2022: 2-step DRSS @wk24

Note: Two Tyrosine Kinase and a Plasma Kallikrein Inhibitors failed as orals in Phase 2 due to dose limiting adverse events (e.g., liver and cardiovascular)

✓ *Completed* ○ *Ongoing* × *Discontinued*

APX3330 Differentiation

- **Mechanism:** Dual MOA targeting validated retinal pathways of angiogenesis and inflammation
- **Human exposure:** >10,000 subject days of systemic exposure in humans at 600mg/day dose
- **Favorable safety and tolerability**

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- Company websites and www.clinicaltrials.gov (as of July 31, 2023)

Landscape of Invasive Therapies (IVT/Suprachoroidal) for Diabetic Retinopathy

Eylea®/Lucentis® Approved, But Not Used in Patients with NPDR; Rarely Used in Mild PDR

Company	Drug	Target/MOA	Route of Administration	Phase 1	Phase 2	Phase 3	Commercial
REGENERON	Eylea® (aflibercept)	VEGF-A/B; PlGF	Intravitreal	✓	✓	✓	✓ *1
Roche	Lucentis® (ranibizumab)	VEGF-A	Intravitreal	✓	✓	✓	✓ *2
KODIAK	KSI-301 (Tarcocimab)	VEGF	Intravitreal	✓	N/A	○	
EyePoint Pharmaceuticals	EYP-1901	Voloronib * (TKI)	Intravitreal	✓	○		
Boehringer Ingelheim	BI 764524	Anti-Sema3A Ischemia modulator	Intravitreal	✓	○		
Ocular Therapeutix	OTX-TKI	Axitinib * (TKI)	Intravitreal	✓	○		
REGENXBIO	RGX-314	AAV8-VEGF	Suprachoroidal (Gene Therapy)	✓	✓		

* Failed as oral/systemic treatments in retina due to dose limiting toxicity

✓ *Completed* ○ *Ongoing* X *Discontinued*

*Trials to Support Approval
[1] Panorama Clinical Trial
[2] Protocol I & T and Rise & Ride

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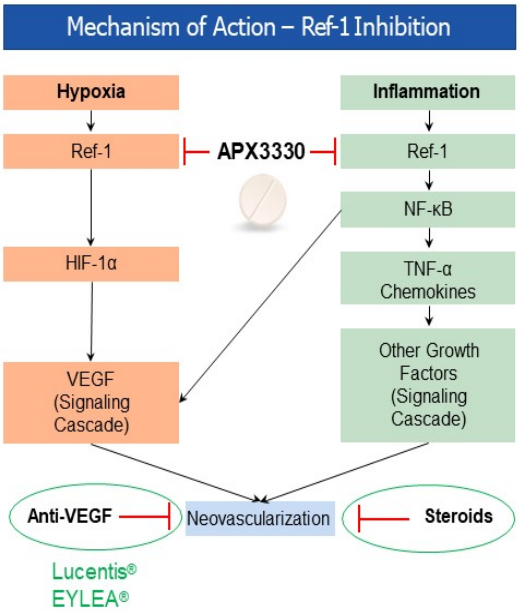
- Company websites and www.clinicaltrials.gov (as of July 31, 2023)
- Eylea® is trademark of Regeneron and Lucentis® is trademark of Genentech

APX3330 Background

APX3330 History and Ref-1 Inhibition Mechanism

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



- Ref-1 (reduction-oxidation effector factor-1), a novel target for retinal diseases, is a transcription factor regulator of angiogenesis (VEGF) and inflammation (NFkB)
- **Unique dual MOA decreases abnormal angiogenesis and inflammation**
- **Anti-VEGF injections *do not* target inflammation**
- Previously developed by Eisai for hepatic inflammatory indications and by Apexian for solid tumors in **11 Phase 1 and 2 trials**
- Extensively studied in over **20 in-vitro and animal studies** with favorable efficacy and safety

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

APX3330: Drug Development History and Patents

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

APX3330
New Chemical Entity

12*
Phase 1 & Phase 2 Trials

Exposure in Humans
>10,000
Subject Days at 600mg/day

Patents to
2034+

☑	☑	☑	☑	☑	☐	☐
Preclinical Efficacy & Toxicology Package	APX3330 IND	6 Phase 1 Trials	5 Phase 2 Trials	Phase 2 Trials	Phase 3 Registration	NDA Filing

Studied in inflammation/hepatitis & cancer patients
(Studied by Eisai & Apexian, respectively)

Focus on Ophthalmology

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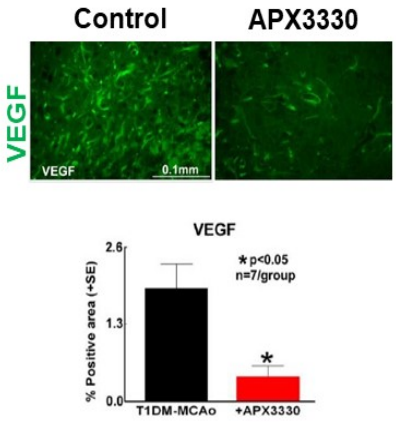
* Includes ZETA-1 trial

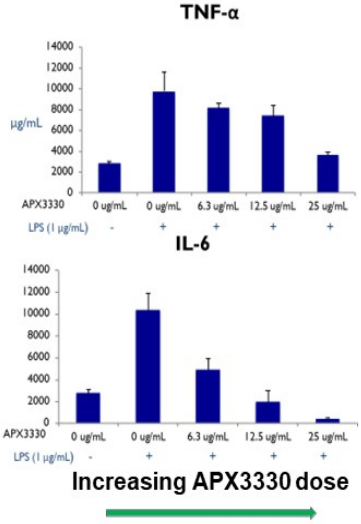
In-vitro Validation of Mechanism of Action

APX3330 Reduces VEGF levels and Inflammatory Cytokines; Provides Neuronal Protection

APX3330 reduces VEGF protein expression in preclinical stroke model

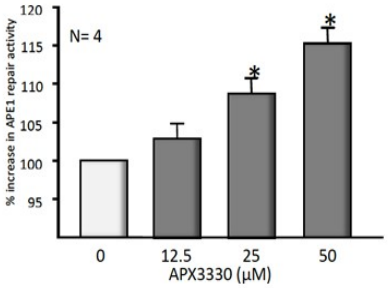


APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages



Increasing APX3330 dose

APX3330 increases DNA oxidative repair and neuronal protection

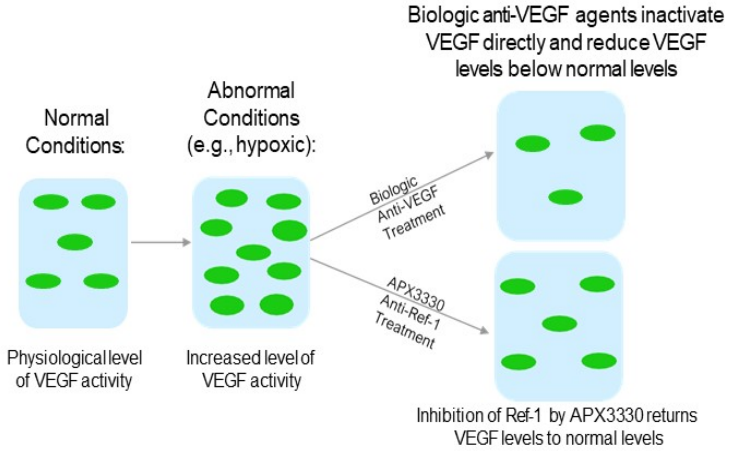


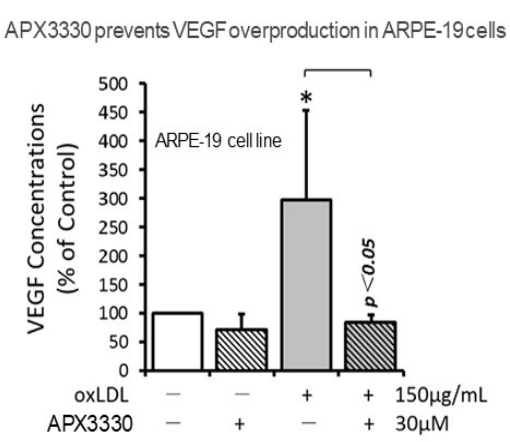
APX3330 enhances Ref-1 endonuclease activity in dorsal root ganglion neurons

- 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).

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 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

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

APX3330 ZETA-1 Clinical Trial

ZETA-1: Phase 2 Trial of Oral AP3330 in Subjects With Diabetic Retinopathy

Multi-center, Randomized, Double-Masked, Placebo-Controlled 24-Week Trial

Eligibility Criteria

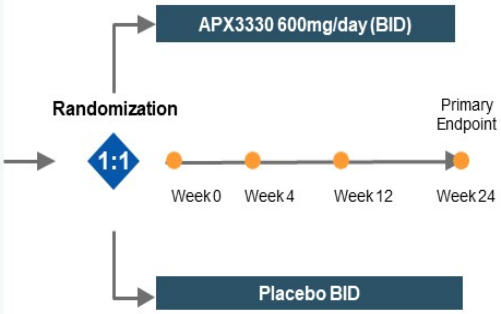
- 25 US sites
- N = 103 participants with moderately severe to severe NPDR or mild PDR (DRSS 47, 53, 61)

Key inclusion:

- ≥ 18 years of age
- DRSS 47, 53, or 61
  - Noncentral DME permitted[2]
- ETDRS BCVA ≥ 60 letters (20/63)

Key exclusion:

- OCT CST >320 µm[2]
- Center involved DME allowed in fellow eye
- Anti-VEGF within past 6 months[3]
- HbA1c ≥ 12.0%



Endpoints

Primary:

- % subjects with ≥ 2 step improvement on DRSS (Diabetic Retinopathy Severity Scale[1]) at week 24

Secondary:

- DRSS improvement ≥1, ≥2, ≥3, ≥4 study eye, fellow eye, binocular
- DRSS worsening ≥1, ≥2, ≥3, ≥4, study eye, fellow eye, binocular
- Progression to vision threatening complications
- Central subfield thickness (CST)
- Best Corrected Distance Visual Acuity (BCDVA)
- DME fellow eye status
- Safety and tolerability

Exploratory:

- Inflammatory cytokines

103 subjects enrolled (FPFV Apr 2021 to LPLV Aug 2022)
Topline announced in January 2023

1. *By Central Reading Center*
2. *Center-Involved DME in Fellow Eye is Acceptable*
3. *Includes Systemic or IVT VEGF*

www.clinicaltrials.gov (NCT04692688); Eylea® is registered trademark of Regeneron
NPDR = non-proliferative diabetic retinopathy PDR = proliferative diabetic retinopathy

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ZETA-1: Baseline Demographics and Systemic Characteristics

Well-Balanced Across Arms

Demographics

	APX3330 n=51	Placebo n=52
Age (years) mean (range)	54.3 (26-81)	58.3 (24-78)
Sex: Male n (%)	24 (47%)	26 (50%)
Race: White n (%)	40 (78%)	41 (79%)
Ethnicity: Hispanic or Latino n (%)	28 (55%)	23 (44%)
Diabetes Status (years) mean (range)	15 (0-36)	16 (0-58)
Systolic Blood Pressure (mmHg) mean	136	139
Diastolic Blood Pressure (mmHg) mean	82	80
Heart Rate (beats/min) mean	77	76
Hemoglobin A1C (%) mean	8.4	8.3
Body Mass Index (kg/m^2) mean	31	31

DRSS Scores

	APX3330 n=49	Placebo n=52
DRSS Score – Study Eye		
47 (Moderately severe to severe NPDR)	22 (43%)	18 (35%)
53 (Moderately severe to severe NPDR)	25 (49%)	28 (54%)
61 (Mild proliferative diabetic retinopathy)	4 (8%)	6 (12%)
DRSS Score – Fellow Eye		
43 or Lower (Mild to moderate NDPR or better)	**15 (31%)**	**13 (25%)**
47 (Moderately severe to severe NPDR)	15 (31%)	20 (38%)
53 (Moderately severe to severe NPDR)	12 (25%)	10 (19%)
61 (Mild proliferative diabetic retinopathy)	1 (2%)	4 (8%)
65 or Higher (Moderate to severe prolif. DR)	**6 (12%)**	**5 (10%)**

Note: 15 fellow eyes were CST>320microns (center-involved DME eyes)

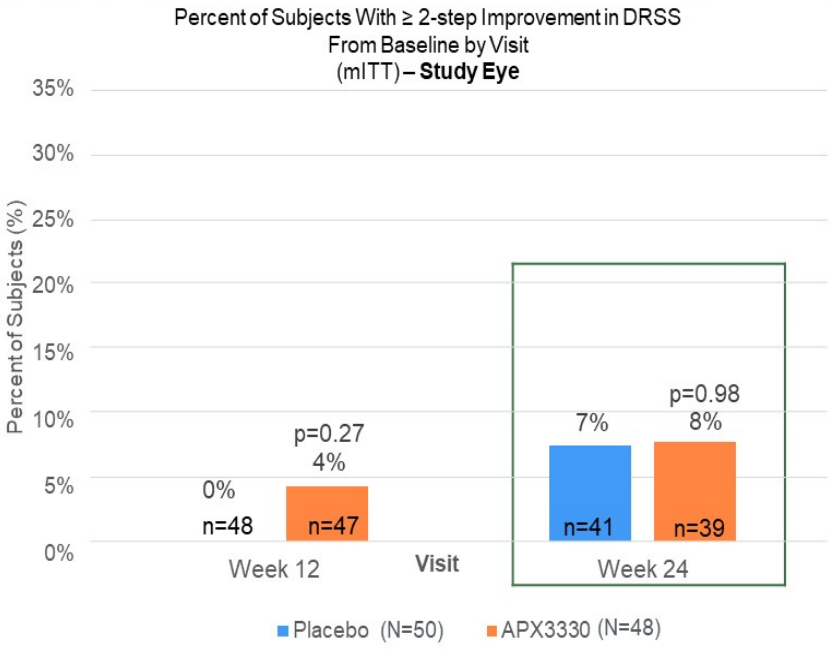
Key Visual Metrics

	APX3330 n=51	Placebo n=52	Total n=103
BCVA Study Eye *Letters (mean)*	**81**	**78**	**80 (20/25 Snellen)**
BCVA Fellow Eye *Letters (mean)*	76	77	77 (20/32 Snellen)
OCT CST Study Eye *(µm)*	**270**	**271**	**271**
OCT CST Fellow Eye *(µm)*	292	286	289
Intraretinal Fluid in the Center of SE	Y – 21 N – 26	Y – 12 N – 31	Y – 33 N – 57
Intraretinal Fluid at the Foveal Center of SE	Y – 1 N – 20	Y – 1 N – 11	Y – 2 N – 31
Intraocular Pressure in Study Eye (mmHg)	15	16	15

Good Visual Acuity Fluid Below 320µm

Percent of Subjects With ≥ 2-Step Improvement in DRSS From Baseline

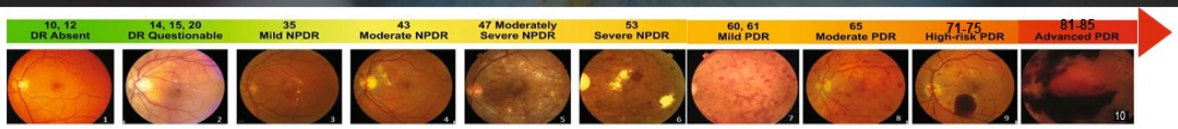
ZETA-1 Did Not Meet the Week 24 Phase 2 Primary Endpoint (based on Anti-VEGF Precedence for DR)



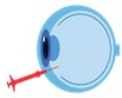
- ZETA-1 Clinical Trial
- Note: Large "N" indicates total number of participants within each arm for the mITT population. Small "n" indicates total number of evaluable eyes for each respective endpoint and arm.

Clinically Meaningful Registration Endpoints in DR

Systemic Drugs Should Evaluate DRSS Change in Both Eyes; To Be Formally Confirmed at EOP2 FDA Meeting



FDA accepts improvement OR worsening (prevention of progression)[1] of the disease AND DRSS is an established surrogate endpoint for DR



Local Drugs (Intravitreal Injections)

Precedent approvable endpoint for locally-delivered drugs (Non-Systemic) in DR:

- ≥ 2-step DRSS improvement in study eye
  - Aflibercept (PANORAMA trial)
  - Ranibizumab (RISE/RIDE/DRCR trials)

Systemic Drugs

Potential approvable endpoints for systemic drug in DR (to be confirmed at the EOP2 FDA meeting) include:

- ≥ 3-step binocular DRSS improvement
- ≥ 3-step binocular DRSS worsening

End-of-Phase 2 meeting with FDA to align on binocular ≥ 3-step DRSS worsening (i.e., sum of right and left eye change in DRSS) as an acceptable primary endpoint for registration

This endpoint is distinct from historical anti-VEGF IVT precedent due to different delivery

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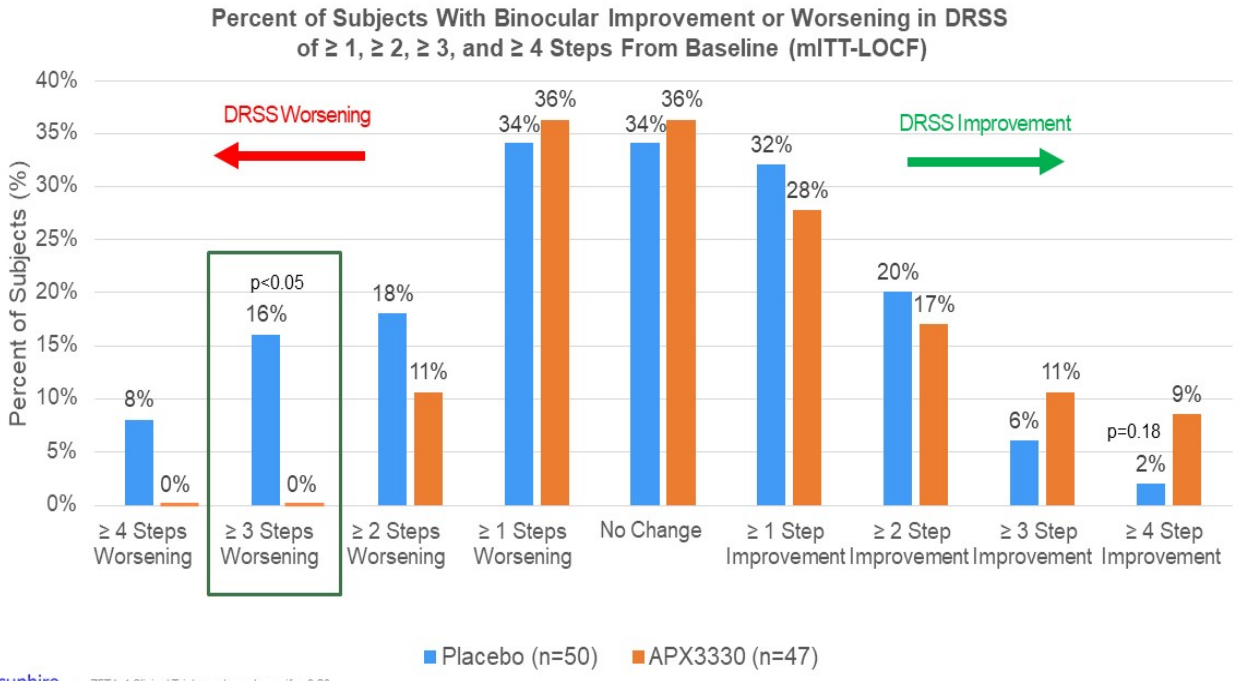
Source: ZETA-1 Clinical trial

1. Nair P, Aiello LP, Gardner TW, Jampol LM, Ferris FL III. Report From the NEI/FDA. Diabetic Retinopathy Clinical Trial Design and Endpoints Workshop. Invest Ophthalmol Vis Sci. 2016 Oct 1;57(13):5127-5142. doi: 10.1167/iovs.16-20356. PMID: 27699406; PMCID: PMC6016432.

Percent of Subjects with Binocular Improvement or Worsening in DRSS at Wk 24

APX3330 Demonstrated Statistical Efficacy on the Pre-Specified, Planned Phase 3 Registration Endpoint



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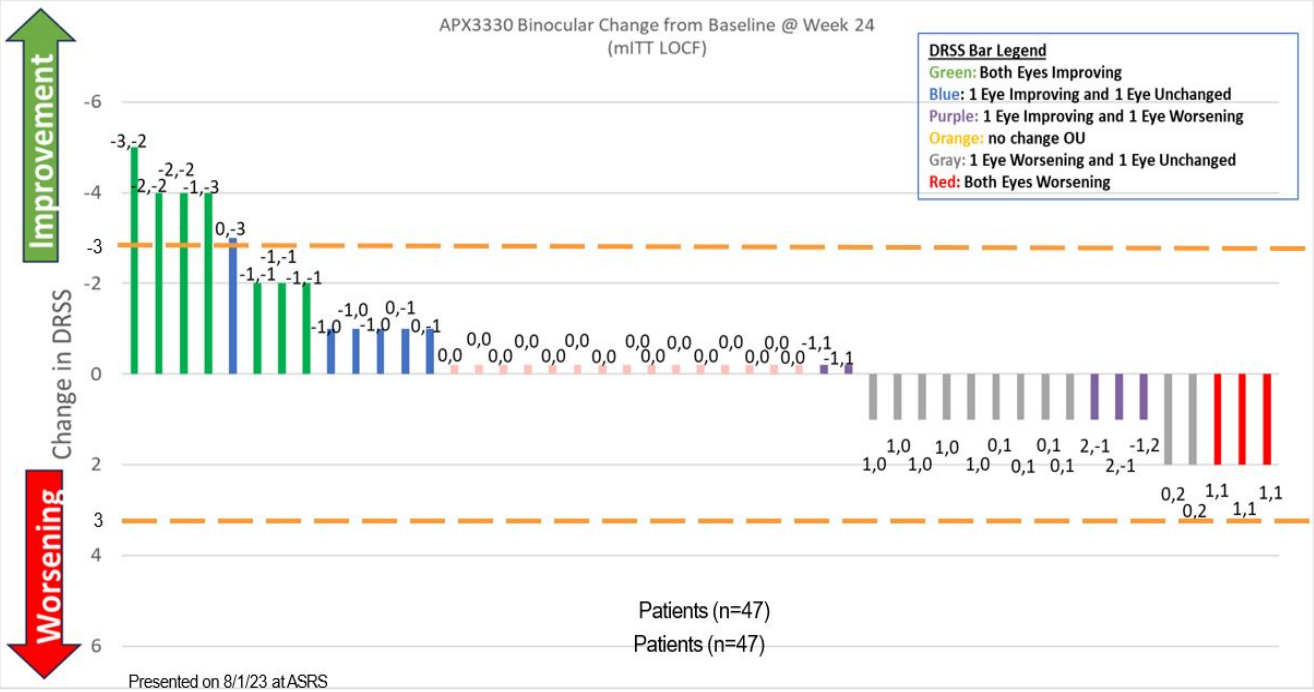
- ZETA-1 Clinical Trial; p values shown if p<0.20
- Table 14.2.2.7, March 2023

Change in DRSS Score by Patient by Eyes

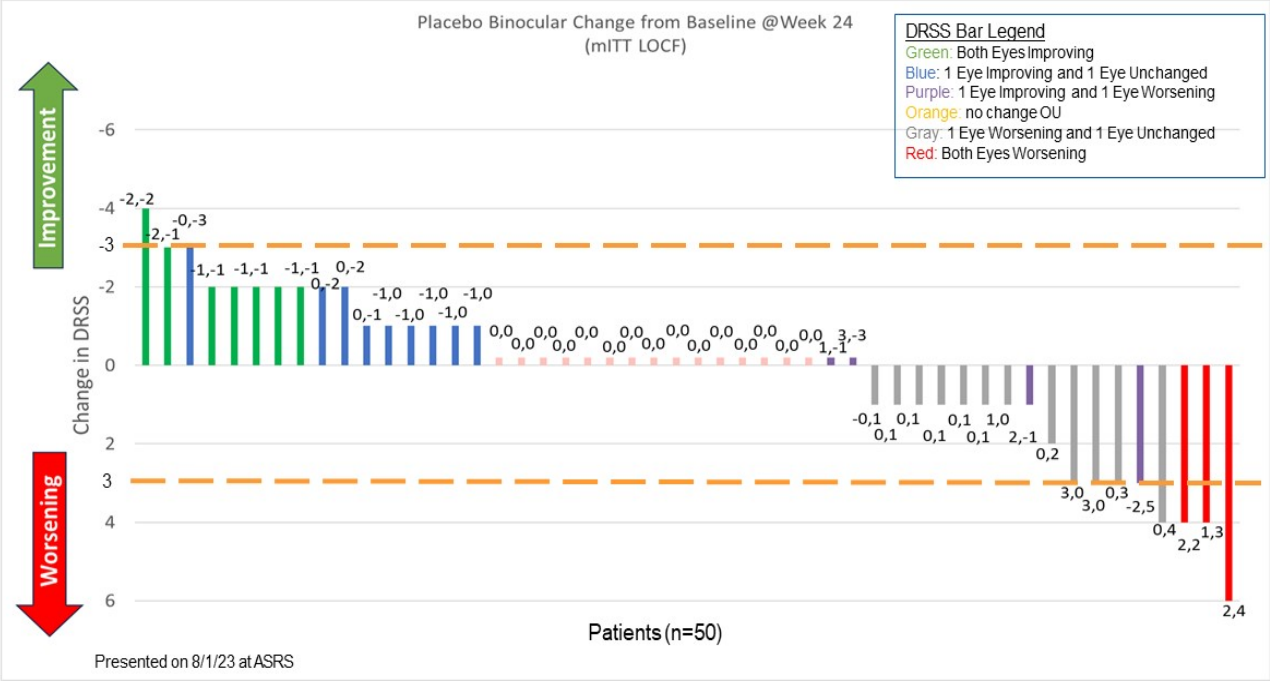
0% Patients in APX3330 Treatment Group had Binocular 3-Step Worsening



Presented on 8/1/23 at ASRS

Change in DRSS Score by Patient by Eyes

16% Patients in Placebo Treatment Group had Binocular 3-Step Worsening

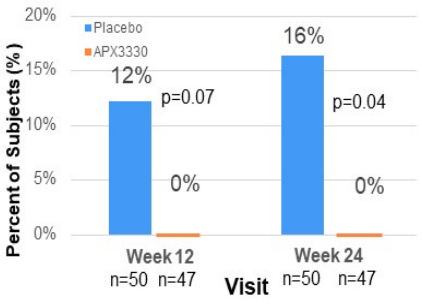


Presented on 8/1/23 at ASRS

% of Subjects With Binocular ≥ 3-Step Worsening in DRSS and Progression to PDR

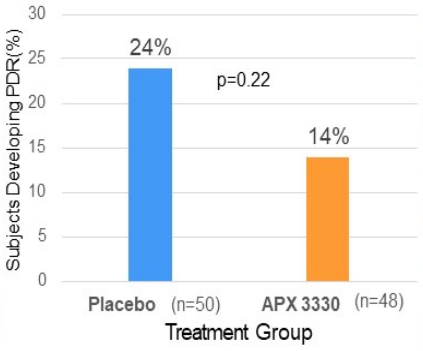
APX3330 Prevented Progression of Structural Retinal Abnormalities

Percent of Subjects With Worsening in DRSS of ≥3 Steps From Baseline by Visit Binocular Eyes (mITT-LOCF)



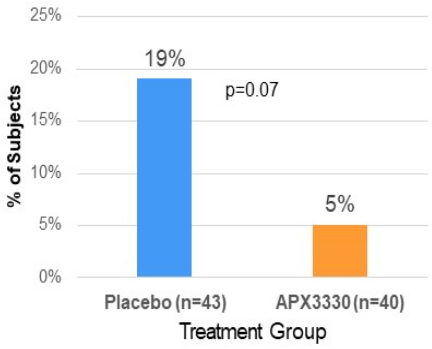
It is estimated ~25% of untreated patients may progress by ≥ 3 steps in binocular DRSS over 1 year[1]

Percentage of Subjects Developing PDR (mITT Population) at week 24



APX3330 reduced the percentage of subjects who developed PDR over the course of 24 weeks

Percentage of Subjects with ≥ 5 Letters of BCVA Lost at Week 24 (Safety Population)



BCVA data shows **fewer APX3330 treated subjects losing visual acuity** compared to placebo at week 24

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- ZETA-1 Clinical Trial
- [1] Sun JK, Evidence for DR Progression and Regression from Clinical Trials. Presented at NDI/FDA DR Clinical Trials Design and Endpoints Workshop, June 26, 2015.

ZETA-1: Treatment Emergent Adverse Events

Oral APX3330 Showed a Favorable Safety and Tolerability Profile Consistent with Prior Trials

	Placebo (n=52)	APX3330 (n=51)
Total AEs	120	91
#of Subjects with AEs	35 (67%)	29 (57%)
Treatment-related AEs	17 (14%)	14 (15%)
Serious AEs	11 (9%)	3 (3%)
Subjects Withdrawals Due to AEs	1 (2%)	2 (4%)
Deaths	1 (2%)	0 (0%)
AEs in >5% of Subjects*		
| *Eye disorders* | Diabetic Retinal Edema	5 (10%)	2 (4%)
Diabetic Retinopathy	6 (12%)	1 (2%)
Vitreous detachment	3 (6%)	0 (0%)
Cataract	1 (2%)	3 (6%)
Pruritus	1 (2%)	6 (12%)
Rash	1 (2%)	3 (6%)
COVID-19	5 (10%)	1 (2%)

<u>APX3330 Safety Profile</u>:

- Limited AEs, most mild in severity
  - Pruritis: Mild and resolved without APX3330 dose de-escalation or discontinuation
- AEs similar to or less than placebo
- Few serious treatment-related AEs, all unrelated to study medication
- No ocular AEs other than expected DR progression
  - Lower incidence of clinical DR/DME worsening with APX3330
- **Patients continued routine medications to manage their diabetes comorbidities**

- APX3330 SAEs: Dyskinesia, TIA, Chest pain
- Placebo SAEs: Vertigo, Asthenia, Multiple organ dysfunction, Bradycardia, CAD, Cholelithiasis, COVID-19 pneumonia, Cellulitis, Respiratory failure, Skin ulcer, Peripheral embolism
- AEs → Withdrawal APX3330: Presyncope, Dyspnea; Placebo: DME (both eyes)
- *Preferred Term within Organ Class

APX3330 - Phase 2 Summary and Next Steps

ZETA-1 Summary

- APX3330 demonstrated favorable safety and tolerability with compelling potential to slow progression of diabetic retinopathy
- ZETA-1 statistically significant results on potential Phase 3 registration endpoint:
  - 0% APX3330-treated patients had a binocular ≥ 3-step worsening of DRSS from baseline compared with 16% for placebo-treated patients (p=0.04)

APX3330 Next Steps

- Further analysis of ZETA-1 Phase 2 data, including insights for Phase 3 trial design
- Prepare for EOP2 FDA meeting in Q4 2023 to formally confirm Phase 3 design and registration endpoint
- Advance APX3330 into Phase 3 program with long-term exposure (up to 2 years)

Our Goal for Patients

To have a clinically meaningful impact on ***preventing progression*** to reduce likelihood of vision loss in diabetic retinopathy patients

APX3330 Key Takeaways

- DR is one of the largest markets in retina with 10M patients in US and over 100M worldwide
- Majority of the NPDR patients are not candidates for approved biologics treatments and are left untreated
- APX3330 first-in-class oral drug that inhibits Ref-1 which reduces VEGF and inflammatory cytokines to normal physiological levels
- Prevention of worsening is a clinically meaningful potential registration endpoint that was met in ZETA-1 study
  - No subjects (0%) treated with APX3330 had a binocular ≥ 3-step DRSS worsening from baseline compared with 16% for placebo (p=0.04) after 24 weeks of treatment
- APX3330 demonstrated favorable safety & tolerability in diabetic patients
- **An EOP2 meeting with FDA is confirmed in Q4 2023**
- APX3330 has the potential to be an early, non-invasive preventative treatment for the 8 million NPDR patients with the potential to treat other organs affected by diabetes (e.g., kidney disease, peripheral neuropathy)
- Broad prescriber base including general ophthalmology, optometry and primary care due to favorable safety

Nyxol

Global Partnership with Viatris for Nyxol

Viatris Has Selected Nyxol to be a Key Element of its Global Eye Care Division

Partner for Nyxol global commercialization

Fully funded development and commercialization costs for all 3 Nyxol indications

Allows Ocuphire to focus on APX3330 development

Strengthens cash position into 2025

- **$35 million upfront**
- **Funding for potentially all R&D and commercialization for all 3 indications globally**
- **$130 million in regulatory and sales milestones**
  - First potential $10 million milestone payment on FDA approval in RM
- **Tiered double digit royalties through 2040**

RM

Reversal of Mydriasis (RM)

P

Presbyopia

1 Nyxol as a Single Drop

2 Nyxol with LDP Adjunctive Therapy

DLD

Dim Light or Night Vision Disturbances (DLD)

Summary of Nyxol Trial Results

Comprehensive Body of Clinical Data Supporting Efficacy and Safety Across 3 Indications

Indication & Status	Primary Endpoint	Efficacy Data	Key Secondary Endpoint(s)	Safety & Tolerability
RM PDUFA 9/28/23	Return to baseline pupil diameter at 90 minutes after dilation	**Met Phase 3 primary endpoint** **MIRA-3**: 58% Nyxol vs. 6% placebo **MIRA-2**: 49% Nyxol vs. 7% placebo (p<0.0001) **MIRA-4**: 64% Nyxol vs. 25% placebo	Efficacy across all mydriatic agents, iris color, 1 or 2 drops, and all ages (3-80)	• No headaches • No blurry vision • ~5% mild redness • No change in IOP • No SAEs • Most AEs were mild
Presbyopia (Nyxol Alone) Phase 3	≥3 line gain in near vision with loss of no more than 1 line in distance vision	**Met planned Phase 3 primary endpoint** **VEGA-1**: 29% Nyxol vs.12% placebo at 12 hrs post-Nyxol dose (p=0.02)	Durable near vision (18hrs) Optimal pupil size Pupillary light reflex	
Presbyopia (Nyxol + LDP) Phase 3		**Met Phase 2 primary endpoint** **Met planned Phase 3 primary endpoint** **VEGA-1**: 61% combo post-LDP dose (30 min) + post-Nyxol dose (12 hrs) vs. 14% placebo (p<0.0001)	Durable near vision gain Optimal pupil size Pupillary light reflex	
DLD 2nd Phase 3	≥3 lines (eye test) of improvement in mesopic low contrast best-corrected distance visual acuity (mLCVA)	**Met Phase 3 primary endpoint** **LYNX-1**: 13% Nyxol vs. 3% placebo at Day 8 (p<0.05) and 21% in Nyxol vs.3% placebo at Day 15 (p<0.01)	Improvement visual acuity measures (distance and near) in dim light conditions	

Corporate Highlights

- ***Late-Stage Retinal Pipeline*** *Represents* ***Multi-Billion Dollar Opportunity*** *in Unmet NPDR Patients*
- ***APX3330 – Novel, Non-Invasive, Safe Oral Tablet*** *to Treat Diabetic Retinopathy*
- *APX Pipeline Driven by a* ***Paradigm Changing, Dual Target Ref-1 Platform*** *for Retinal Diseases*
- ***Global License Agreement with Viatris*** *to Fund Development and Commercialization of Nyxol for All Refractive Indications*
- ***Strong Financial Position*** *to Fund Operations into 2025*


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Appendix
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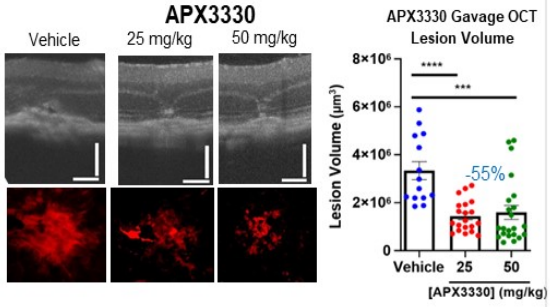
Preclinical Data: Oral APX3330 Blocks Neovascularization

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

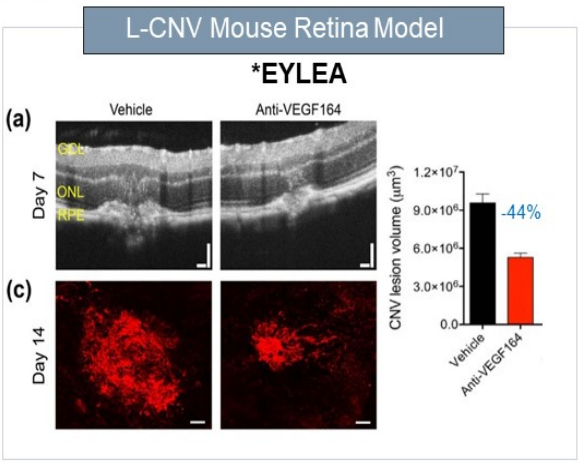
L-CNV Mouse Retina Model

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 <u>intravitreal</u> injection of 20µM APX3330 in mouse L-CNV model****
- ✓ **Efficacy was also seen after dosing <u>intraperitoneal</u> 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 <u>intravitreal</u> injection of 20µM APX3330 in Vldlr $^{-/-}$ mice model******

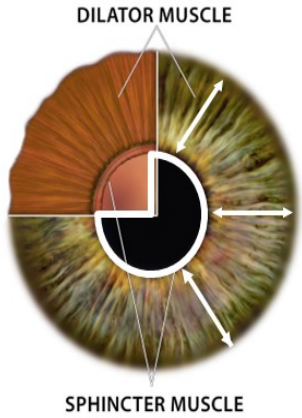
Ocuphire Pharma

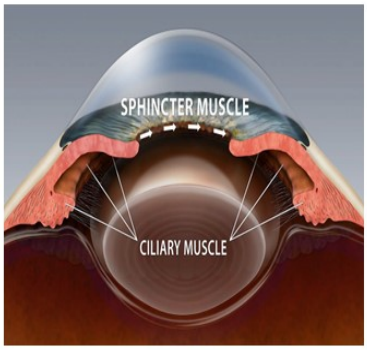
- Silva et al. ARVO 2021 Annual Meeting
- *Published data on EYLEA. This study was performed independently from APX3330 study and is a cross-study comparison.
- **Li 2014; *** Pasha 2018; ****Jiang 2011 (*Vldlr*$^{-/-}$: Very Low-Density Lipoprotein receptor knock-out mice)

Nyxol's Differentiated MOA as an Alpha-1 Blocker

No Engagement of Ciliary Muscle, No Headaches and Lower Risk of Retinal Detachment

Phentolamine is the Active Ingredient in Nyxol: a non-selective α Antagonist





Phentolamine blocks α1 receptors on the **Iris Dilator Muscle up to 24 hours**

↓

Decreases pupil size (moderately) **without affecting the iris sphincter or ciliary muscles**

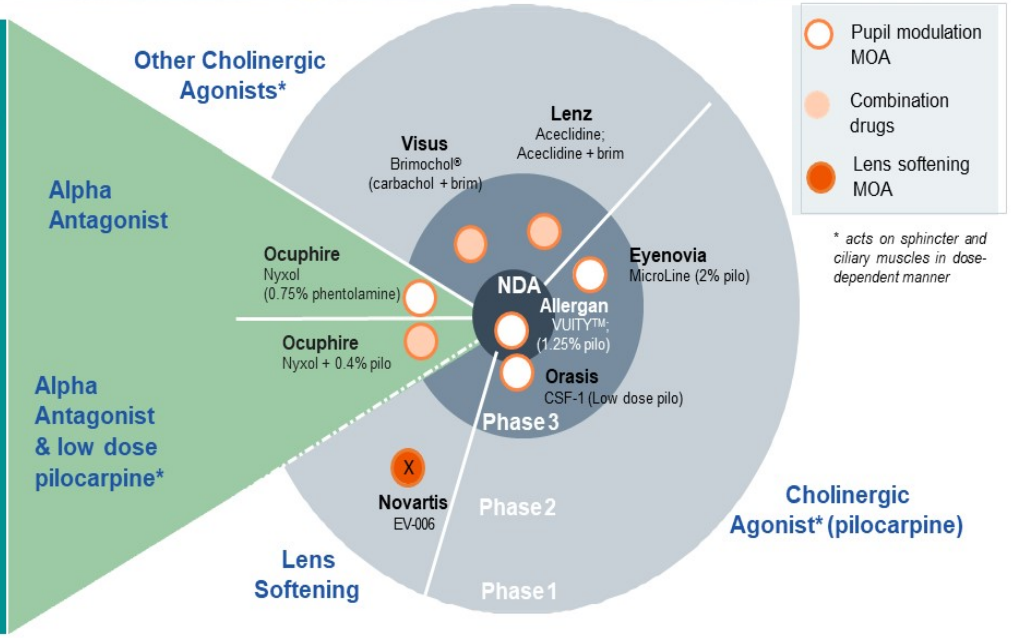
↓

Allows for 3 indications: **RM, Presbyopia and DLD**

505(b)(2) Regulatory Pathway Supported by Prior Phentolamine Approvals in non-ophthalmic Indications

A New, Differentiated MOA and Combination Therapy Offers Tunability

- **Nyxol's potential differentiation:**
  1) **New MOA class** (iris dilator muscle inhibitor)
  2) **Favorable safety and tolerability** (e.g.: no headaches, no accommodative spasm, no risk of retinal detachment)
  3) **24-hour durability**
  4) **Broad range of patients including high myopes**
  5) **Improvement in night vision disturbances**
- **Nyxol+LDP may offer added efficacy and tunability**



Management Team with Decades of Drug Development Experience

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Interim CEO

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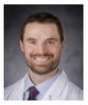

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