

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 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): **November 2, 2023**

Ocuphire Pharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or
organization)

001-34079
(Commission File Number)

11-3516358
(I.R.S. 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)

(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	Name of 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 November 2, 2023, Ocuphire Pharma, Inc. (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 8.01 Other Events.

On November 2, 2023, the Company issued a press release announcing the successful outcome of an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, supporting the advancement of oral APX3330 for the treatment of diabetic retinopathy into Phase 3 studies based on the recently completed Phase 2 ZETA-1 trial.

A copy of the press release is attached hereto as Exhibit 99.2 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
<u>99.1</u>	Corporate Presentation, dated November 2, 2023.
<u>99.2</u>	Press release issued by Ocuphire Pharma, Inc. on November 2, 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: November 2, 2023

By: /s/ Dr. George Magrath
Dr. George Magrath
Chief Executive Officer



November 2023





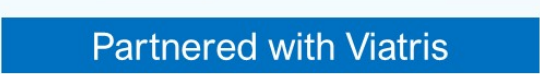
Ocuphire Corporate Presentation

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 Phentolamine Ophthalmic Solution (POS) to be a "best in class" presbyopia drop, and timing of planned future clinical trials for APX3330, APX2009 and APX2014, the advancement to Phase 3 registration path for APX3330, FDA agreement on Special Protocol Assessment, 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 and the ability of APX3330 to slow 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 Viatriis 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.

Ocuphire Pipeline

Product Candidate	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Regulatory Approval	Upcoming Milestones
APX3330 Oral Pill	Diabetic Retinopathy (DR)						<input checked="" type="checkbox"/> EOP2 Mtg October 2023 <input type="checkbox"/> Special Protocol Assessment (SPA) Submission
APX3330 Local Delivery	Retina						<input type="checkbox"/> Select retinal drug delivery technology
APX2009 and APX2014 Local Delivery	Retina						<input type="checkbox"/> Select retinal drug delivery technology
Phentolamine Ophthalmic Solution 0.75% Eyedrops	Pharmacologically-Induced Mydriasis						<input checked="" type="checkbox"/> APPROVED (RYZUMVI™) Sept 2023
	Presbyopia (P)						<input type="checkbox"/> VEGA-2 Phase 3 Topline Data Q4 2023
	Dim Light or Night Vision Disturbances (DLD)						<input checked="" type="checkbox"/> SPA Submitted <input type="checkbox"/> LYNX-2 2 nd Phase 3 trial (n=150+)

Management Team with Decades of Drug Development Experience



George Magrath, MD, MBA
CEO



Ronil Patel, MTech, MS
SVP, Operations and BD



Charlie Hoffmann, MBA
SVP, Corporate Development



Amy Rabourn, CPA
SVP, Finance



Drey Coleman
VP, Clinical Operations



Mitch Brigell, PhD
Head, Clinical Development and Strategy



Barbara Withers, PhD
VP, Clinical and Regulatory Strategy



Bindu Manne
Head, Market Development and Commercialization



Chris Ernst
Global Head, QA and Manufacturing



Laura Gambino
Director, Project Management



Daniela Oniciu, PhD
Global Head, R&D, Chemistry and Product Development



Corporate Highlights



Late-Stage Clinical Candidate for Retinal Diseases Represents 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 showed APX3330 prevented or slowed progression of Diabetic Retinopathy (DR)*
- *Successful EOP2 meeting with the FDA and a Special Protocol Assessment (SPA) to be submitted*



Phentolamine Ophthalmic Solution 0.75% (POS) for Refractive Disorders

- Global license agreement with Viatris to fund all development and commercialization for phentolamine indications:
 - ***RYZUMVI™ (Phentolamine Ophthalmic Solution) 0.75% for the treatment of pharmacologically-induced mydriasis received FDA approval in September 2023***
 - *Approval triggered \$10M milestone payment*
 - ***Presbyopia and Dim Light Disturbances*** currently in Phase 3



Experienced Retina Drug Development Team to Advance APX3330 into Phase 3

Diabetic Retinopathy Market and Unmet Need

Diabetic Eye Disease is a 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

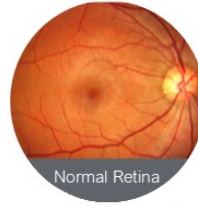


Type 1 diabetes (T1D): The body produces very little or no insulin, which means that patients need daily insulin injections to maintain blood glucose levels

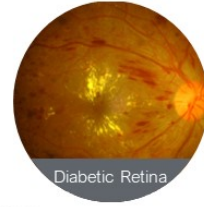


Type 2 diabetes (T2D): The most common form of diabetes - either the body does not produce enough insulin, or resists insulin

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



Normal Retina



Diabetic 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

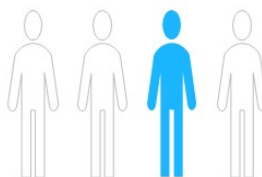
Diabetic Retinopathy at a Glance

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

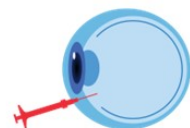


Physicians have **no non-invasive options** for NPDR with current standard being wait-and-monitor



Prevention of Progression is favored by payors with chronic diseases such as diabetes which is the primary driver of increased healthcare costs

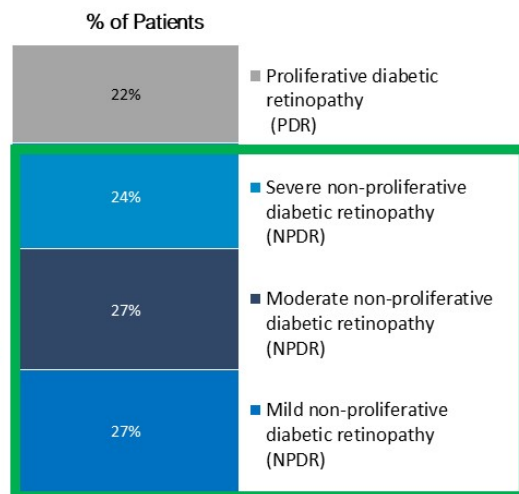
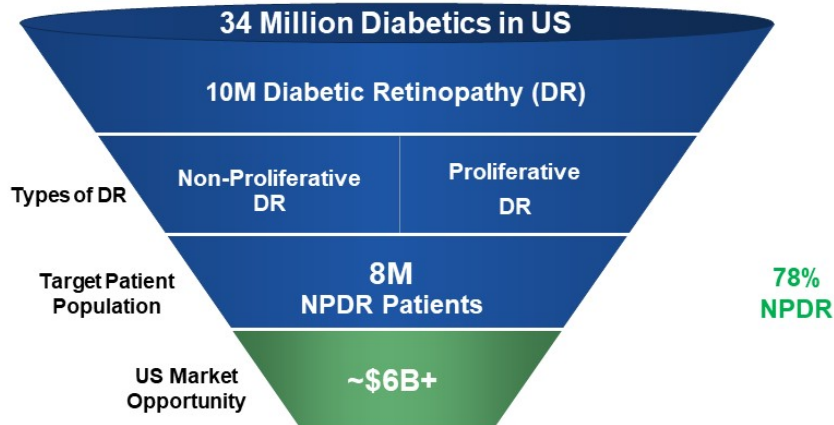
Majority of moderate to severe patients with DR are **not treated with anti-VEGF** due to injection burden and no benefit to visual acuity



U.S Diabetic Retinopathy Market

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

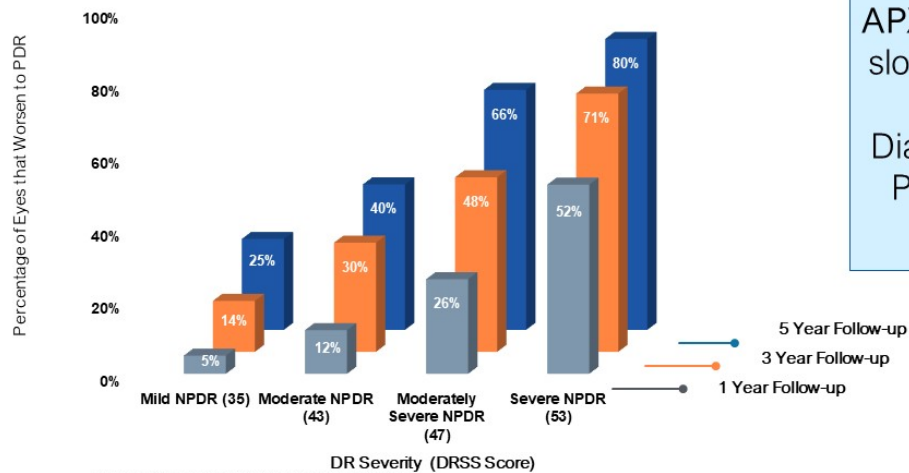
Real-World Chart Review of DR Patients in US



Progression of DR Severity Measured up to 5 Years

NPDR Patients are Rarely Treated with anti-VEGF Intravitreal Injections Due to Treatment Burden

Regardless of severity, all eyes worsen over time



Early Intervention with APX3330 can potentially slow the **progression** of Non-Proliferative Diabetic Retinopathy to Proliferative Diabetic Retinopathy

Diabetic Retinopathy Treatment Landscape

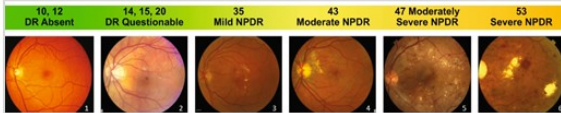
Current Standard of Care Based on Severity

Currently, There Are No Non-Invasive Treatments Approved for Early Intervention or Slowing the Progression

2021 ASRS PAT Survey
Closely monitor retinopathy and encourage systemic glycemic control

59.5%
60.5%

Mild to Moderate NPDR



Wait and Monitor for Progression

NPDR patients are monitored for progression requiring visits to the office every 4-6 months



Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

PDR









Anti-VEGF Injections

Gold standard Eylea® and Lucentis® injections are effective treatments in the first year for PDR

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

Landscape of Investigational Non-Invasive Therapies for Diabetic Retinopathy

Ocuphire's APX3330 is the Most Advanced 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-angiogenesis & Anti-inflammatory)	DR	Oral	✓	✓ 2022		2020: 2-step DRSS @wk24
 Roche	RG7774	CB2 receptor (cannabinoid)	DR	Oral	✓	X 2023		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
 Vantage	VX-01	AOC-3 inhibitor	DR	Oral	✓	○		2022: Not Disclosed
 OcUTERRA	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 is the **ONLY** candidate with validated retinal pathways of **angiogenesis** and **inflammation**.

Human exposure >10,000 subject days of systemic exposure at 600mg/day dose and a **favorable safety and tolerability profile**.



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 Therapeutics	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



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

*Trials to Support Approval

¹Panorama Clinical Trial

²Protocol I & T and Rise & Ride

APX3330 Background

APX3330 - Mechanism of Action Targeting Ref-1 Inhibition

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

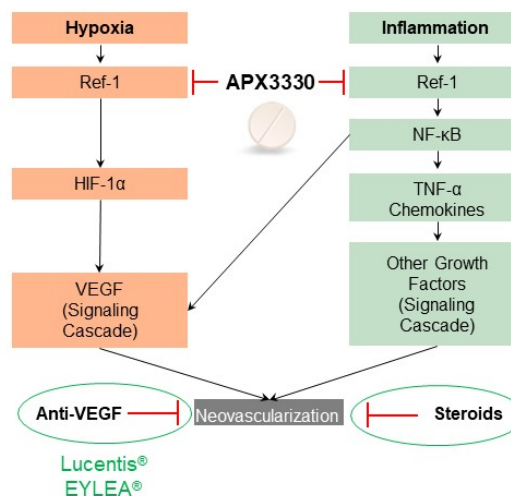
Ref-1 (reduction-oxidation effector factor-1)

A novel target for retinal diseases, is a transcription factor regulator of angiogenesis (VEGF) and inflammation (NFkB)

• Unique MOA decreases abnormal angiogenesis and inflammation

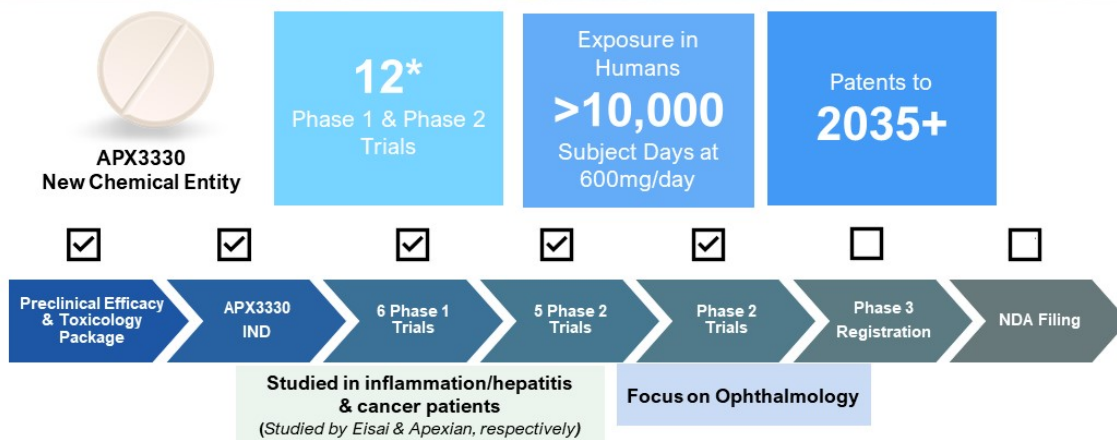
- APX3330 does not deplete the VEGF levels but rather normalizes VEGF levels to physiologic levels
- Anti-VEGF injections *do not* target inflammation

Mechanism of Action – Ref-1 Inhibition



APX3330: Drug Development History and Patents

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

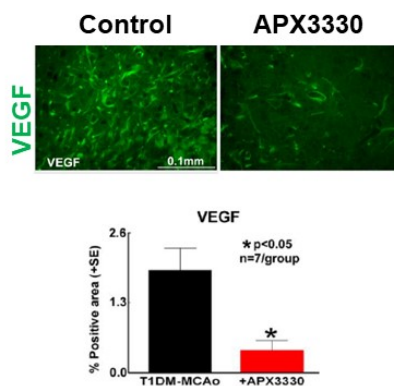


- Previously developed by Eisai for hepatic inflammatory indications and by Apexian for solid tumors in **11 Phase 1 and 2 trials**
- Extensively studied in over **20 in-vitro and animal studies** with favorable efficacy and safety results

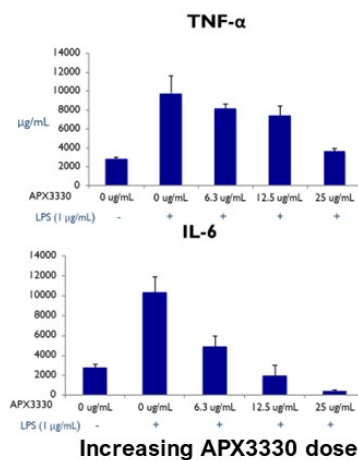
In-vitro Validation of Mechanism of Action

APX3330 Reduces VEGF levels and Inflammatory Cytokines; Provides Neuronal Protection

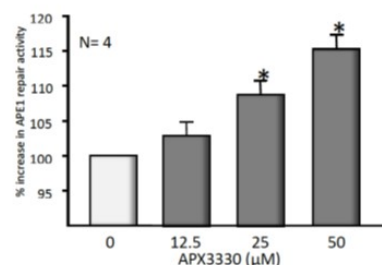
APX3330 reduces VEGF protein expression in preclinical stroke model



APX3330 reduces pro-inflammatory cytokines in LPS stimulated macrophages



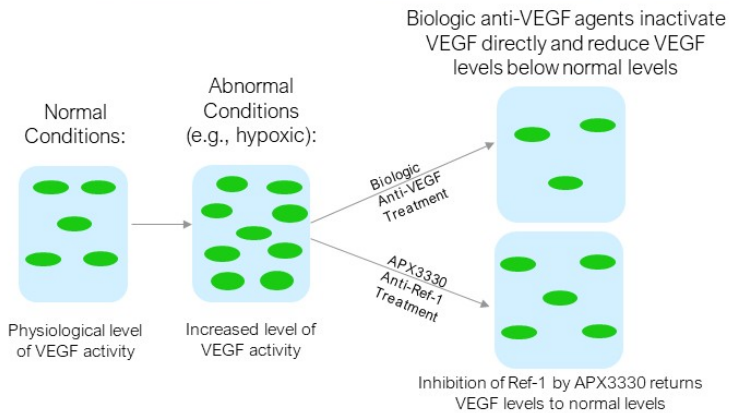
APX3330 increases DNA oxidative repair and neuronal protection



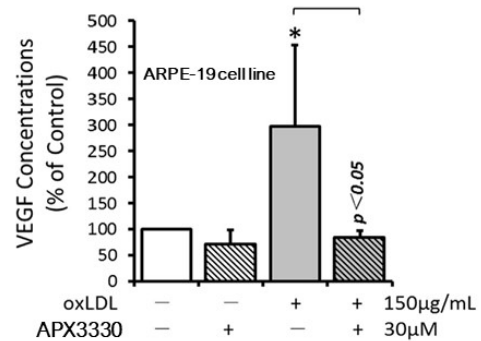
APX3330 enhances Ref-1 endonuclease activity in dorsal root ganglion neurons

APX3330 VEGF Effects in Normal Cells

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



APX3330 prevents VEGF overproduction in ARPE-19 cells



- 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

APX3330 ZETA-1 Clinical Trial

ZETA-1: Phase 2 Trial of Oral APX3330 in Subjects With Diabetic Retinopathy

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

Eligibility Criteria

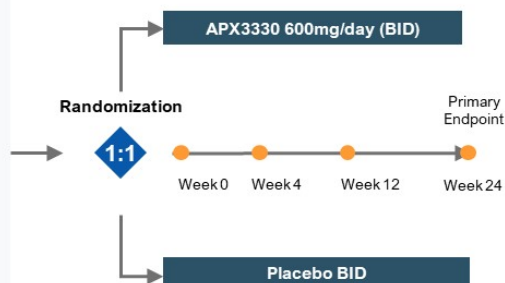
- 25 US sites
- N = 103 participants with moderately severe to severe NPDR or mild PDR (DRSS 47, 53, 61)

Key inclusion:

- ≥ 18 years of age
- DRSS 47, 53, or 61
 - Noncentral DME permitted²
- ETDRS BCVA ≥ 60 letters (20/63)

Key exclusion:

- OCT CST $> 320 \mu\text{m}^2$
- Center involved DME allowed in fellow eye
- Anti-VEGF within past 6 months³
- HbA1c $\geq 12.0\%$



Endpoints

Primary:

- % subjects with ≥ 2 step improvement on DRSS (Diabetic Retinopathy Severity Scale¹) at week 24

Secondary:

- DRSS improvement $\geq 1, \geq 2, \geq 3, \geq 4$ study eye, fellow eye, binocular
- DRSS worsening $\geq 1, \geq 2, \geq 3, \geq 4$, 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 data 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

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/m²) 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 NPDR 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 proliferative DR)	6 (12%)	5 (10%)

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

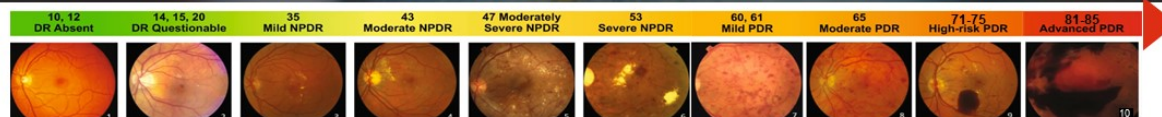
Key Visual Metrics

	APX3330 n=51	Placebo n=52	Total n=103
BCVA Study Eye <i>Letters (mean)</i>	81	78	80 (20/25 Snellen)
BCVA Fellow Eye <i>Letters (mean)</i>	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

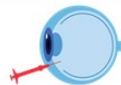
Good Visual Acuity
Fluid Below 320μm

Clinically Meaningful Registration Endpoints in DR

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



FDA accepts improvement OR worsening (slowing or 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 trials)



Systemic Drugs

Approvable endpoints for systemic drug in DR include either:

- ≥ 3-step DRSS improvement on a binocular scale
- ≥ 3-step DRSS worsening on a binocular scale

For oral administration, the binocular DRSS endpoint is distinct from anti-VEGF IVT precedent due to different delivery

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/iov.16-20356. PMID: 27699406; PMCID: PMC6016432.

End-of-Phase 2 Meeting Outcome

FDA Accepts the Binocular DRSS Person Scale For Phase 3 APX3330 DR Program

DRSS is a Validated Surrogate Endpoint

Level (worse eye/better eye)	Description	Scale Step
10/10	No DR	1
20/<20 20/20	Microaneurysms only, one or both eyes	2-3
35/<35 35/35	Mild NPDR, one or both eyes	4-5
43/<43 43/43	Moderate NPDR, one or both eyes	6-7
47/<47	Moderately severe NPDR, one eye	8
47/47	Moderately severe NPDR, both eyes	9
53/<53	Severe or very severe NPDR, one eye	10
53/53	Severe or very severe NPDR, both eyes	11
60 or 61/<60	Mild PDR and/or SPC, one eye	12
60 or 61/60 or 61	Mild PDR and/or SPC, both eyes	13
65/<65 65/65	Moderate PDR, one or both eyes	14-15
71+/<71 71+/71+	High risk PDR, one or both eyes	16-17+

In the binocular Person Scale, the worse eye is weighted instead of calculating the sum of both eyes

A 3-step change on this scale is considered clinically meaningful by FDA

Baseline 47,43 = Step 8

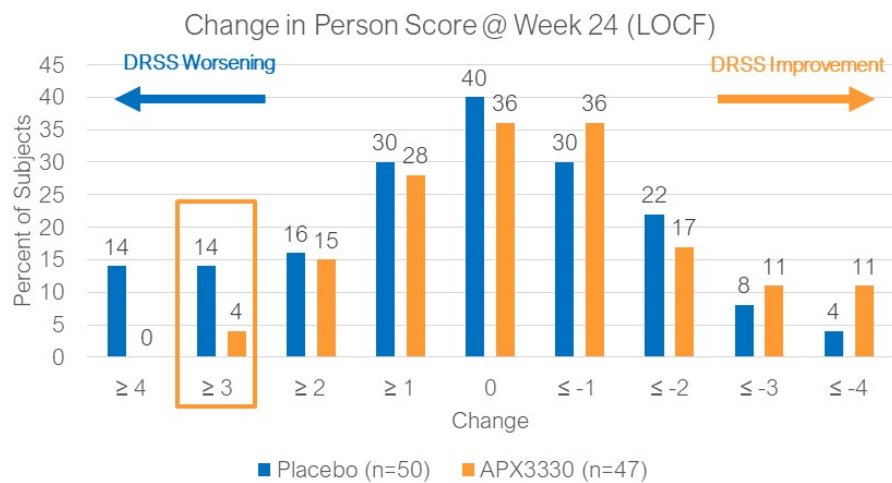
Final 47,47 = Step 9 (1-step change)

Final 53,43 = Step 10 (2-step change)

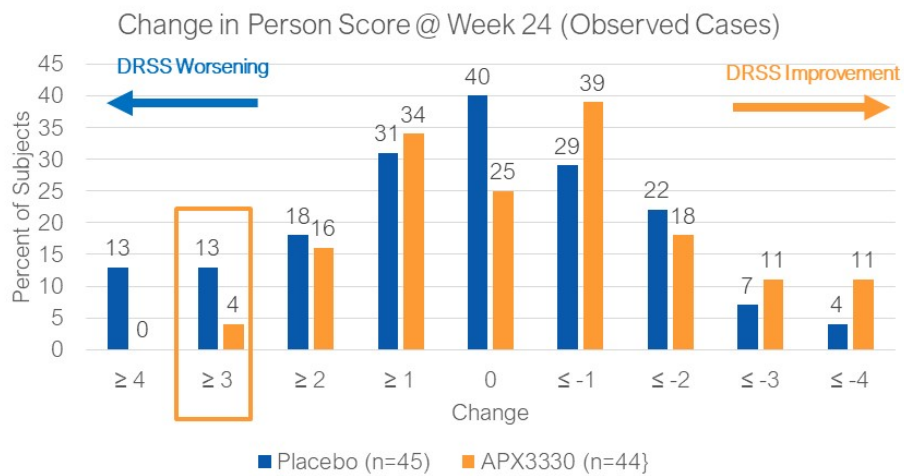
Final 61,43 = Step 12 (4-step change)

Final 61,53 = Step 12 (4-step change)

ZETA-1: Percent of Subjects with Improvement or Worsening in DRSS at Wk 24 on the Binocular Person Scale (LOCF)

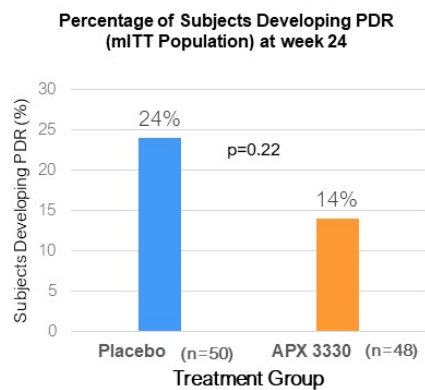


ZETA-1: Percent of Subjects with Improvement or Worsening in DRSS at Wk 24 on the Binocular Person Scale (Observed Cases)

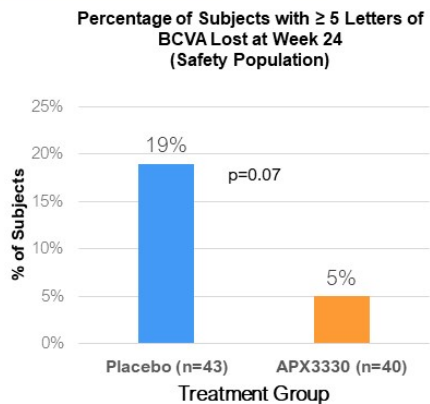


APX3330 Reduced % of Subjects Developing PDR and % Losing BCVA

APX3330 Prevented Progression of Structural Retinal Abnormalities



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



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

ZETA-1: Treatment of 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*		
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%)

Eye disorders

APX3330 Safety Profile:

- Limited AEs, most mild in severity
 - Pruritus: 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 Milestones

- Successful EOP2 FDA meeting completed in October 2023; agreement that a 3-step change on the binocular person scale is an approvable registration endpoint
- Submit Special Protocol Assessment (SPA)
- 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 *slowing or preventing progression* to reduce likelihood of vision loss in diabetic retinopathy patients

DR and 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 with unique MOA that inhibits Ref-1 which reduces VEGF and inflammatory cytokines to normal physiological levels
- Prevention of worsening is a clinically meaningful potential registration endpoint
- APX3330 demonstrated favorable safety and tolerability in diabetic patients
- **Successful EOP2 meeting with the FDA and a Special Protocol Assessment (SPA) to be submitted**
- 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

Phentolamine Ophthalmic Solution 0.75%

Global Partnership with Viatris for Phentolamine Ophthalmic Solution 0.75%

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



Partner for global commercialization



Fully funded development and commercialization costs for all 3 phentolamine indications



Allows Ocuphire to focus on APX3330 development



Strengthens cash position into 2025


- **\$35 million upfront**
- **Fully funded development and commercialization for all 3 indications**
- **\$130 million in regulatory and sales milestones**
 - First milestone payment of \$10 million on FDA approval for pharmacologically-induced mydriasis indication
- **Tiered double digit royalties through 2040**



**Phentolamine
Ophthalmic Solution
0.75%**

THREE INDICATIONS

**NEW
PARTNERSHIP
WITH VIATRIS**



Treatment of Pharmacologically-Induced Mydriasis

APPROVED



**RYZUMVI™ (Phentolamine Ophthalmic Solution)
0.75% for the Treatment of Pharmacologically-
Induced Mydriasis Produced by Adrenergic
Agonists (e.g., Phenylephrine) or
Parasympatholytic (e.g., Tropicamide) Agents**

Presbyopia

1

POS as a Single
Drop



2

POS with LDP
Adjunctive Therapy



Dim Light or Night Vision Disturbances (DLD)



Summary of Phentolamine Ophthalmic Solution 0.75% 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
Ryzumvi™ Approved September 2023	Return to baseline pupil diameter at 90 minutes after dilation	Met Phase 3 primary endpoint MIRA-3: 58% POS vs. 6% placebo MIRA-2: 49% POS vs. 7% placebo (p<0.0001) MIRA-4: 64% POS vs. 25% placebo	Efficacy across all mydriatic agents, iris color, 1 or 2 drops, and all ages (3-80)	<ul style="list-style-type: none"> No headaches No blurry vision ~5% mild redness No change in IOP No SAEs Most AEs were mild
Presbyopia (POS 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% POS vs. 12% placebo at 12 hrs post-POS dose (p=0.02)	Durable near vision (18 hrs) Optimal pupil size Pupillary light reflex	
Presbyopia (POS + LDP) Phase 3		Met Phase 2 primary endpoint Met planned Phase 3 primary endpoint VEGA-1: 61% combo post-LDP dose (30 min) + post-POS 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% POS vs. 3% placebo at Day 8 (p<0.05) and 21% in POS 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



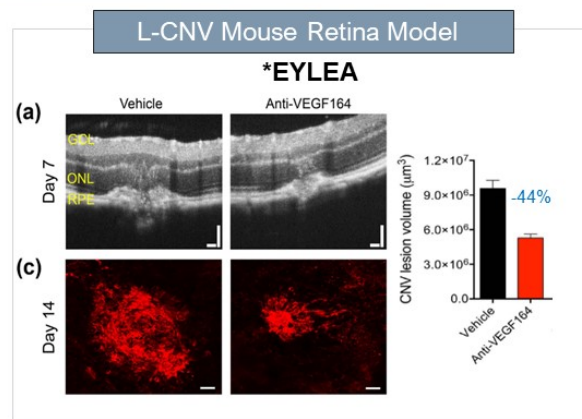
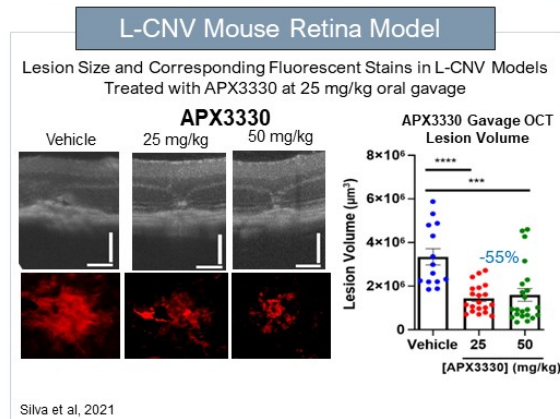
Global License Agreement with Viatris to Fund Development and Commercialization of Phentolamine Ophthalmic Solution 0.75% for All Refractive Indications



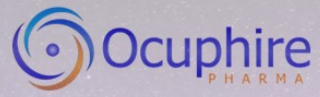
Strong Financial Position to Fund Operations into 2025

Preclinical Data: Oral APX3330 Blocks Neovascularization

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



- ✓ Efficacy was also seen after single intravitreal injection of 20µM APX3330 in mouse L-CNV model**
- ✓ Efficacy was also seen after dosing intraperitoneal injection of 50 mg/kg twice daily, 5 days on/2 days off, for 2 weeks in mouse L-CNV model***
- ✓ Efficacy was also seen after single intravitreal injection of 20µM APX3330 in Vldlr^{-/-} mice model****



Restore Vision & Clarity

www.ocuphire.com

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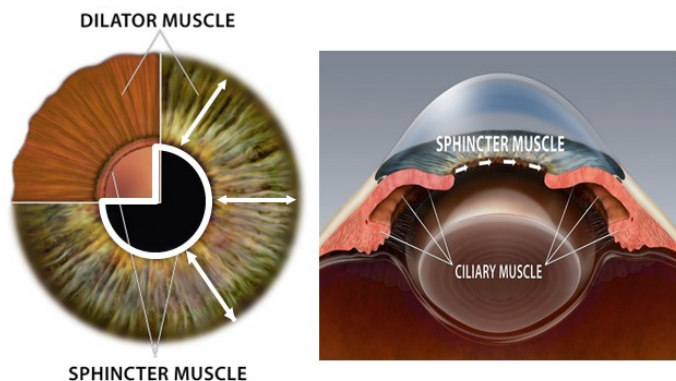
Ocuphire Pharma

Appendix

Phentolamine Ophthalmic Solution 0.75%'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 POS: a non-selective α Antagonist



Phentolamine blocks $\alpha 1$ receptors on the **Iris Dilator Muscle up to 24 hours**



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

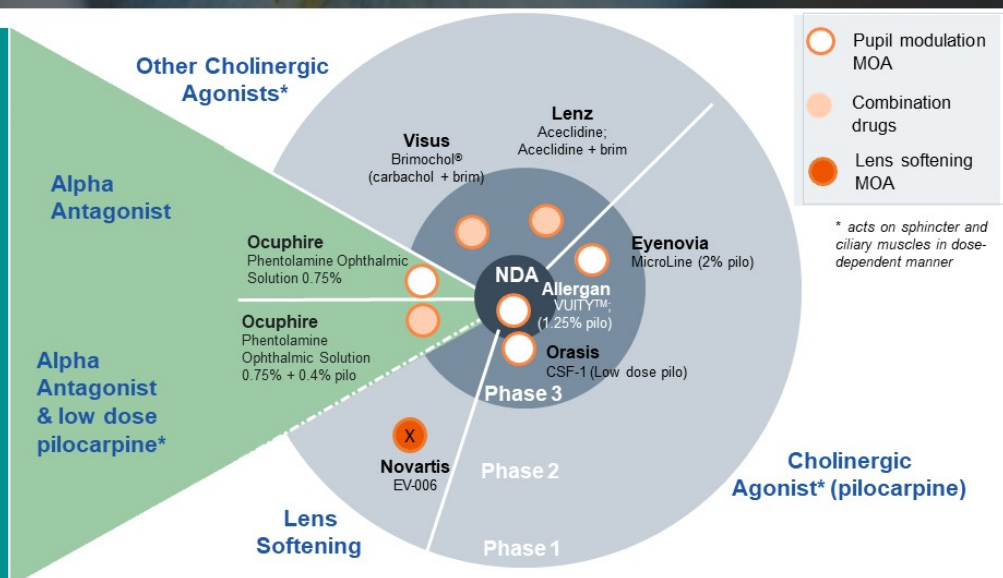
505(b)(2) Regulatory Pathway Supported by Prior Phentolamine Approvals in Non-Ophthalmic Indications

A New, Differentiated MOA and Combination Therapy Offers Tunability

➤ POS'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

➤ POS+LDP may offer added efficacy and tunability



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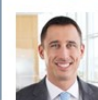
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Ocuphire Pharma Announces Successful End-of-Phase 2 Meeting with FDA for Oral APX3330 in Diabetic Retinopathy

Agreement on Phase 3 Primary Endpoint of 3-step Worsening on Binocular Diabetic Retinopathy Severity Scale (DRSS) Score

Company Plans to Submit a Special Protocol Assessment (SPA)

APX3330 has the Potential to be the First Oral Option for 8M Non-Proliferative Diabetic Retinopathy (NPDR) Patients in the US

FARMINGTON HILLS, Mich., November 2, 2023 (GLOBE NEWSWIRE) -- Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of retinal and refractive eye disorders, today announced the successful outcome of an End-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA), supporting the advancement of oral APX3330 for the treatment of diabetic retinopathy (DR) into Phase 3 studies based on the recently completed Phase 2 ZETA-1 trial.

"We are pleased to have FDA agreement on the primary endpoint for Phase 3 pivotal trials of APX3330 which we believe is the most advanced oral therapy currently in development for diabetic retinopathy," said George Magrath, M.D, MBA., M.S., Chief Executive Officer of Ocuphire. "Results from our Phase 2 ZETA-1 results demonstrate that oral APX3330 has the potential to slow or prevent clinically meaningful progression of diabetic retinopathy, as measured by the percentage of subjects with ≥ 3 -step worsening on a binocular diabetic retinopathy severity scale (DRSS), which will be the Phase 3 primary endpoint. As recommended by the FDA, Ocuphire plans to submit a Special Protocol Assessment to agree on the clinical trial protocol and statistical analysis plan for the Phase 3 trials and will share specifics on the study design parameters and anticipated timing once agreed with the FDA. We are grateful for the FDA's support and guidance and look forward to continued collaboration as we advance APX3330 into Phase 3 development."

The EOP2 meeting was supported by results from the previously completed Phase 2 ZETA-1 trial. The randomized, double-masked, placebo-controlled Phase 2 trial was designed to evaluate the efficacy and safety of oral APX3330 in diabetic retinopathy patients. A higher percentage of placebo-treated patients had ≥ 3 -step worsening on binocular DRSS from baseline compared to APX3330-treated patients at 24 weeks. APX3330 demonstrated favorable safety and tolerability in diabetic patients.

David Brown, M.D., F.A.C.S., co-chairman of the medical leadership board at Retina Consultants of America (RCA) said, “Given the increasing number of DR patients and current treatment options, I am encouraged by the results of the ZETA-1 trial showing that APX3330 can potentially slow or prevent progression to vision threatening diseases such as Proliferative Diabetic Retinopathy. The current treatment paradigm for NPDR patients is for physicians to monitor progression every 4-6 months depending on DR severity. Approved anti-VEGF therapies are not widely utilized in NPDR patients because of the necessity for consistent intravitreal injections in asymptomatic patients. A safe convenient oral medication that could slow or prevent diabetic retinopathy would be a major advance in our fight against diabetic blindness.”

About APX3330

APX3330 is a first-in-class, small molecule, oral inhibitor of the transcription factor regulator Ref-1 (reduction-oxidation effector factor-1). With a novel dual mechanism of action, APX3330 blocks the downstream pathways regulated by Ref-1 – which involve angiogenesis (VEGF) and inflammation (NFkB) – to decrease abnormal activation of both angiogenesis and inflammatory pathways that are implicated across several ocular diseases, including DR, DME, and age-related macular degeneration (AMD). APX3330 has shown a favorable safety and tolerability profile in 12 clinical trials conducted in healthy, hepatitis, cancer, and diabetic subjects.

About Ocuphire Pharma

Ocuphire Pharma, Inc. is a clinical-stage ophthalmic biopharmaceutical company focused on developing and commercializing small-molecule therapies for the treatment of retinal and refractive eye disorders.

Ocuphire’s lead retinal product candidate, APX3330, is a first-in-class small-molecule inhibitor of Ref-1 (reduction oxidation effector factor-1 protein). Ref-1 is a regulator of transcription factors such as HIF-1a and NF-kB. Inhibiting REF-1 reduces levels of vascular endothelial growth factor (“VEGF”) and inflammatory cytokines which are known to play key roles in ocular angiogenesis and inflammation. Through inhibition of Ref-1, APX3330 normalizes the levels of VEGF to physiologic levels, unlike biologics that deplete VEGF below the levels required for normal function. APX3330 is an oral tablet administered twice per day for the treatment of diabetic retinopathy (“DR”). A Phase 2 study in subjects with DR and an End-of-Phase 2 meeting have recently been completed, and a Special Protocol Assessment is planned to be submitted with the U.S. Food and Drug Administration (FDA).

DR affects approximately 10 million people with diabetes and is projected to impact over 14 million Americans by 2050. DR is classified as Non-Proliferative Diabetic Retinopathy (“NPDR”), the early stage of the disease in which symptoms may be mild or non-existent or Proliferative Diabetic Retinopathy (“PDR”) which is the more advanced stage of diabetic eye disease that can be highly symptomatic with loss of vision. Approximately 80% of DR patients have NPDR that will progress to PDR if left untreated. Despite the risk for visual loss associated with this disease, over 90% of NPDR patients currently receive no course of treatment apart from observation by their eye care specialist until they develop sight-threatening complications. This is due to the treatment burden of the frequent eye injections required with currently approved therapies for this disease. APX3330 as an oral tablet has the potential to be an early, non-invasive treatment for the 8 million NPDR patients in the US. Treatment with APX3330 is expected to delay or prevent progression of NPDR, thereby reducing the need for expensive intravitreal injections with anti-VEGF therapies and reducing the likelihood of vision loss due to DR.

Ocuphire has also in-licensed APX2009 and APX2014, which are second-generation analogs of APX3330. The unique dual mechanism of action of these Ref-1 inhibitors of reducing angiogenesis and inflammation could potentially be beneficial in treating other retinal diseases such as age-related macular degeneration, and geographic atrophy. Ocuphire is currently evaluating local delivery routes in addition to the systemic (oral) route as part of its pipeline expansion in retinal therapies.

Ocuphire has a partnership with Viatriis, Inc. to develop and commercialize phentolamine ophthalmic solution 0.75%. Phentolamine is a non-selective alpha-1 and alpha-2 adrenergic antagonist designed to reduce pupil size by uniquely blocking the alpha-1 receptors found on the iris dilator muscle without affecting the ciliary muscle. In September 2023, the FDA approved RYZUMVI™ (phentolamine ophthalmic solution 0.75%) to treat pharmacologically induced mydriasis produced by adrenergic agonists (e.g., phenylephrine) or parasympatholytic agents (e.g., tropicamide). Phentolamine ophthalmic solution 0.75% is also in Phase 3 clinical development for the treatment of presbyopia and dim light (night) vision disturbances.

For more information, 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 the End-of-Phase 2 meeting with the FDA to confirm Phase 3 registration endpoints, study parameters for Phase 3 pivotal studies, and FDA agreement on Special Protocol Assessment. 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) risks that the Viatriis partnership may not facilitate the commercialization or market acceptance of Ocuphire’s product candidates; (x) the success and timing of commercialization of any of Ocuphire’s product candidates and (xi) the maintenance of Ocuphire’s intellectual property rights. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by Ocuphire from time to time with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Ocuphire undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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