

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): March 27, 2024

Ocuphire Pharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation)	001-34079 (Commission File Number)	11-3516358 (IRS Employer Identification No.)
37000 Grand River Avenue, Suite 120 Farmington Hills, MI (Address of principal executive offices)		48335 (Zip Code)

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

(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, \$0.0001 par value 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

Representatives of Ocuphire Pharma, Inc. (the “*Company*”) plan to share the Investor Presentation attached hereto as Exhibit 99.1 in upcoming meetings with investors and others.

The information in this Item 7.01 of this Current Report on Form 8-K, and Exhibit 99.1, is furnished and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “*Exchange Act*”), nor shall it be deemed incorporated by reference in any filing made by the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Investor Presentation March 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

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

Dated: March 27, 2024

OCUPHIRE PHARMA, INC.

By: /s/ Dr. George Magrath

Name: Dr. George Magrath

Title: Chief Executive Officer









Ocuphire Investor Presentation
March 2024

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 End-of-Phase 2 meeting with the FDA to align on late-stage registration endpoints and study parameters, the launching of RYZUMVI, the continued development of PS and LDP, our partnership with Viatriis, the strength of our cash position, and the potential of APX3330 as an oral treatment for patients with non-proliferative diabetic retinopathy. These forward-looking statements relate to us, our business prospects and our results of operations and are subject to certain risks and uncertainties posed by many factors and events that could cause our actual business, prospects and results of operations to differ materially from those anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described under the heading "Risk Factors" included in our Annual Report on Form 10-K. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this presentation. In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "ongoing," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. We undertake no obligation to revise any forward-looking statements in order to reflect events or circumstances that might subsequently arise. 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: the success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; regulatory requirements or developments; changes to or unanticipated events in connection with clinical trial designs and regulatory pathways; delays or difficulties in the enrollment of patients in clinical trials; substantial competition and rapid technological change; our development of sales and marketing infrastructure; future revenue losses and profitability; our relatively short operating history; changes in capital resource requirements; risks related to the inability of Ocuphire to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; domestic and worldwide legislative, regulatory, political and economic developments; employee misconduct; changes in market opportunities and acceptance; reliance on third-parties; future, potential product liability and securities litigation; system failures, unplanned events, or cyber incidents; the substantial number of shares subject to potential issuance associated with our Equity Line of Credit arrangement with LPC; risks that our partnership with Viatriis, or our other licensing arrangements, may not facilitate the commercialization or market acceptance of Ocuphire's product candidates; future fluctuations in the market price of our common stock; the success and timing of commercialization of any of Ocuphire's product candidates; and obtaining and maintaining 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. Readers are urged to carefully review and consider the various disclosures made by us in this presentation and in our reports filed with the SEC that advise interested parties of the risks and factors that may affect our business. All forward-looking statements contained in this presentation 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.

Positioned to Transform the Treatment of Diabetic Retinopathy

	Diabetic retinopathy market is large and underserved	<ul style="list-style-type: none"> DR is the leading cause of blindness in working age adults, impacting 10M patients in the US^{1,2} Most patients have early-stage disease (non-proliferative diabetic retinopathy), which is generally untreated and represents a \$6B market³
	Oral APX3330 targets earlier-stage DR via multiple pathways	<ul style="list-style-type: none"> Current therapies are invasive, often reserved for advanced DR, and do not address multiple disease pathways APX3330 may represent a promising oral option for slowing DR progression by inhibiting Ref-1, simultaneously addressing angiogenesis, oxidative stress, and inflammation
	Phase 2 efficacy of APX3330 in slowing DR progression	<ul style="list-style-type: none"> Fewer APX3330-treated subjects experienced DR worsening compared to placebo, demonstrating efficacy on the FDA-confirmed endpoint of ≥ 3-step DRSS worsening on binocular scale Fewer APX3330-treated subjects developed proliferative diabetic retinopathy (advanced DR) compared to placebo
	Primed for upcoming pivotal Phase 2/3 study	<ul style="list-style-type: none"> End-of-phase 2 meeting completed with FDA alignment on primary endpoint SPA submitted to secure alignment on study design and statistical analysis plan
	Proven development team	<ul style="list-style-type: none"> Over 60 years of combined Ophthalmology experience Senior management involved in the research, development, and approval of numerous Ophthalmic products, including Vabysmo®, Syfovre®, Miebo™, Oxervate®, Ryzumvi™, Xiidra®, Eysuvis®, and Inveltys®
	Revenue-generating partnership	<ul style="list-style-type: none"> In partnership with Viatriis, Ryzumvi™ expected to launch 1H 2024 for reversal of pharmacologically-induced mydriasis and two ongoing, funded Phase 3 studies in decreased visual acuity under low light conditions and presbyopia Provides for potential double-digit royalties and milestone payments

NPDR market calculated based on total DR market size of \$ 3.96 in 2023 and NPDR revenue share of 70.38% in 2023.
 AMD, age-related macular degeneration; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; FDA, Food & Drug Administration; GA, geographic atrophy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; SPA, Special Protocol Assessment.
 Vabysmo® is a trademark of Genentech, Inc.; Syfovre® is a registered trademark of Apellis Pharmaceuticals, Inc.; Miebo™ is a trademark of Bausch + Lomb Incorporated or its affiliates; Oxervate® is a registered trademark of Dompé Farmaceutici S.p.A.; RYZUMVI™ is a trademark of Ocuphire Pharma, Inc.; Xiidra® is a registered trademark of Bausch + Lomb Incorporated or its affiliates; Eysuvis® and Inveltys are registered trademarks of Alcon, Inc.
 1. Flaxel CJ, et al. Diabetic retinopathy preferred practice pattern®. Ophthalmology. 2020;127:85-145. 2. Prevalence of diabetic retinopathy. Centers for Disease Control and Prevention. Accessed December 21, 2023. <https://www.cdc.gov/visionhealth/visioncare/manifestations-prevalence.html> 3. Data on file

APX3330 is the Foundation of Our Retina Pipeline

PRODUCT CANDIDATE	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	REGULATORY APPROVAL	MILESTONES
APX3330 Oral pill	Diabetic Retinopathy						<ul style="list-style-type: none"> EOP2 meeting ✓ SPA submission ✓
APX2009	Geographic Atrophy						<ul style="list-style-type: none"> Preclinical proof-of-concept
APX2014	Retina						<ul style="list-style-type: none"> Select drug delivery technology and evaluate target disease
 (phentolamine ophthalmic solution) 0.75% Eye drop Licensed to Viatris	Reversal of pharmacologically-induced mydriasis						<ul style="list-style-type: none"> Approved (Sept 2023) ✓ Launch expected 1H 2024
	Presbyopia						<ul style="list-style-type: none"> VEGA-2 Ph 3 topline data (Q4 2023) ✓
	Decreased visual acuity under low light (mesopic) conditions						<ul style="list-style-type: none"> SPA Agreement ✓ LYNX-2 pivotal studies

*RYZUMVI™ is indicated for the treatment of pharmacologically-induced mydriasis produced by adrenergic agonists (eg, phenylephrine) or parasympatholytic agents (eg, tropicamide).
 EOP, end of Phase; SPA, Special Protocol Assessment.
 RYZUMVI™ is a trademark of Ocuphire Pharma, Inc.

Diabetic Retinopathy is the Leading Cause of Vision Loss in Working-Age Adults in the US



What
is DR?

Common complication of diabetes, and results from damage to blood vessels in the retina, progressively leading to vision loss and impaired quality of life

	NPDR Non-proliferative Diabetic Retinopathy	PDR Proliferative Diabetic Retinopathy
CLINICAL PRESENTATION	Blood vessels weaken, bulge, close off, or leak into the retina	Growth of new abnormal blood vessels in the retina (neovascularization), vitreous hemorrhage, and scar tissue
COMMON SYMPTOMS	Asymptomatic (early stages) Floaters, blurry vision, dark spots (later stages)	Vision loss, blindness
TREATMENT	"Watch and wait" is SoC IVI anti-VEGF injections (advanced disease)	IVI anti-VEGF injections Panretinal laser photocoagulation Vitreotomy surgery

anti-VEGF, anti-vascular endothelial growth factor therapy; DR, diabetic retinopathy; IVI, intravitreal injection; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; SoC, standard of care.

1. Diabetic Eye Disease. National Institute of Diabetes and Digestive and Kidney Diseases. <https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/diabetic-eye-disease#:~:text=Diabetic%20retinopathy%20is%20the%20most,of%20blindness%20by%2095%20percent>. Accessed on March 20, 2024. 2. Diabetic retinopathy: Causes, symptoms, treatment. American Academy of Ophthalmology. Accessed on December 22, 2023. <https://www.aao.org/eye-health/diseases/what-is-diabetic-retinopathy> 3. Flaxel CJ, et al. *Ophthalmology*. 2020;P66-P145.



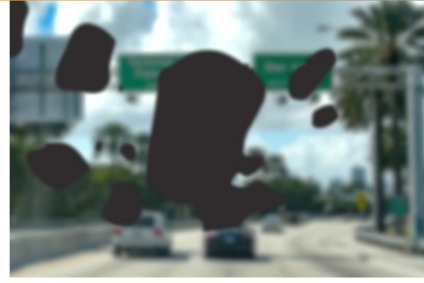
DR Progression Can Have a Significant Impact On Functional Vision

NPDR

Minimal visual disruption



PDR
Significant vision loss

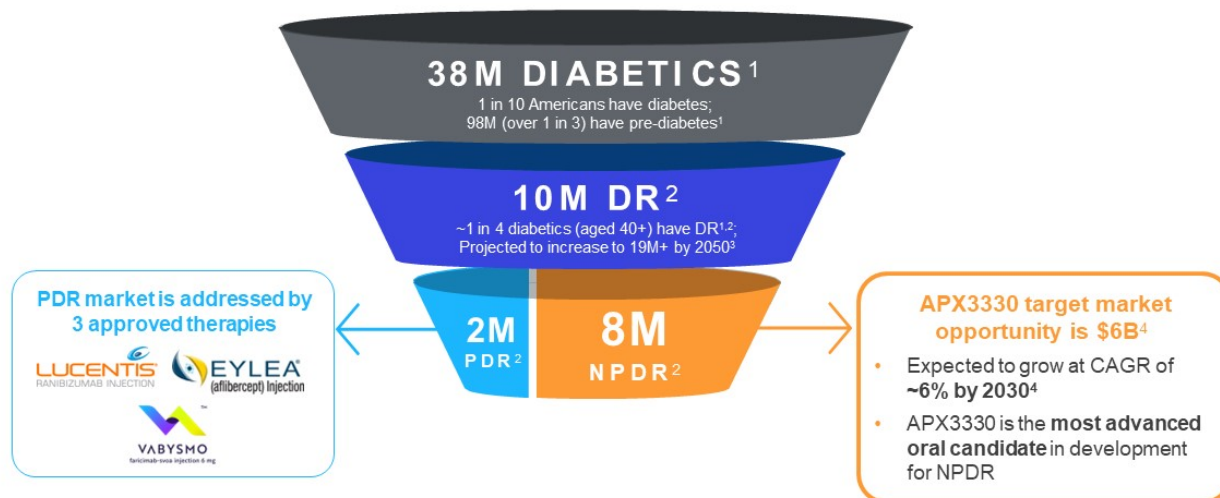


~50% of patients with severe NPDR will progress to PDR in 1 year¹

Treating diabetic retinopathy early can reduce the risk of blindness by 95%²

NOTE: The severity of vision loss varies between individuals with DR.
DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.
1. [No authors listed]. ETDRS report number 12. *Ophthalmology*. 1991;98:623-633. 2. Diabetic Eye Disease. National Institute of Diabetes and Digestive and Kidney Diseases. <https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/diabetic-eye-disease#:~:text=Diabetic%20retinopathy%20is%20the%20most,of%20blindness%20by%2095%20percent>. Accessed on March 5, 2024.

NPDR Represents a Large Segment of the Growing DR Market
















NPDR market calculated based on total DR market size of 8.9B in 2023 and NPDR revenue share of 70.38% in 2023.⁴

CAGR, compound annual growth rate; DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Lucentis® is a registered trademark of Genentech, Inc.; Eylea® is a registered trademark of Regeneron Pharmaceuticals, Inc.; Vabysmo® is a trademark of Genentech, Inc.

1. Diabetes. A report card. Centers for Disease Control and Prevention. Accessed December 21, 2023. <https://www.cdc.gov/diabetes/library/socialmedia/infographics/diabetes.html> 2. Prevalence of diabetic retinopathy. Centers for Disease Control and Prevention. Accessed December 21, 2023. <https://www.cdc.gov/visionhealth/vehsa/estimates/diabetic-retinopathy-prevalence.html> 3. Lundeen EA, et al. JAMA Ophthalmol. 2023;141(8):747-754. 4. Grand View Research. Diabetic retinopathy market analysis, 2018-2023. 2023. <https://www.grandviewresearch.com/industry-analysis/diabetic-retinopathy-market>

APX3330 has the Potential to be the First Oral Treatment for DR

Non-invasive therapies	COMPANY	DRUG	PHASE	TARGET	ROA
		APX3330	Phase 2/3	Ref-1 inhibitor	Oral
		Runcaciguat	Phase 2	Guanylate cyclase activator	Oral
		OPL-0401	Phase 2	ROCK 1/2 inhibitor	Oral
		VX-1	Phase 2	AOC-3 inhibitor	Oral
		RG7774	Discontinued	CB2 receptor (cannabinoid)	Oral
Invasive therapies (IVT/suprachoroidal)		OTT166	Phase 2 <i>Missed efficacy endpoint</i>	Integrin inhibitor	Eye drop
	COMPANY	DRUG	PHASE	TARGET	ROA
		Eylea® (afibercept)*	Commercial	VEGF-A/B; PlGF	Intravitreal
		Lucentis® (ranibizumab)†	Commercial	VEGF-A	Intravitreal
		KSI-301 (tarcocimab)	Phase 3	VEGF	Intravitreal
		EYP-1901	Phase 2	Voloronib (TKI)‡	Intravitreal
		BI 764524	Phase 2	Anti-Sema3A	Intravitreal
		OTX-TKI	Phase 1	Axitinib (TKI)‡	Intravitreal
		RGX-314	Phase 2	AAV8 VEGF	Suprachoroidal (gene therapy)

AAV8, adeno-associated virus 8; AOC-3, Amine oxidase copper-containing 3; CB2, cannabinoid receptor 2; DR, diabetic retinopathy; PlGF, placental growth factor; Ref-1, reduction-oxidation effector factor-1;

ROCK, rho kinase; Sema3A, semaphorin3A; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.

Eylea® is a registered trademark of Regeneron Pharmaceuticals, Inc.; Lucentis® is a registered trademark of Genentech, Inc.

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).

*Trials to support approval: Panorama clinical trial; †Trials failed as orals in Phase 2 due to dose limiting adverse events (e.g., liver and cardiovascular); ‡Failed as oral/systemic treatments in retina due to dose limiting toxicity

Sources: Company websites and www.clinicaltrials.gov

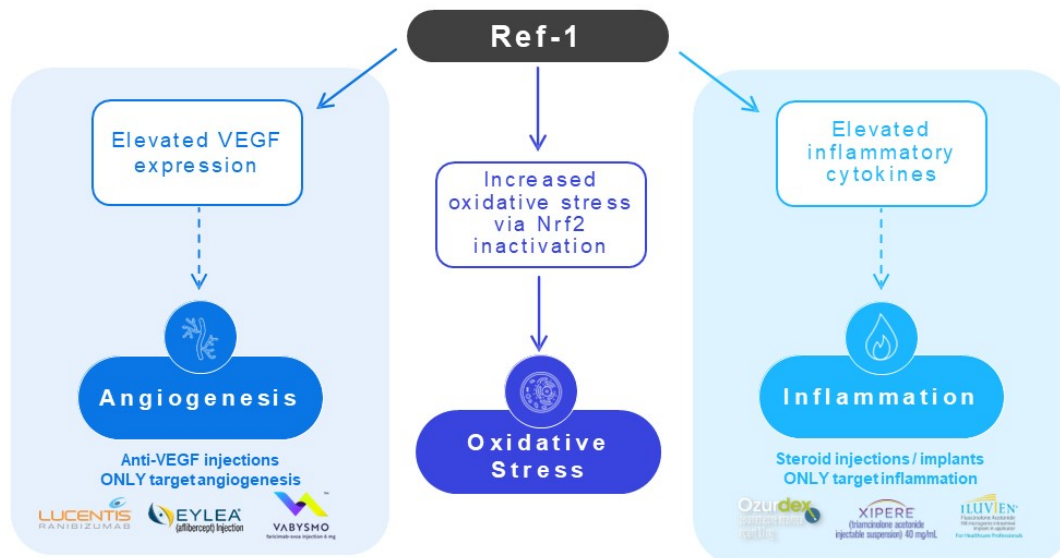
APX3330

The most advanced oral program currently in development for diabetic retinopathy



Ref-1 Mediates Multiple Pathways Involved in DR

Current Invasive Treatments Only Target a Single Pathway



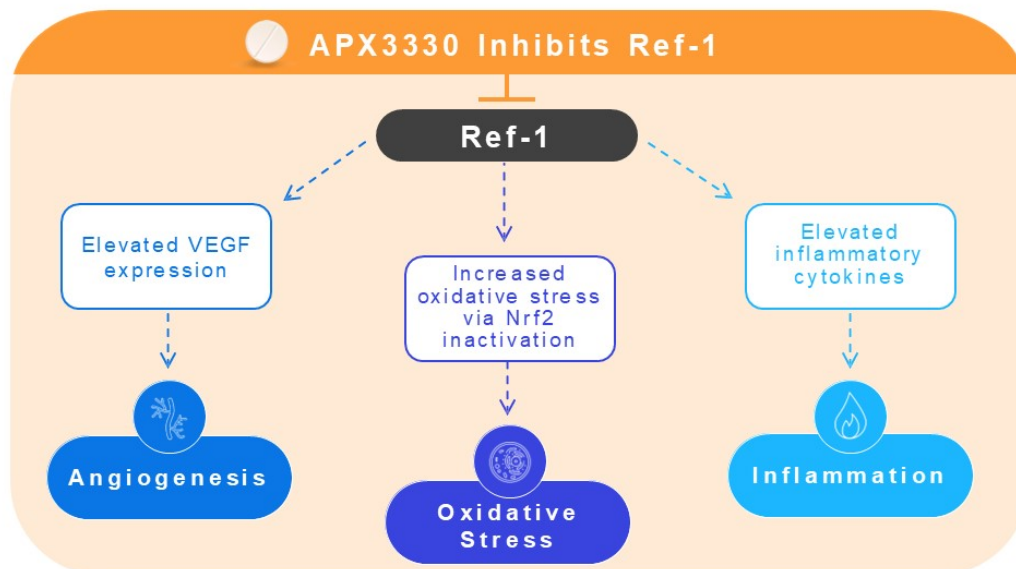
NOTE: Ozurdex®, Xipere®, and Iluvien® are not indicated for the treatment of DR.

Lucentis® is a registered trademark of Genentech, Inc.; Eylea® is a registered trademark of Regeneron Pharmaceuticals, Inc.; Vabysmo® is a trademark of Genentech, Inc.; Ozurdex is a registered trademark of Allergan, Inc., an AbbVie company; Xipere® is a registered trademark of Clearside Biomedical, Inc.; Iluvien is a registered trademark of Alimera Sciences, Inc.

Nrf2, nuclear factor erythroid 2-related factor 2; Ref-1, reduction-oxidation effector factor-1; VEGF, vascular endothelial growth factor.

1. Logsdon DP, et al. *Sci Rep*. 2018;8:13759. 2. Li Y, et al. *Redox Biology* 2. 2014;485-494. FDA.

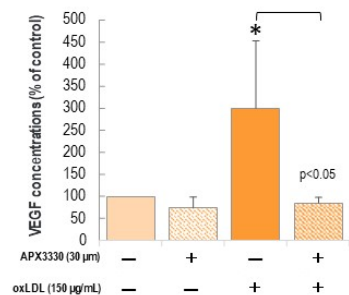
APX3330 Inhibits Ref-1-mediated Angiogenesis, Oxidative Stress, and Inflammation



Nrf2, nuclear factor erythroid 2-related factor 2; Ref-1, reduction-oxidation effector factor-1; TNF- α , tumor necrosis factor alpha; VEGF, vascular endothelial growth factor.
1. Logsdon DP, et al. *Sci Rep*. 2018;8:13759. 2. Li Y, et al. *Redox Biology* 2. 2014;4:85-494. FDA

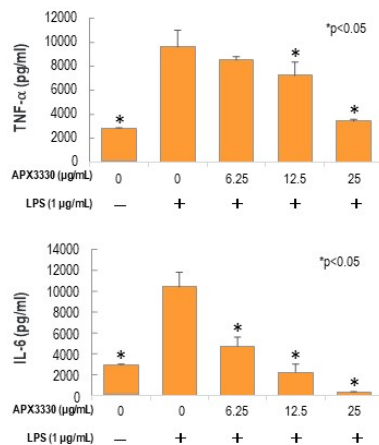
In vitro Data Validates Three Clinically Meaningful Pathways in DR

1 APX3330 restores physiologic VEGF levels¹

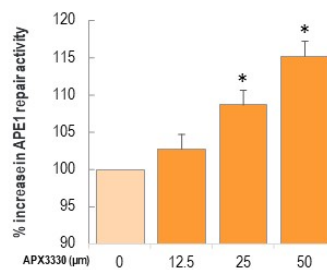


Restoration of physiologic VEGF treats pathologic disease while allowing a favorable tolerability profile

2 APX3330 reduces pro-inflammatory cytokines (in macrophages)²



3 APX3330 increases DNA oxidative repair and neuronal protection³



Reduced oxidative stress should improve integrity of the neurovascular unit

APE-1, apyrimidinic endonuclease 1; ARPE, spontaneously arising retinal epithelial cell line; LPS, lipopolysaccharide; oxLDL, oxidized low density lipoprotein; TNF-α, tumor necrosis factor-α; IL-6, interleukin 6; VEGF, vascular endothelial growth factor.
¹ Li Y, et al. *Redox Biology* 2. 2014;485-494. ² Jedinak A, et al. *Anticancer Research*. 2011;379-386. ³ Kelley MR, et al. *PLoS One*. 2014;9:e106485.

ZETA-1 Clinical Trial

A Phase 2 Randomized, Placebo-Controlled,
Double-Masked Study of APX3330 in DR is Complete



ZETA-1 Phase 2 Study Design and Demographics

- **Primary endpoint:** % of subjects with a ≥ 2 step improvement in monocular ETDRS DRSS at week 24
- **Study eye:** DR graded moderately severe to severe NPDR or mild PDR (monocular DRSS 47, 53, or 61)
- **Fellow eye:** No exclusion*

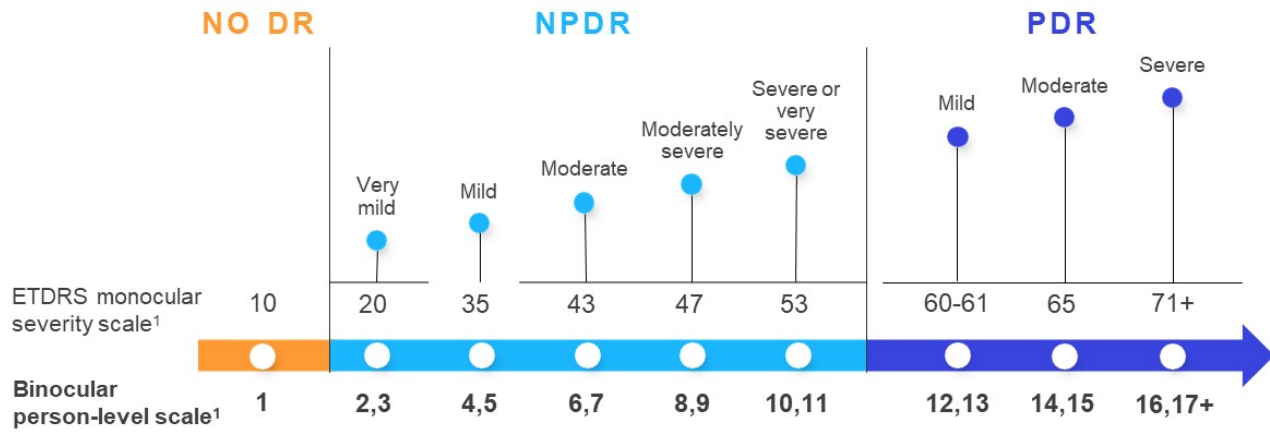


Baseline DRSS Scores		Placebo (n=52)	APX3330 (n=51)
DRSS Score – Study Eye			
47	Moderately severe to severe NPDR	18 (35%)	22 (43%)
53	Moderately severe to severe NPDR	28 (54%)	25 (49%)
61	Mild PDR	6 (12%)	4 (8%)
DRSS Score – Fellow Eye			
43 or Lower	Mild to moderate NPDR or better	12 (23%)	15 (29%)
47	Moderately severe to severe NPDR	22 (42%)	15 (29%)
53	Moderately severe to severe NPDR	11 (21%)	14 (28%)
61	Mild PDR	4 (8%)	1 (2%)
65 or Higher	Moderate to severe PDR	3 (6%)	4 (8%)

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

*Two APX3330 subjects did not have available DRSS scores in the fellow eye at screening.
 BID, twice-daily; CST, central subfield thickness; DME, diabetic macular edema; DRSS, Diabetic Retinopathy Severity Scale; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.
 Source: ZETA-1 Table 14.1.2.1

Binocular DRSS is a Validated and Well-Established Scale to Evaluate Systemic Therapies



≥ 3-step worsening on the binocular DRSS is considered clinically meaningful

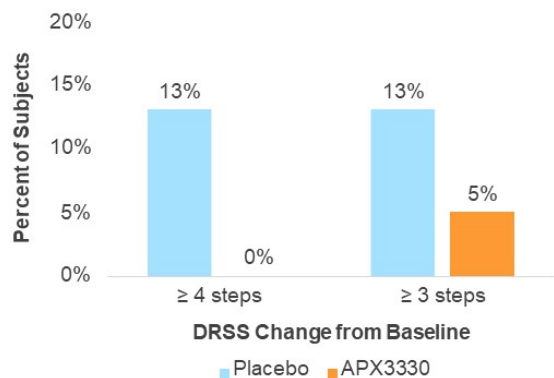
Subjects graded based on fundus photographs (images of the retina taken with a fundus camera).

DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

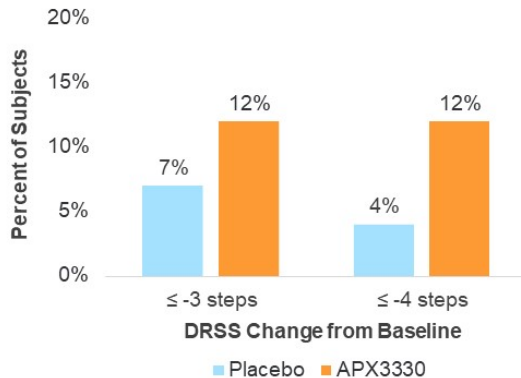
1. Chew EY, et al. *N Engl J Med*. 2010;363:233-44.

ZETA-1 Analysis: Fewer APX3330-treated Subjects Worsened and More Improved

Percentage of Subjects with Worsening at Week 24 on the Binocular DRSS Person-Level Scale (Observed Cases)

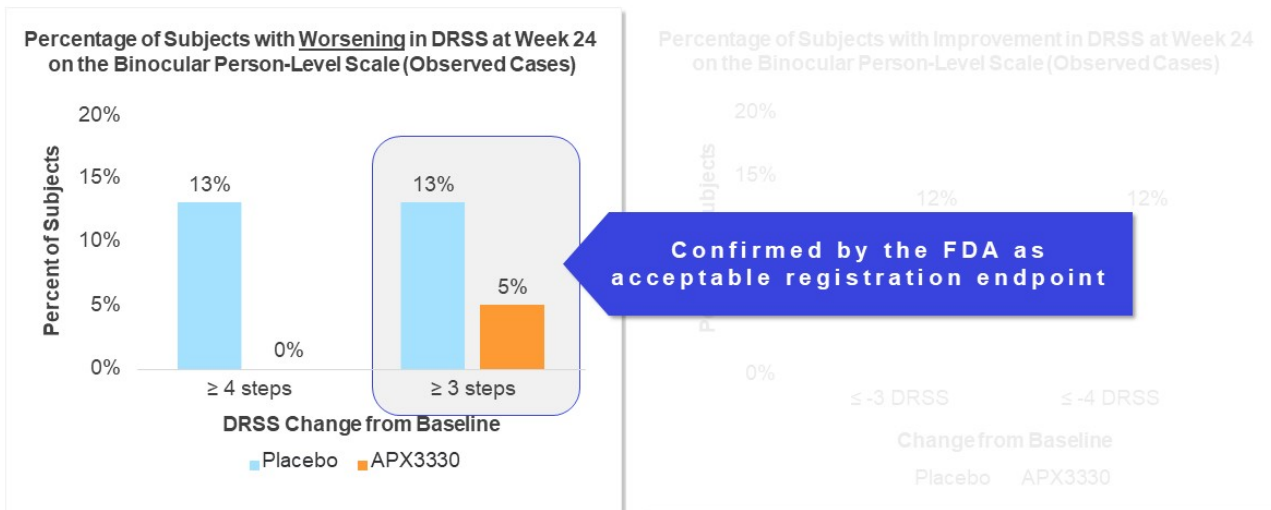


Percentage of Subjects with Improvement at Week 24 on the Binocular DRSS Person-Level Scale (Observed Cases)



Observed differences between groups were not statistically significant.
DRSS, Diabetic Retinopathy Severity Scale.
Observed cases: Subjects with DRSS scores at week 24.
Source: Zeta 1 Table 14.2.2.9.2

ZETA-1 Analysis: Fewer APX3330-treated Subjects Worsened

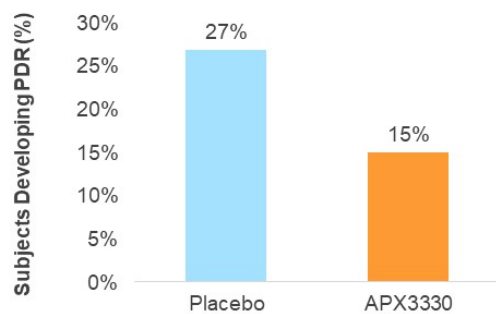


Observed differences between groups were not statistically significant.
DRSS, Diabetic Retinopathy Severity Scale; FDA, Food & Drug Administration.
Observed cases: Subjects with DRSS scores at week 24.
Source: Zeta 1 Table 14.2.2.9.2

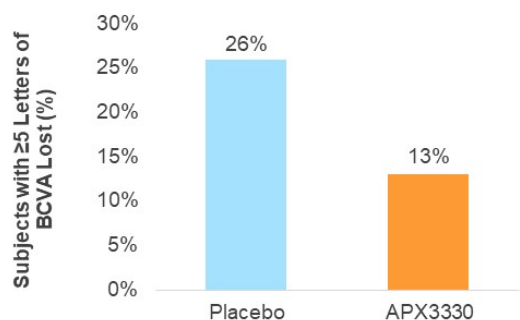
APX3330 Decreased Rates of Developing PDR and Vision Loss

APX3330 prevented progression of structural retinal abnormalities

Percentage of Subjects Developing PDR
by Week 24 (mITT Population)



Percentage of Subjects with ≥ 5 Letters of BCVA Lost
at Week 24 (Observed Cases)



Observed differences between groups were not statistically significant.
BCVA, best-corrected visual acuity; mITT, modified intention-to-treat; PDR, proliferative diabetic retinopathy.
Observed cases: Subjects with DRSS score at week 24.
Source: ZETA-1 Table 14.2.6.7.2; Table 14.3.6.5

APX3330 Demonstrated a Favorable Safety and Tolerability Profile Consistent with Prior Studies

	Placebo (n=52)	APX3330 (n=51)
Total AEs	120	91
Total treatment-related AEs	14	14
Subjects with treatment-related AEs	10 (20%)	10 (19%)
Withdrawals due to treatment-related AEs	1 (2%)	1 (2%)

AEs in >5% of Subjects

	All AEs		Treatment-related AEs	
	Placebo (n=52)	APX3330 (n=51)	Placebo (n=52)	APX3330 (N=51)
Ocular AEs				
DME	5 (10%)	2 (4%)	1 (2%)	0
DR	6 (12%)	1 (2%)	1 (2%)	0
Vitreous detachment	3 (6%)	0	0	0
Cataract	1 (2%)	3 (6%)	0	0
Non-ocular AEs				
Pruritus (itching)	1 (2%)	6 (12%)	1 (2%)	3 (6%)
Rash	1 (2%)	3 (6%)	1 (2%)	2 (4%)
COVID-19	5 (10%)	1 (2%)	0	0
SARS CoV-2 test positive	3 (6%)	0	0	0

APX3330 Safety Profile

- Ocular AEs similar between APX3330 and placebo
- Lower incidence of clinical DME/DR worsening with APX3330
- Pruritus was mild and resolved without APX3330 dose de-escalation or discontinuation
- Subjects with DR continued routine medications to manage comorbid conditions

AE, adverse event; DME, diabetic macular edema, DR, diabetic retinopathy.
Source: ZETA-1 Clinical Trial. Tables: 14.3.1.1, 14.3.1.7, 14.3.1.10, 16.2.7.

ZETA-2 Clinical Trial

A Phase 2/3 Randomized, Placebo-Controlled,
Double-Masked Study of APX3330 in NPDR is Planned

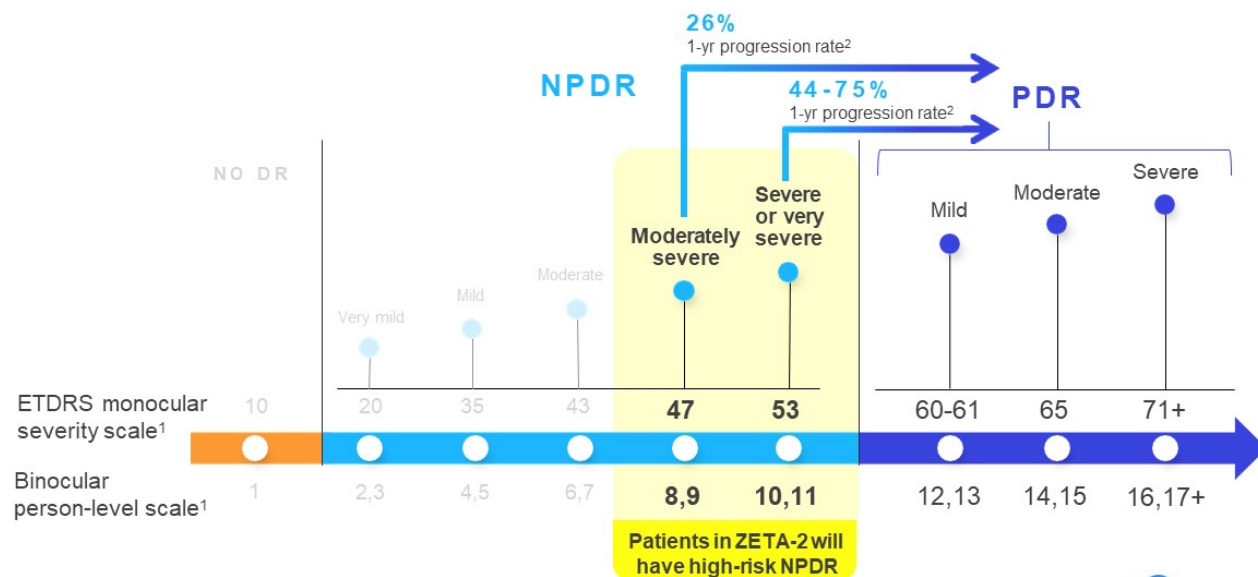


Optimizing ZETA-2 for Success

	Phase 2 ZETA-1	Phase 2/3 ZETA-2
Duration	24 weeks (6 months)	48 weeks (12 months)
Eligibility	Study eye (1 eye)	Binocular (2 eyes)
Sample size	N=103	N=300
Primary endpoint	≥ 2-step DRSS improvement in the study eye	≥ 3-step DRSS worsening on a binocular person-level scale
Baseline DRSS score	47, 53, 61 in study eye; Fellow eye no exclusion	47 or 53 in one eye; Fellow eye 43, 47, 53
Key exclusion	DME in study eye	PDR or DME in either eye

DME, diabetic macular edema; DRSS, Diabetic Retinopathy Severity Scale; PDR, proliferative diabetic retinopathy.

High-Risk NPDR Patients are More Likely to Progress Thereby Providing an Enriched Study Population for ZETA-2



DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.
 1. Chew EY, et al. *N Engl J Med*. 2010;363:233-44. 2. [No authors listed]. ETDRS report number 12. *Ophthalmology*. 1991;98:823-833.

Observed Rates of Progression Increase as DR Severity Increases

Based on Landmark NEI ETDRS Study of Over 3,700 Patients

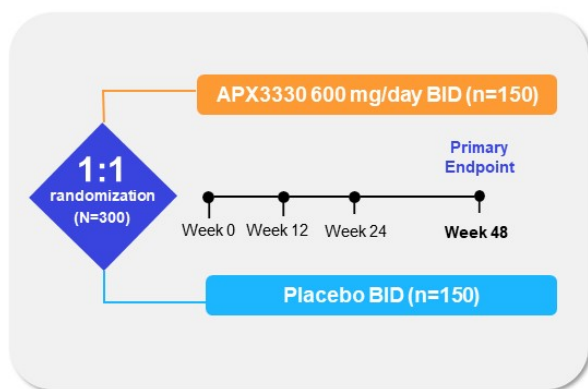
Placebo
progression
rate
≥3 steps
correlates
with PDR
development

DRSS level		1-year progression rate to ANY PDR ¹	1-year progression rate to HIGH-RISK PDR ²
43	Moderate NPDR	12%	3%
47	Moderately severe NPDR	26%	9%
53a to d	Severe NPDR	44 – 51%	15%
53e	Very Severe NPDR	75%	45%
61	Mild PDR	–	22%
≥65	Moderate PDR	–	46%

In ZETA-1, 13% of placebo patients worsened by ≥3 steps at 6 months, consistent with observed rates in this landmark study³

DR, diabetic retinopathy; NEI, National Eye Institute; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.
1. [No authors listed]. ETDRS report number 12. *Ophthalmology*. 1991;98:823-833. 2. ETDRS report number 9. *Ophthalmology*. 1991;98:766-785. 3. Data on file.

Optimized Study Design Positions ZETA-2 for Success



- ✓ **Enriched patient population** of high-risk NPDR progressors
- ✓ **≥3 step worsening** is associated with a higher likelihood of PDR progression in the proposed study population
- ✓ **Significant placebo progression rates expected** due to duration and population
- ✓ **Study is powered above 80%** to detect delta between APX3330 and placebo, similar to ZETA-1

Globally Recognized Retina Specialists Support APX3330 Development



"If ZETA-1 results are repeated in Phase 3, I would **place virtually all of my diabetic patients on oral APX3330** and treat locally only as needed."

Jeff Heier, MD

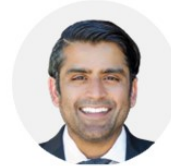
Ophthalmic Consultants of Boston



"Ref-1 biology targets three pillars of diabetic eye disease: **angiogenesis, inflammation, and oxidative stress**. This is promising in the quest to provide non-invasive, early options for patients."

Peter Kaiser, MD

Cleveland Clinic



"I enjoy working with the team to develop an **innovative protocol design to enroll the patients most likely to have progressive disease** while keeping the study practical to help enrollment."

Arshad Khanani, MD

Sierra Eye Associates

Partnership with Viatris

Ryzumvi™ (phentolomine ophthalmic solution) 0.75%



RYZUMVI™ is a trademark of Ocuphire Pharma, Inc.

Global Partnership with Viatris for Ryzumvi™



Partner for global commercialization



Fully-funded development; Viatris responsible for commercialization



Allows Ocuphire to focus on APX3330 and pipeline



Strengthens cash position

- Ryzumvi approved for the reversal of pharmacologically-induced mydriasis and expected to launch in 1H 2024
- Licensing agreement provides funding for 2 additional indications, with Viatris responsible for commercialization
- Two Phase 3 studies ongoing in presbyopia and dim light disturbances
- Received \$35M upfront cash payment upon licensing agreement
- \$120M in potential regulatory and commercial milestone payments → first \$10M milestone met for Ryzumvi approval
- Potential for tiered double-digit royalties

All 3 Indications Have Sizeable Potential US Patient Populations



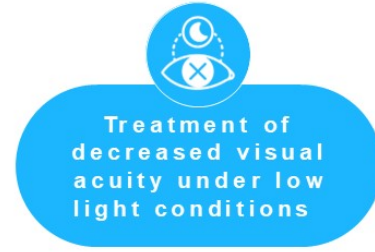
100M

eye dilations conducted
every year²



133M

presbyopes³



600-700K

laser vision correction
procedures per year⁴

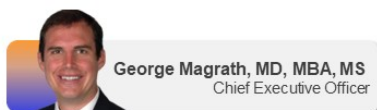
35% of LASIK patients
report dim light disturbances⁵

*RYZUMVI™ is indicated for the treatment of pharmacologically-induced mydriasis produced by adrenergic agonists (eg, phenylephrine) or parasympatholytic agents (eg, tropicamide).

RYZUMVI™ is a trademark of Ocuphire Pharma, Inc.
1. Ryzumvi. Prescribing Information. Ocuphire Pharma, Inc.; 2023. 2. Wilson FA, et al. *J Ophthalmol*. 2015;2015:435606. 3. Berdahl J, et al. *Clin Ophthalmol*. 2020;14:3439-3450. 4. Lindstrom RL. Millennials will be the next target for laser vision correction. *Ocular Surgery News*. April 1, 2019. Accessed December 12, 2023. <https://www.healio.com/news/ophthalmology/20190329/millennials-will-be-the-next-target-for-laser-vision-correction> 5. Marmalis N. *J Cataract Refract Surg*. 2014;40:343-344.



Highly Experienced Team with Meaningful Expertise



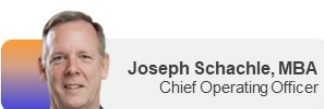
George Magrath, MD, MBA, MS
Chief Executive Officer



Nirav Jhaveri, MBA
Chief Financial Officer



Ash Jayagopal, PhD, MBA
Chief Scientific & Development Officer



Joseph Schachle, MBA
Chief Operating Officer



Ophthalmic Experts

- Over 60 years of proven clinical, commercial, and transaction experience
- Involved in the research, development, and approval of numerous Ophthalmic products:



Vabysmo® is a trademark of Genentech, Inc.; Syfovre® is a registered trademark of Apellis Pharmaceuticals, Inc.; RYZUMVI™ is a trademark of Ocuphire Pharma, Inc.; Eysuvis® and Inveltys are registered trademarks of Alcon, Inc.; Miebo™ is a trademark of Bausch + Lomb Incorporated or its affiliates; Oxervate® is a registered trademark of Dompé Farmaceutici S.p.A.; Xiidra® is a registered trademark of Bausch + Lomb Incorporated or its affiliates;

Ocuphire is Positioned to Transform the Treatment of Diabetic Retinopathy



Extensive understanding of large, underserved DR market



Addressing unmet needs by targeting multiple DR pathways with oral treatment



Demonstrated efficacy in slowing DR progression in completed Phase 2 study



Primed for pivotal Phase 2/3 study with FDA-confirmed endpoint



Proven development team with decades of Ophthalmic expertise



Revenue-generating partnership strengthens cash position

DR, diabetic retinopathy; FDA, Food and Drug Administration.