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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

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**FORM 6-K**

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**REPORT OF FOREIGN ISSUER  
PURSUANT TO RULE 13a-16 OR 15d-16  
OF THE SECURITIES EXCHANGE ACT OF 1934**

For the month of January, 2025

Commission File No. 001-39621

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**OPTHEA LIMITED**  
(Translation of registrant's name into English)

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Level 4  
650 Chapel Street  
South Yarra, Victoria, 3141  
Australia  
(Address of registrant's principal executive office)

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Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F.  
Form 20-F  Form 40-F

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**Explanatory Note**

On January 13, 2025, Opthea Limited (the "**Company**") posted an updated corporate presentation on the Company's website. Investors may access the presentation by visiting the "Investor Relations" section of the Company's website at [ir.opthea.com](http://ir.opthea.com).

In the corporate presentation, the Company announced that, based on current estimates, as of December 31, 2024, the Company had cash and cash equivalents of US\$130 million. These estimates are preliminary, unaudited and are subject to change upon completion of the Company's financial statement closing procedures. The review of the Company's financial statements for the three months ended December 31, 2024 is ongoing and could result in changes to this amount. The Company's registered public accounting firm has not audited, reviewed or performed any procedures with respect to these preliminary results and, accordingly, does not express an opinion or any other form of assurance about them.

The information contained in the corporate presentation is summary information that is intended to be considered in the context of the Company's filings with the Securities and Exchange Commission, the Australian Securities Exchange, and other public announcements that the Company makes, by press release or otherwise, from time to time.

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### Cautionary Statement Regarding Forward Looking Statements

Any statements in this report about future expectations, plans and prospects for the Company, including statements about the Company's estimated, unaudited cash and cash equivalents at December 31, 2024, and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "opportunity," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the completion of the Company's financial statement closing procedures and other risks and uncertainties included in the risk factors section of the Company's Annual Report on Form 20-F, filed with the U.S. Securities and Exchange Commission (the "**SEC**") on August 30, 2024, and other filings the Company makes with the SEC from time to time available at [www.sec.gov](http://www.sec.gov). All forward-looking statements contained in this report speak only as of the date on which they were made. The Company undertakes no obligation and does not intend to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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EXHIBIT INDEX

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<u>Exhibit</u>	<u>Description</u>
99.1	<a href="#">Opthea Corporate Presentation - Jan 2025</a>

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**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, thereto duly authorized.

**OPTHEA LIMITED**  
(Registrant)

By: /s/ Frederic Guerard  
Name: Frederic Guerard  
Title: Chief Executive Officer

Date: 01/13/2025

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# Transforming Patient Outcomes with Superior Vision Gains

Corporate Overview | January 2025

NASDAQ (OPT); ASX (OPT.AX)



# Disclaimer and Forward-looking Statements

This presentation includes general background information about the activities of Opthea Limited (ABN 32 006 340 567) ("Opthea" or "Company") and its affiliates and subsidiaries (together, the "Opthea Group"). The information contained in this presentation is in summary form and does not purport to be complete or to contain all material information about the Opthea Group which a prospective investor or purchaser may require in evaluating a possible investment in Opthea or acquisition of securities in Opthea. This presentation should be read in conjunction with Opthea's other period corporate reports and continuous disclosure announcements filed with the Australian Securities Exchange, the Australian Securities and Investments Commission and the U.S. Securities and Exchange Commission. The information in this presentation remains subject to change without notice. No member of the Opthea Group nor any director, officer, employee, adviser, agent or representative of any member of the Opthea Group (each an Opthea Party and together, the Opthea Parties) has any obligation to update or correct this presentation.

This presentation contains forward-looking statements within the meaning of the U.S. federal securities laws that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the therapeutic and commercial potential and size of the estimated market opportunity of the Company's product in development, the potential for Priority Review for the Company's product candidate, the viability of future opportunities, future market supply and demand, the expected timing of top-line data, expected intellectual property and exclusivity protections for the Company's product candidate, the future cash runway, the financial condition, results of operations and business of Opthea, including estimated cash and cash equivalents at December 31, 2024, certain plans, objectives, expectations and strategies of management of Opthea, including with respect to the current and planned clinical trials of its product candidate and the timing thereof, and the expected timing for planned regulatory submissions and potential approvals, and the future performance of Opthea, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "opportunity," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Opthea may not actually achieve the plans, intentions or expectations disclosed in the forward-looking statements, and you should not place undue reliance on the forward-looking statements as predictions of future events. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect Opthea's current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law. Please refer to information, including risk factors, set forth in Opthea's Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission on August 30, 2024, and other future filings with the U.S. Securities and Exchange Commission, the Australian Securities and Investments Commission and the Australian Securities Exchange for key factors that could cause actual results to differ materially from those projected in the forward-looking statements contained herein including risks associated with: future capital requirements and ability to continue as a going concern, the completion of Opthea's financial statement closing procedures, the development, testing, production, marketing and sale of drug treatments, regulatory risk and potential loss of regulatory approvals, ongoing clinical studies to demonstrate sozinibercept safety, tolerability and therapeutic efficacy, clinical research organization and labor costs, intellectual property protections, the development, testing, production, marketing and sale of drug treatments, and other factors that are of a general nature which may affect the future operating and financial performance of the Company.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

The information contained in this presentation does not constitute investment or financial product advice (nor taxation or legal advice) and is not intended to be used as the basis for making an investment decision. The presentation is for informational purposes only and is not a prospectus or other disclosure document under Australian law or the law of any other jurisdiction and does not contain all the information which would be required to be disclosed in a prospectus or other disclosure document. The information presented in this presentation may differ materially from that presented in any disclosure document prepared in connection with any offer of securities. It does not take into account the investment objectives, financial situation, taxation position or needs of any particular investor, which should be considered when deciding if an investment is appropriate. You must consider your own investment objectives, financial situation and needs and conduct your own independent investigations and enquiries, including obtaining taxation, legal, financial or other professional advice in relation to the information contained in this presentation as appropriate to your jurisdiction. This presentation should not be relied upon by the Recipient in considering the merits of any particular transaction.

This presentation does not constitute an offer to sell, or the solicitation of an offer to buy, any securities in the United States or any other jurisdictions in which such an offer would be unlawful prior to registration or qualification under the U.S. Securities Act of 1933, as amended, or the securities laws of any state or other jurisdiction of the United States.

This presentation may contain trademarks and trade names of third parties, which are the property of their respective owners. Third party trademarks and trade names used in this presentation belong to the relevant owners and use is not intended to represent sponsorship, approval or association by or with any of the Opthea Group.

# Sozinibercept Has the Potential to Be the First Product in 20 Years to Deliver Superior Visual Outcomes

## Addressing High Unmet Need

- Despite wide use of anti-VEGF-A therapy, wet AMD patients still experience loss in vision long term<sup>1</sup>
- Every letter of vision counts to improve quality of life and reduce mortality

## Proprietary Technology

- First-in-class VEGF-C/D 'trap' inhibitor intended for combination with standard of care anti-VEGF-A therapies
- Composition of Matter and Methods of Use Patents through 2034; opportunities to extend beyond 2034\*

## Superior Lead Asset

- Phase 2b demonstrated superiority in combination with SOC therapy, with well tolerated safety profile
- Sozinibercept has the potential to improve vision for millions of patients with wet AMD

## Topline Data from Pivotal Trials in 2025

- Topline data anticipated for COAST (n=998) in early 2Q CY2025 and ShORe (n=986) in mid-CY2025
- Current cash expected to fund operations into 3Q CY2025<sup>2</sup>

## Substantial Market Opportunity

- Multibillion dollar commercial opportunity in a growing market with an established clinical practice
- Sozinibercept developed for use in combination with any anti-VEGF-A; will not compete directly with SOC therapies

AMD – age-related macular degeneration; MOA – Mechanism of Action; SOC – Standard of care

<sup>1</sup>CATT Research Group; Maguire MG et al. Ophthalmology. 2016 Aug.

<sup>2</sup>Additional funding will be required to reach commercialization of sozinibercept and to meet obligations under the Development Funding Agreement ("DFA"). As a result of obligations under the DFA and applicable law regarding liquidity, the Company may raise or obtain additional capital in one or more transactions, earlier than 3Q CY 2025 or anticipated topline data readout dates.

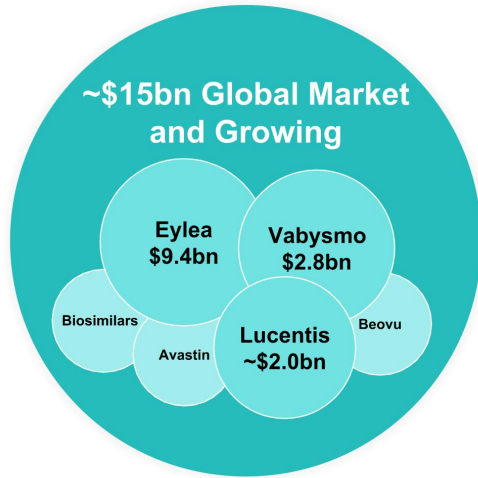
\*Potential for Patent Term Extensions & Data and Market Exclusivity (12 Years for Biologic)

# Sozinibercept Designed to Deliver Superior Visual Outcomes in Combo with VEGF-A Inhibitors; Potential to Create New Multi-Billion Dollar Medicine

Global Marketed VEGF-A Inhibitors



Sozinibercept is a VEGF-C/D “Trap” Inhibitor



Potential value proposition:

**Targeting Improved Visual Function**

*Critical for Patients, Physicians and Payors*

**Fits Seamlessly into Physician Practice**

**Potential Use with Any VEGF-A Inhibitor**

**Multi-Billion Dollar Commercial Opportunity**

The \$15bn global market comprised of Eylea, Vabysmo, Lucentis revenue plus an estimate for biosimilars, Avastin off-label, and Beovu of ~\$1bn



# Experienced Leadership Team

Expertise and Track Record to Make a Positive Impact on the Retinal Community

## Management Team



**Fred Guerard, PharmD, MS**  
Chief Executive Officer



**Tom Reilly**  
Chief Financial Officer



**Parisa Zamiri, MD, PhD**  
Chief Medical Officer



**Megan Baldwin, PhD, MAICD**  
Founder, Chief Innovation Officer



**Mike Campbell**  
Chief Commercial Officer



## Chief Medical Advisor



**Arshad M. Khanani, MD, MA, FASRS**  
Managing Partner, Director of Clinical Research and Director of Fellowship at Sierra Eye Associates, and Clinical Professor at the University of Nevada, Reno School of Medicine

## Clinical Advisory Board



**Charles C. Wykoff, MD, PhD**  
Director of Research, Retina Consultants of Texas, Chairman of Research and Clinical Trials Committee, Retina Consultants of America



**Tim Jackson, PhD, MB, ChB, FRCophth**  
National Health Service, Consultant at Kings Hospital College Hospital, London

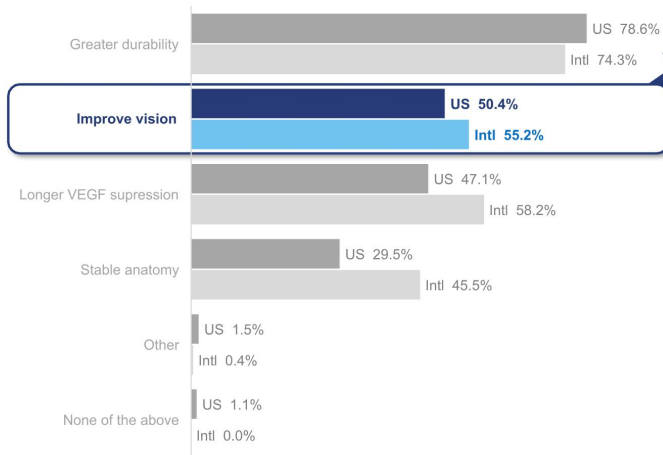


**Jason Slakter, MD**  
Clinical Professor at New York University School of Medicine and partner at Vitreous Retina Macula Consultants of New York

# Improving Vision Now the Largest Unmet Need in Wet AMD for Retina Specialists

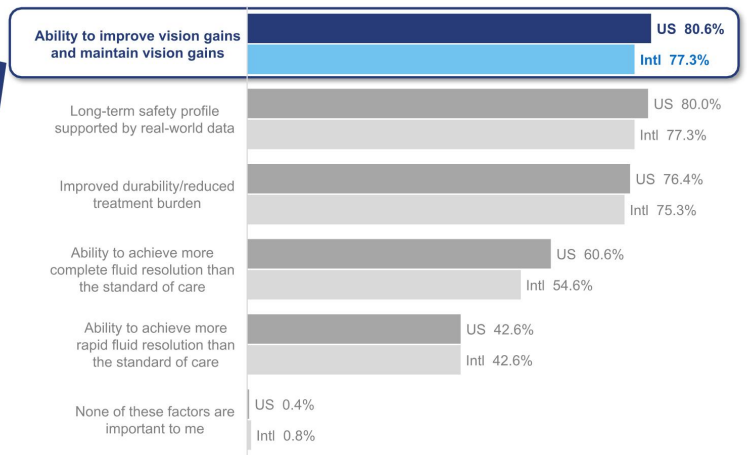
## ASRS PAT Survey 2023

What are the greatest unmet needs in treating wet AMD and DME?  
n=1,012



## ASRS PAT Survey 2024

Which factors are more important to you when selecting an anti-VEGF agent?  
n=1,021



American Society of Retina Specialists (ASRS) annual Preferences and Trends (PAT) survey.  
AMD, age-related macular degeneration; DME, diabetic macular edema; VEGF, vascular endothelial growth factor; US, United States of America; Intl, international

# Despite Treatment with Standard of Care Anti-VEGF-A Therapies, the Majority of Patients Achieve Suboptimal Vision Outcomes

## Despite treatment with anti-VEGF-A therapy\*

**>45%** do not achieve significant vision gains

**>60%** will have **persisting macular fluid**

**25%** will have **further vision loss at 12+ months**



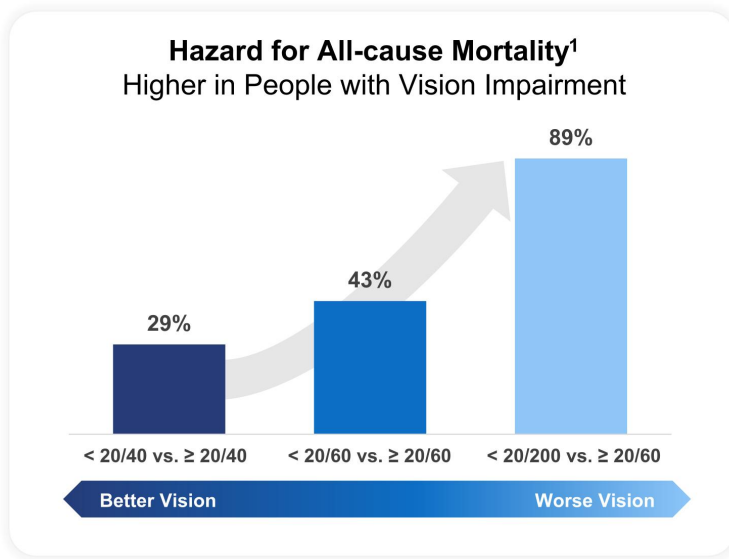
The majority of patients fail to achieve 20/40 vision<sup>1</sup>



Suboptimal vision is associated with decrease in Instrumental Activities of Daily Living (IADL) skills<sup>2</sup>

\*Based on randomised, controlled clinical trial data; >45% fail to achieve  $\geq 2$  lines improvement in Best Corrected Visual Acuity (BCVA); Persisting fluid: SD-OCT CST  $\geq 300$   $\mu\text{M}$  or Time-Domain OCT CST  $\geq 250$   $\mu\text{M}$   
IADL: Instrumental activities of daily living (complex activities related to the ability to live independently)  
<sup>1</sup>Mettu PS, et al. Prog Retin Eye Res. 2021  
<sup>2</sup>Hochberg C, et al. Invest Ophthalmol Vis Sci. 2012 May 31.

# Every Letter Counts; Vision Loss Associated with Increased Mortality Risk



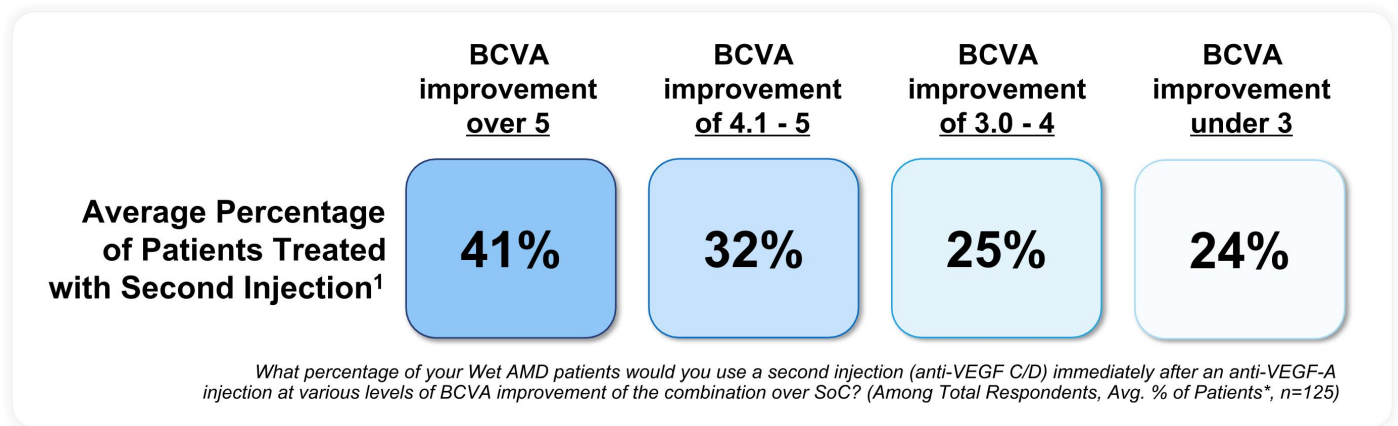
**Decrease of 1 ETDRS letter per year expected to increase mortality risk by 16%<sup>2</sup> associated exclusively with IADL levels**

IADL – Instrumental activities of daily living; ETDRS – Early Treatment Diabetic Retinopathy Study chart

<sup>1</sup>Ehrlich JR et al. "Association between vision impairment and mortality: a systematic review and meta-analysis." *Lancet Glob Health*. 2021.

<sup>2</sup>Christ SL, et al. "Longitudinal relationships among visual acuity, daily functional status, and mortality: the Salisbury Eye Evaluation Study." *JAMA Ophthalmol*. 2014.

# U.S. Retina Specialists Willing to Administer Second Injection to at Least 24% of Their Patients for Additional BCVA Improvement



**Estimate 1% Share of Wet AMD TAM Equals ~\$100M+ in Sales Per Annum**

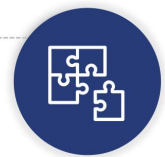
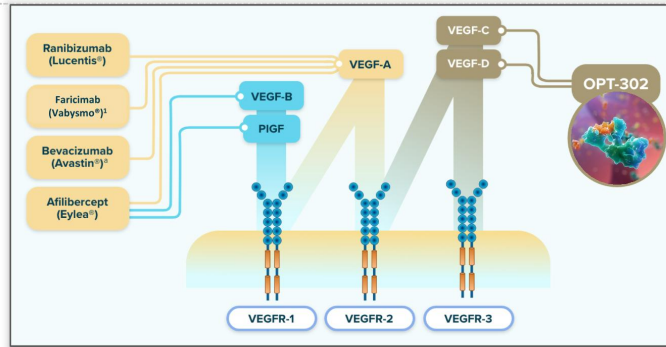
BCVA – Best Corrected Visual Acuity  
TAM – Total Addressable Market  
<sup>1</sup>Source: InCrowd Awareness Trial and Usage (ATU) Report, June 2024  
\*Averages calculated using the midpoints of each % prescribing allocation group.

# Sozinibercept, a First-In-Class VEGF-C/D “Trap” Inhibitor, Has the Potential to Address the Limitations of Anti-VEGF-A Therapies



## The Problem

Wet AMD is a **multi-factorial disease**. Treatment with VEGF-A inhibitors **upregulates VEGF-C/D**, driving angiogenesis and vascular permeability.



## The Solution

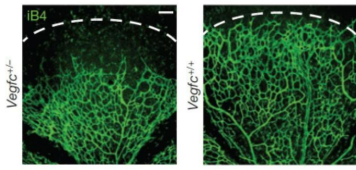
When used in combination with any VEGF-A inhibitor, **OPT-302 completely blocks VEGFR-2 and VEGFR-3 signaling**.

<sup>1</sup> Faricimab also has inhibitory effect on Ang-2.

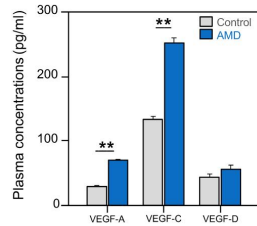
<sup>2</sup> Bevacizumab is used 'off-label' for the treatment of neovascular (wet) AMD

# Published Evidence Supports Broader VEGF Pathway Inhibition with Sozinibercept

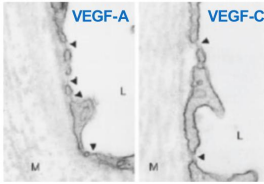
## VEGF-C Stimulates Retinal Angiogenesis<sup>^</sup>



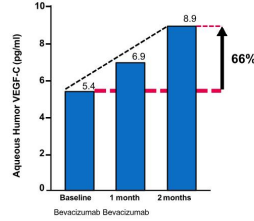
## Circulating VEGF-C Levels Significantly Elevated in AMD Patients<sup>+</sup>



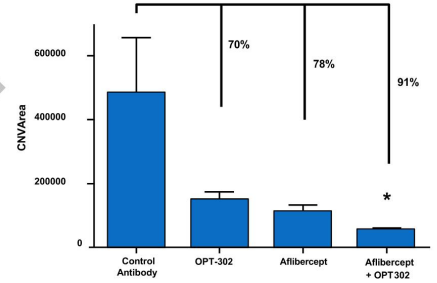
## VEGF-A and VEGF-C Induce Vascular Leakage/permeability<sup>#</sup>



## Elevated VEGF-C in Aqueous Humor Following Anti-VEGF-A therapy in Wet AMD Patients<sup>\*</sup>



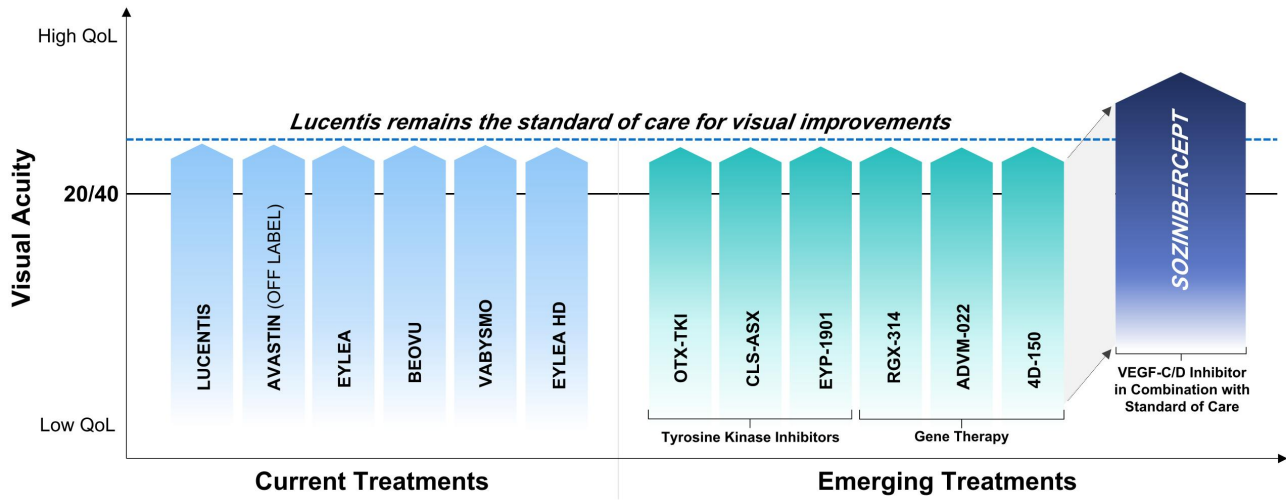
## Additive Benefit of VEGF-A and VEGF-C/D Inhibition in Mouse Wet AMD Model



<sup>^</sup>Tammela et al., Nature Cell Biology, 2011; <sup>#</sup>Zhou et al. BMC Ophthalmology (2020) 20:15; <sup>+</sup>Cao et al., Circ Res., 2004; <sup>†</sup>Lashkari et al, 2013 ARVO Annual Meeting, 4999-A0128; <sup>\*</sup>Cabral et al., 2018 Ophthalmology Retina (2018).

# Sozinibercept Has Demonstrated Improvement in Vision Gains and Reduction in Vision Loss

Opportunity in Wet AMD Market for an *Overall Shift* Towards Superior Visual Outcomes



QoL – Quality of Life

Jackson, Timothy L., et al. "A randomized controlled trial of OPT-302, a VEGF-C/D inhibitor for neovascular age-related macular degeneration." *Ophthalmology*. June 2023.

Jung, Eric, et al. "The future of wet AMD therapeutics." *Retina Today*. November/December 2023.

Comparison of historical data; other than Lucentis, comparative data is not from the same study. These results are presented from different clinical trials at different points in time with differences in trial design. Cross-trial comparisons must be interpreted with caution, and as a result, conclusive cross-trial comparisons cannot be made.



# Long-term Value Opportunities for Sozinibercept

Main Patent Family Extends through 2034, with Expansion Opportunities Beyond 2034\*

PROGRAM	DEVELOPMENT PHASE				ANTICIPATED MILESTONES
	RESEARCH / PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	
<b>Wet Age-Related Macular Degeneration (Wet AMD)</b>					
<b>Sozinibercept</b> For use in combination with anti-VEGF-A therapies					<b>Topline data:</b> COAST (in early 2Q CY2025) ShORe (in mid-CY2025)
<b>Diabetic Macular Edema (DME)</b>					
<b>Sozinibercept</b> For use in combination with anti-VEGF-A therapies					Phase 3 ready
<b>Co-formulation (Sozinibercept + VEGF-A Inhibitor)</b>					
<b>Sozinibercept</b> Co-formulation with VEGF-A Inhibitor					Feasibility underway

\*Potential for Patent Term Extensions & Data and Market Exclusivity (12 Years for Biologic)

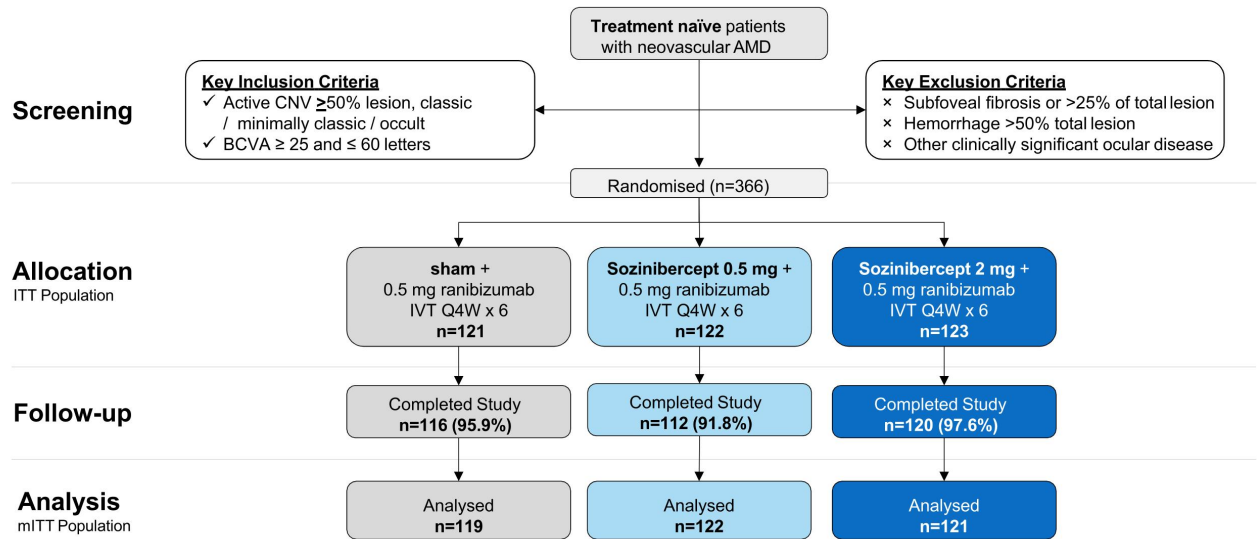
# Advancing Therapeutic Innovations to Transform Patient Outcomes with Superior Vision Gains

We are dedicated to advancing sozinibercept to **improve patients' visual outcomes**

Next Steps	<b>Clinical Milestones</b>	<ul style="list-style-type: none"><li>Phase 3 program enrolled 1,984 patients across COAST and ShORe</li><li>Topline data anticipated for COAST in early 2Q CY2025 and ShORe in mid-CY2025</li></ul>
	<b>Manufacturing Scale-up</b>	<ul style="list-style-type: none"><li>DS PPQ campaign completed Sep-2024; update on DP PPQ in early CY2025</li><li>PPQ validation batches supportive of BLA filing and launch</li></ul>
	<b>Regulatory Preparations</b>	<ul style="list-style-type: none"><li>FDA Fast Track designation allows rolling submission of completed BLA modules</li><li>Potential BLA approval anticipated as early as end of CY2026</li></ul>
	<b>Commercial Readiness</b>	<ul style="list-style-type: none"><li>Strengthen medical expert engagement and develop market access strategy</li><li>Complete development of product launch plan</li></ul>

DS: Drug Substance; DP: Drug Product

# Robust Phase 2b Trial in Wet AMD Demonstrated Superiority in Visual Outcome



CNV – choroidal neovascularisation; IVT – intravitreal; Q4W – once every 4 weeks; ITT – Intent to Treat Population, all participants who were randomised into the study irrespective of whether study medication was administered or not; Safety Population - all participants in the ITT but excluding those who did not receive at least one dose of study medication; mITT – Modified ITT Population, all participants in the Safety Population but excludes any participant without a Baseline VA score and/or any participant who did not return for at least one post-baseline visit

# Phase 2b Primary and Secondary Endpoints

## Pre-Specified Anatomical Sub-Groups Informed Enrichment of Phase 3 Program

### Primary Endpoint

**Mean change from baseline in BCVA at week 24**

### Key Secondary Endpoints

Proportion of patients gaining  $\geq 15$  letters from baseline at week 24

Change in central subfield thickness (CST) from baseline at week 24

Change in intra-retinal and sub-retinal fluid from baseline to week 24

Safety and tolerability

### Select Pre-specified Subgroups

**Predominantly classic, minimally classic, & occult lesions**  
(Stratification Factor)

**Retinal Angiomatous Proliferation (RAP)**  
detected/not detected at baseline

**Polypoidal Choroidal Vasculopathy (PCV)**  
detected/not detected at baseline

## Well-Balanced Phase 2b Trial Demographics and Baseline Characteristics

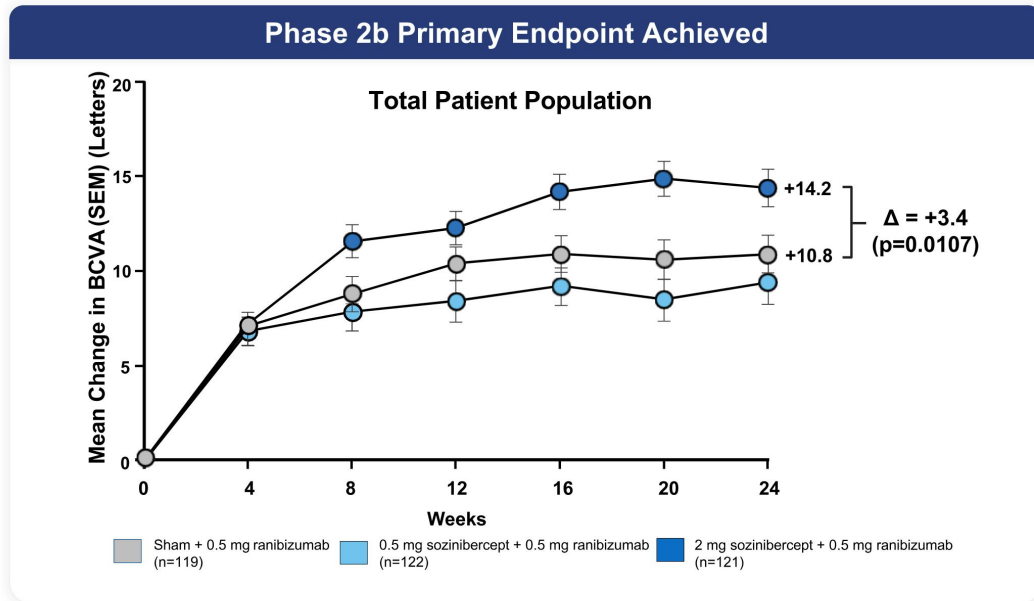
Demographic/Baseline Disease Characteristic	Sham + ranibizumab n=121	0.5 mg sozinibercept + ranibizumab n=122	2 mg sozinibercept + ranibizumab n=123
Mean Age – years ± SD	76.1 ± 9.48	78.8 ± 8.16	77.8 ± 8.82
Sex – n (%)	Male	48 (39.7%)	49 (40.2%)
	Female	73 (60.3%)	73 (59.8%)
Caucasian Race – n (%)	117 (99.2%)	119 (99.2%)	117 (97.5%)
Mean Visual Acuity (BCVA) – letters ± SD	50.7 ± 10.21	51.1 ± 8.96	49.5 ± 10.26
Mean Total Lesion Area - mm <sup>2</sup> ± SD	6.08 ± 3.21	6.48 ± 3.30	6.62 ± 3.39
Lesion Type	Predominantly classic – n (%)	15 (12.4%)	15 (12.3%)
	Minimally classic – n (%)	53 (43.8%)	51 (41.8%)
	Occult - n (%)	53 (43.8%)	56 (45.9%)
	PCV detected <sup>1</sup> – n (%)	20 (16.5%)	24 (19.7%)
	RAP detected <sup>2</sup> – n (%)	15 (12.7%)	22 (18.5%)
Mean central subfield thickness (CST) - mm ±SD	412.10 ± 110.62	425.18 ± 120.45	414.12 ± 123.25
Sub-retinal fluid (SRF) present – % participants	89.3%	84.4%	87.8%
Intra-retinal cysts present – % participants	57.9%	63.9%	56.1%

Intent-to-Treat (ITT) population; SD – standard deviation; BCVA – Best Corrected Visual Acuity

<sup>1</sup>PCV - polypoidal choroidal vasculopathy, detected by SD-OCT, FA and fundus photography.

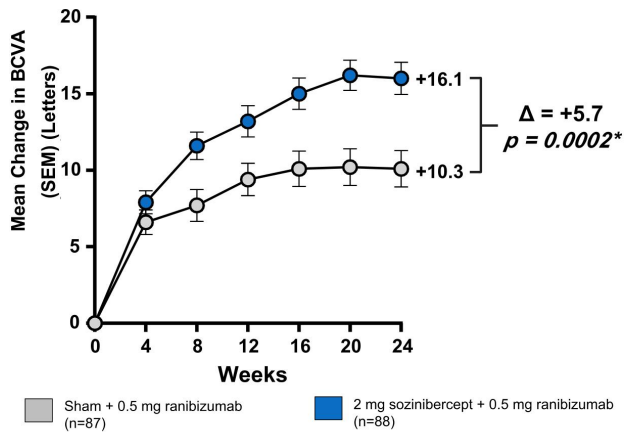
<sup>2</sup>RAP - retinal angiomatous proliferation, detected by SD-OCT, FA and fundus photography.

# Sozinibercept 2 mg Combination Therapy Demonstrated Over 30% Improvement in Visual Acuity over Ranibizumab Monotherapy



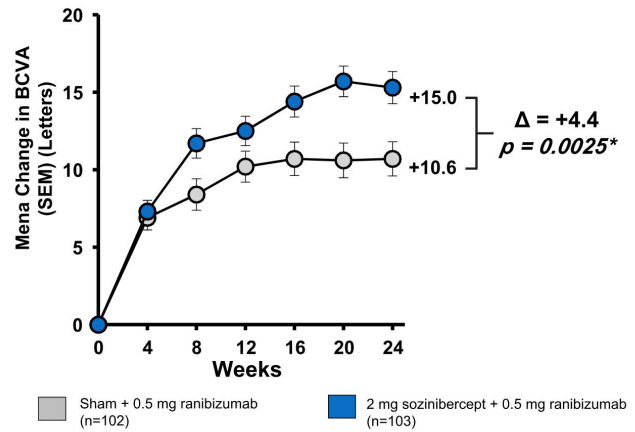
# Phase 2b Superiority Data Informed Enrichment of Phase 3

## Occult & Minimally Classic Lesions (RAP Absent) Represents ~75%<sup>1</sup> of wet AMD patients



1<sup>st</sup> Primary Analysis Population in Phase 3

## Total Patient Population (RAP Absent) Represents ~90%<sup>2</sup> of wet AMD patients



2<sup>nd</sup> Primary Analysis Population in Phase 3

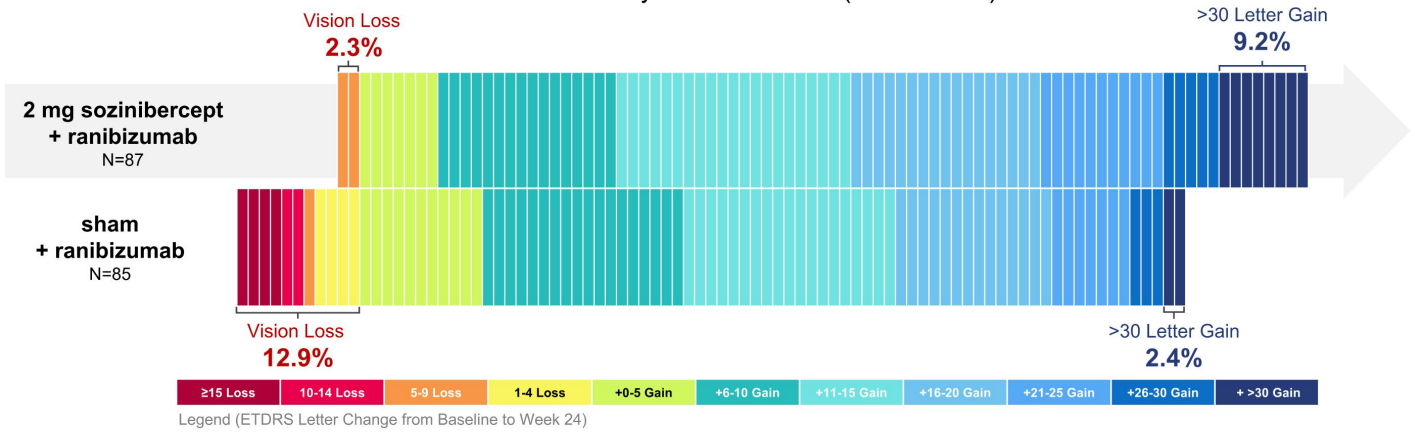
\*Unadjusted p-values

<sup>1</sup>Olsen, Timothy W et al. Fluorescein angiographic lesion type frequency in neovascular Age-Related macular degeneration. Ophthalmology, 111(2), 250 – 255.

<sup>2</sup>Daniel, E. et al. Outcomes in eyes with retinal angiomatous proliferation in the comparison of age-related macular degeneration treatments trials (CATT). Ophthalmology, 123(3), 609–616.

# Greater Proportion of Sozinibercept Patients Gained Substantial Vision and Fewer Experienced Vision Loss

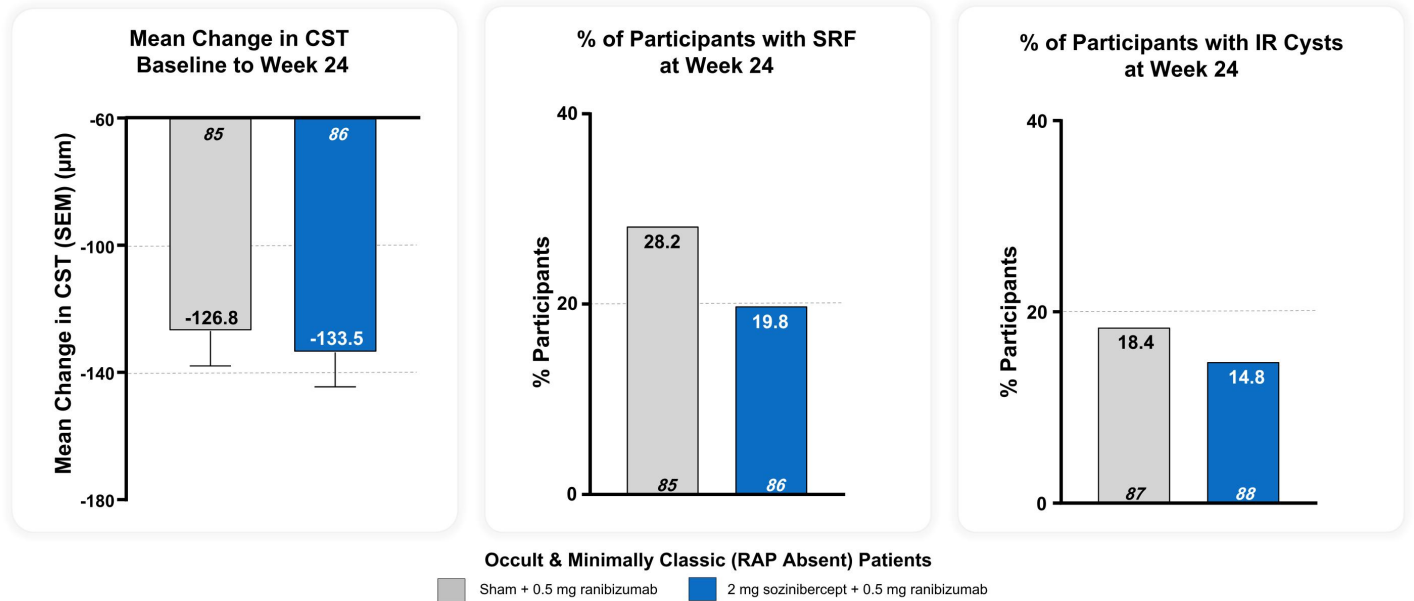
**Change from Baseline to Week 24 (ETDRS Letters, Individual Participants)**  
Occult and Minimally Classic Lesions (RAP Absent)



**42% relative increase in patients achieving 20/40 vision compared to ranibizumab control**

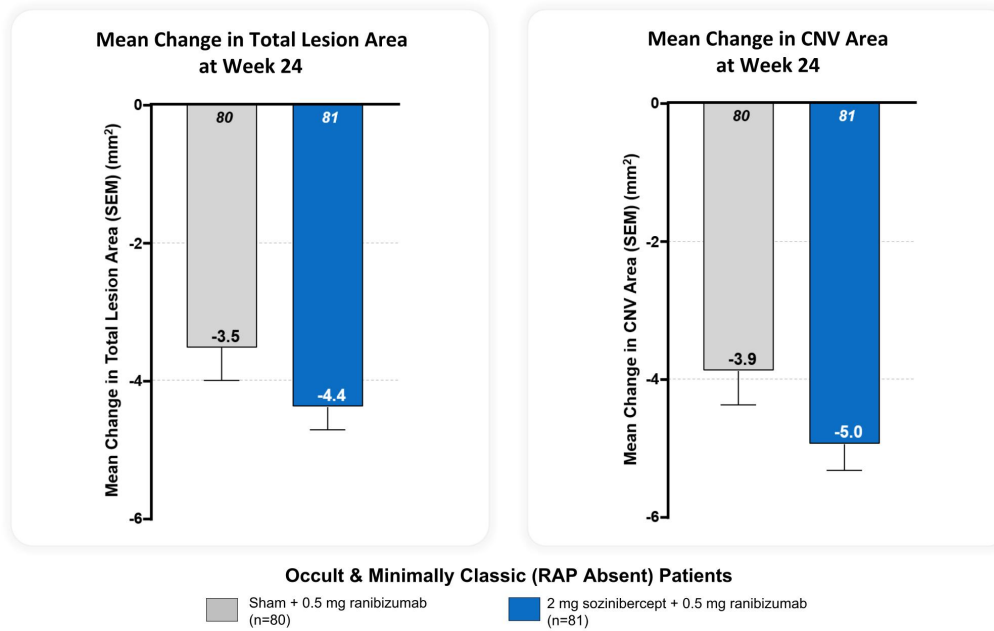


# Sozinibercept Reduced Retinal Thickness and Dried the Retina Better



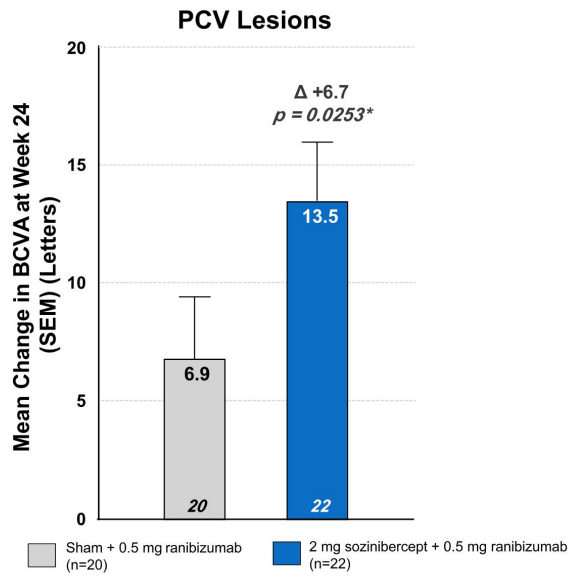
mITT: as observed; top of bar – statistic, bottom of bar – n.  
CST: Central Subfield Thickness; SRF: Subretinal fluid; IR: Intra-retinal.

# Sozinibercept Demonstrated Greater CNV and Lesion Regression



mITT; as observed; top of bar – statistic, bottom of bar – n. CNV: Choroidal Neovascular.

# Superior Vision Gains in Hard-To-Treat PCV Lesion Patients



Polypoidal Choroidal Vasculopathy (**PCV**) is a difficult-to-treat wet AMD subtype; it is often described as the **most prevalent form of wet AMD worldwide**

PCV is **highly prevalent in Asian populations** (up to ~60%), while ~8-13% prevalence in Caucasians

**Phase 3 ShORe and COAST trials enrolled patients with PCV<sup>1</sup>**

\*Unadjusted p-value

<sup>1</sup> Evaluated by color fundus photography (FP), fluorescein angiography (FA), and spectral domain optical coherence tomography (SD-OCT)

# Sozinibercept Was Well Tolerated

## Safety of Combination Therapy Comparable to Standard of Care Monotherapy

N Participants (%)	Sozinibercept Any dose* N=399 (N=1,842 injections)	Sozinibercept 2 mg N=263 (N=1,121 injections)	Sham + anti-VEGF-A control N=170 (N=854 injections)
Ocular TEAEs - Study Eye – related to study product(s)	41 (10.2%)	22 (8.4%)	20 (11.8%)
Ocular TEAEs - Study Eye – Severe	4 (1.0%)	2 (0.8%)	2 (1.2%)
Intraocular inflammation – Study Eye	7 <sup>1,2,3</sup> (1.8%)	3 <sup>1</sup> (1.1%)	3 <sup>1</sup> (1.8%)
Participants with AEs leading to treatment discontinuation	4 <sup>2,4-6</sup> (1.0%)	1 <sup>4</sup> (0.4%)	2 <sup>7,8</sup> (1.2%)
Any APTC event	4 <sup>4,5,9,10</sup> (1.0%)	3 <sup>5,9,10</sup> (1.1%)	2 <sup>11,12</sup> (1.2%)
Deaths	2 <sup>10,13</sup> (0.5%)	2 <sup>10,13</sup> (0.8%)	2 <sup>14,15</sup> (1.2%)

<sup>1</sup>Transient anterior chamber cell (trace 1-4 cells); <sup>2</sup> SAE of endophthalmitis, with AE's of hypopyon and anterior chamber cell (n=1; 0.5 mg); <sup>3</sup> SAE of vitritis (n=1; 0.5 mg); <sup>4</sup>Non-fatal myocardial infarction; <sup>5</sup>Cerebrovascular accident; <sup>6</sup>Enteritis; <sup>7</sup>Abdominal pain; <sup>8</sup>Increased IOP; <sup>9</sup>Non-fatal angina pectoris; <sup>10</sup>Fatal congestive heart failure/myocardial infarction; <sup>11</sup>Non-fatal arterial embolism; <sup>12</sup>Embolitic stroke; <sup>13</sup>Metastatic ovarian cancer; <sup>14</sup>Pneumonia; <sup>15</sup>infective endocarditis.  
\*Any dose (sozinibercept 0.3 mg, 0.5 mg, 1 mg or 2 mg)

# Similar Rate of Intraocular Inflammation Between Standard Of Care and Sozinibercept in Combination Therapy

N Participants (%)	Sozinibercept Any dose* N=399 (N=1,842 injections)	Sozinibercept 2 mg N=263 (N=1,121 injections)	Sham + anti-VEGF-A control N=170 (N=854 injections)
<b>Intraocular Inflammation<sup>1</sup></b>	7 (1.8%)	3 (1.1%)	3 (1.8%)
<b>OPT-302-1001 (Phase 1/2a wet AMD)</b>	2	0	0
Uveitis with anterior chamber cell 1+	1	0	0
Uveitis with anterior chamber cell 2+	1	0	0
<b>OPT-302-1002 (Phase 2b wet AMD)</b>	3	1	2 <sup>a</sup>
Endophthalmitis with anterior chamber 1+ and hypopyon	1	0	0
Vitritis	1	0	0
Anterior chamber cell, trace	1	1	2 <sup>a</sup>
<b>OPT-302-1003 (Phase 1b/2a DME)</b>	2 <sup>b</sup>	2 <sup>b</sup>	1
Iritis with keratic precipitates and anterior chamber cell 2+	1	1	0
Iritis with anterior chamber cell 2+	0	0	1
Anterior chamber cell 4+, associated with cataract extraction/ intraocular lens implant and hyphema	1 <sup>b</sup>	1 <sup>b</sup>	0

Safety population

<sup>1</sup>AEs observations considered to be indicative of intraocular inflammation, defined prior to database lock

<sup>a</sup>Observed during ophthalmic examination, but not reported as TEAEs

<sup>b</sup>Considered associated with lens extraction and not reported as TEAEs

## Phase 3 Clinical Program Is Informed by Phase 2b Results and Optimized for Success



Enriched patient population by excluding RAP lesions (+4.4 letters in Phase 2b); key inclusion and exclusion criteria otherwise unchanged



Hierarchical primary analysis first conducted in the high-responding occult and minimally classic population (+5.7 letters in Phase 2b) followed by total patient population



Two robust pivotal trials studying sozinibercept in combination with Eylea® and Lucentis® in treatment naïve patients with wet AMD



Phase 3 designed to support broad label for use in combination with any VEGF-A inhibitor for all wet AMD patients (treatment naïve and prior treated)

# Global Pivotal Program Involves 33 Countries and ~400 Sites

Multi-center, sham controlled, double-masked trials in **treatment naïve wet AMD patients**

## Key Inclusion Criteria

- ✓ Active CNV >50% lesion: classic, minimally classic, occult
- ✓ BCVA  $\geq 25$  and  $\leq 60$  letters

## Key Exclusion Criteria

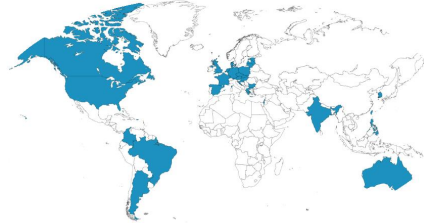
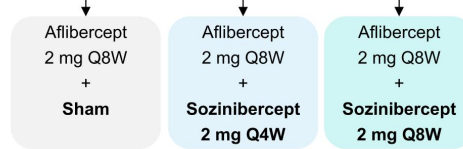
- × Subfoveal fibrosis or >25% of total lesion
- × Hemorrhage >50% total lesion
- × Other clinically significant ocular disease
- × RAP lesions

## COAST

Combination with Aflibercept

Enrolled (N=998)

Randomized (1:1:1)

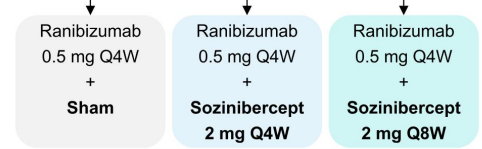


## ShORe

Combination with Ranibizumab

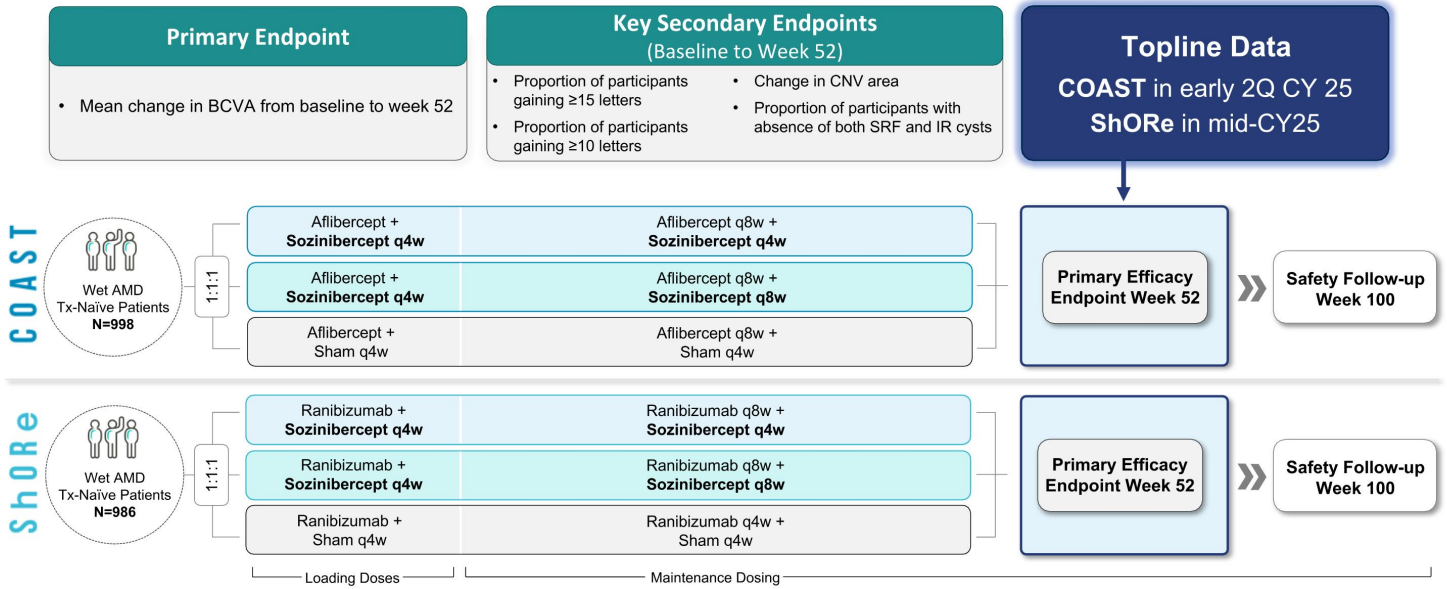
Enrolled (N=986)

Randomized (1:1:1)



CNV – choroidal neovascularization; BCVA – Best Corrected Visual Acuity; RAP – retinal angiomatous proliferation

# Pivotal Trial Design Supports Potential Broad Label for Use With Any Anti-VEGF-A Therapy



Standard of care administered according to approved dosing schedule: aflibercept (2 mg IVT q8w after 3 loading doses) and ranibizumab (0.5 mg IVT q4w after 3 loading doses). Sozinibercept dosed at 2 mg. Note that sham administered at visits when sozinibercept is not administered. Maintenance dosing continued through end of the safety follow-up.



# Phase 3 Enrolled a Higher Proportion of Patients With Best Responding Lesion Types Compared to Phase 2b

Demographic/Baseline Disease Characteristic	Phase 2b		Phase 3	
	Sham + ranibizumab n=121	2 mg sozinibercept + ranibizumab n=123	COAST N=997*	ShORe N=985*
Mean Age – years ± SD	76.1 ± 9.48	77.8 ± 8.82	74.8 ± 8.02	75.4 ± 8.47
Sex – n (%)	Male	48 (39.7%)	45 (36.6%)	442 (44.3%)
	Female	73 (60.3%)	78 (63.4%)	556 (55.7%)
Race – n (%)	Caucasian	117 (99.2%)	117 (97.5%)	859 (86.1%)
	Asian	0 (0.0%)	0 (0.0%)	85 (8.5%)
Mean Visual Acuity (BCVA) – letters ± SD	50.7 ± 10.21	49.5 ± 10.26	52.5 ± 9.43	52.2 ± 9.12
Mean Total Lesion Area - mm <sup>2</sup> ± SD	6.08 ± 3.21	6.62 ± 3.39	6.38 ± 3.20	6.37 ± 3.09
Lesion	Occult - n (%)	53 (43.8%)	54 (43.9%)	555 (55.7%)
	Minimally classic – n (%)	53 (43.8%)	53 (43.1%)	340 (34.1%)
	Predominantly classic – n (%)	15 (12.4%)	16 (13.0%)	102 (10.2%)
	PCV detected <sup>1</sup> – n (%)	20 (16.5%)	22 (17.9%)	261 (26.2%)
	RAP detected <sup>2</sup> – n (%)	15 (12.7%)	14 (11.8%)	—
Mean central subfield thickness (CST) - mm ±SD	412.10 ± 110.62	414.12 ± 123.25	446.5 ± 139.7	451.7 ± 137.8
Sub-retinal fluid (SRF) present – % participants	89.3%	87.8%	95.8%	94.3%
Intra-retinal cysts present – % participants	57.9%	56.1%	78.6%	83.7%

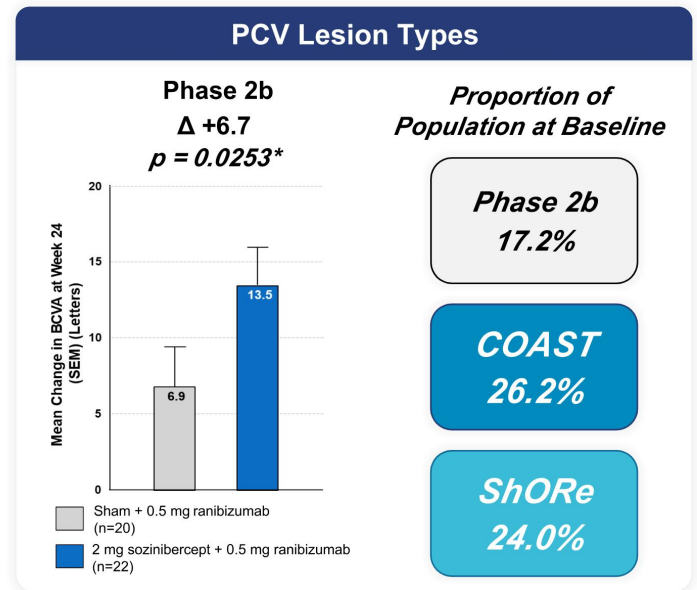
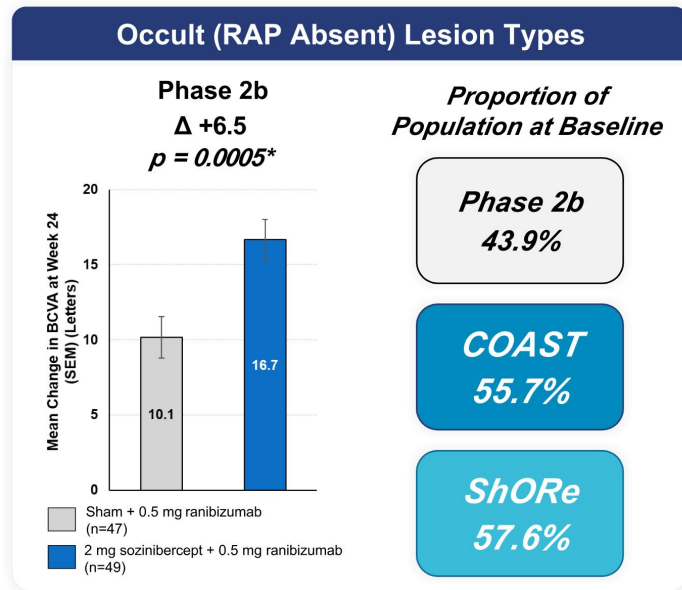
SD – standard deviation; BCVA – Best Corrected Visual Acuity

\*Intent-to-Treat (ITT) population; 1 patient in each of COAST and ShORe was randomized but not treated

<sup>1</sup>PCV - polypoidal choroidal vasculopathy, detected by SD-OCT, FA and fundus photography.

<sup>2</sup>RAP - retinal angiomatous proliferation, detected by SD-OCT, FA and fundus photography.

# Higher Proportion of Patients With Best Responding Lesion Types



\*Unadjusted p-value  
 PCV – Polypoidal Choroidal Vasculopathy

# Cash Runway Through Both Pivotal Topline Data Readouts

## Financial Overview

<b>Ticker</b>	OPT (ASX/NASDAQ)
<b>Shares Outstanding<sup>1</sup></b>	Ordinary Shares: 1,231.1M ADS equivalents: 153.9M
<b>Cash/Cash Equivalents<sup>2</sup></b>	US\$130M
<b>Offices</b>	Melbourne, Australia Princeton, NJ

## Development Funding Agreement (DFA)

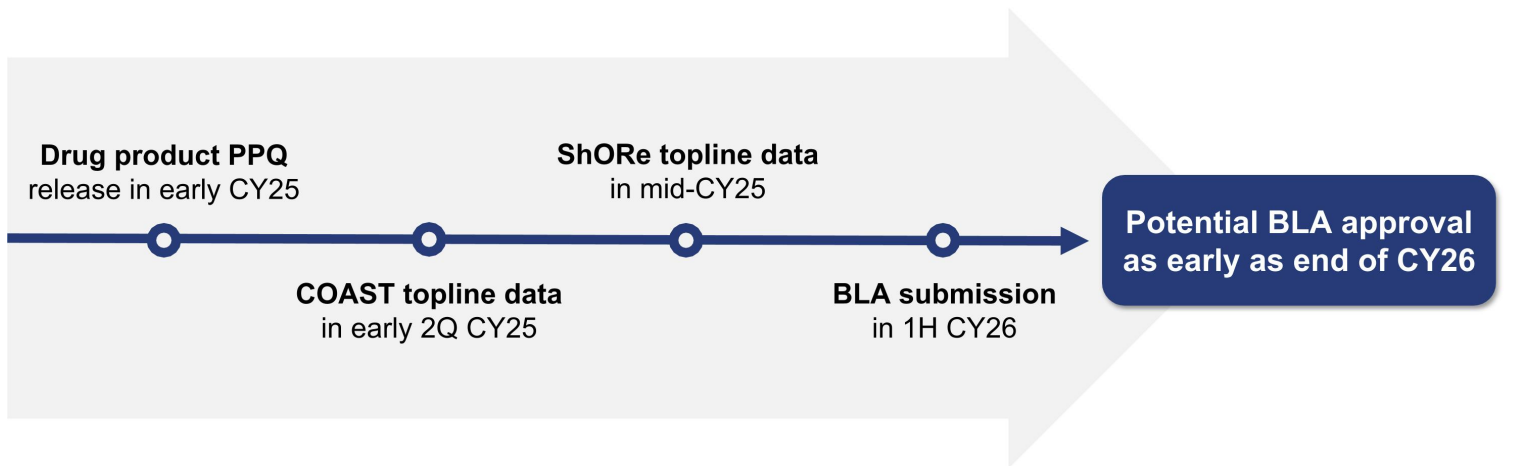
- Total funding drawn under DFA: US\$170M
- Provides non-dilutive funding for development of sozinibercept
- If sozinibercept is approved, repayment is capped at 4x investment and split between fixed payments and variable payments at 7% of revenues
- No amounts owed if the clinical trials do not meet the primary endpoint or if regulatory approval is not received<sup>3</sup>

<sup>1</sup>As of June 30, 2024, pro-forma for the 2024 Retail Entitlement Offer which closed in July 2024.

<sup>2</sup>Preliminary, unaudited estimate as of December 31, 2024, subject to change upon completion of Opthea's financial statement closing procedures.

<sup>3</sup>In certain circumstances, upon or following the termination of the DFA, the Company may owe the DFA investors a multiple of amounts paid to the Company under the DFA. Please refer to the description of the DFA included in the Company's Form 6-K filed with the SEC on August 15, 2022 and the DFA filed as Exhibit 4.14 to the Company's Annual Report on Form 20-F filed with the SEC on September 29, 2022 for more information. Note: Additional funding will be required to reach commercialization of sozinibercept and to meet obligations under the DFA. As a result of obligations under the DFA and applicable law regarding liquidity, the Company may raise or obtain additional capital in one or more transactions, earlier than 3Q CY 2025 or anticipated topline data readout dates.

# Anticipated Clinical and Manufacturing Timelines Support BLA Submission in 1H26 and Potential Approval by End of CY2026



FDA Fast Track designation allows rolling submission of completed BLA modules and potential for Priority Review designation at BLA acceptance



## Thank You.

### UPCOMING EVENT:

#### Opthea Investor Days

*Discuss commercial insights and readiness plans*

<b>Location</b>	<b>Time</b>	<b>Format</b>
New York City	Jan 28 1:30 pm EST	In-person & virtual
Sydney	Feb 3 4:30 pm AEDT	In-person
Melbourne	Feb 5 4:30 pm AEDT	In-person

Details under "Events & Presentations" of the Investor section of Opthea website