



Transforming Patient Outcomes with Superior Vision Gains

Corporate Overview | November 2024

NASDAQ (OPT); ASX (OPT.AX)

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Sozinibercept Has the Potential to Be the First Product in 20 Years to Improve Visual Outcomes

Addressing High Unmet Need

- Despite wide use of anti-VEGF-A therapy, wet AMD patients still experience loss in vision long term¹
- 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 CY2025²

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

¹CATT Research Group; Maguire MG et al. Ophthalmology. 2016 Aug.

²Additional 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 expects to raise or obtain additional capital in one or more transactions, earlier than 3Q CY 2025 or anticipated topline data readout dates.

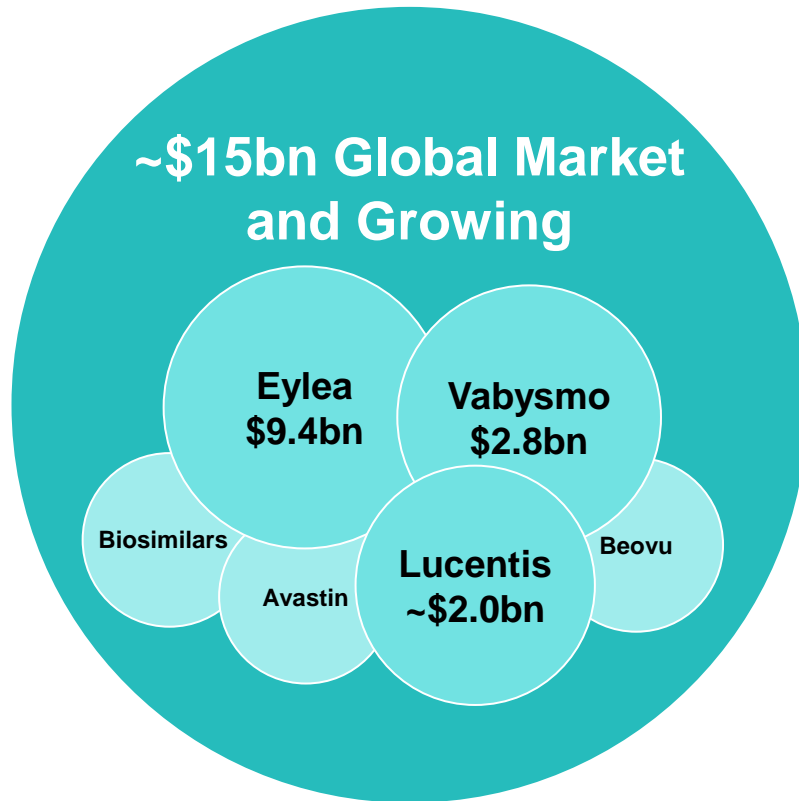
*Potential for Patent Term Extensions & Data and Market Exclusivity (12 Years for Biologic)

Sozinibercept Designed to Improve Visual Outcomes in Combo with VEGF-A Inhibitors; Potential to Create New Multi-Billion Dollar Class

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

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

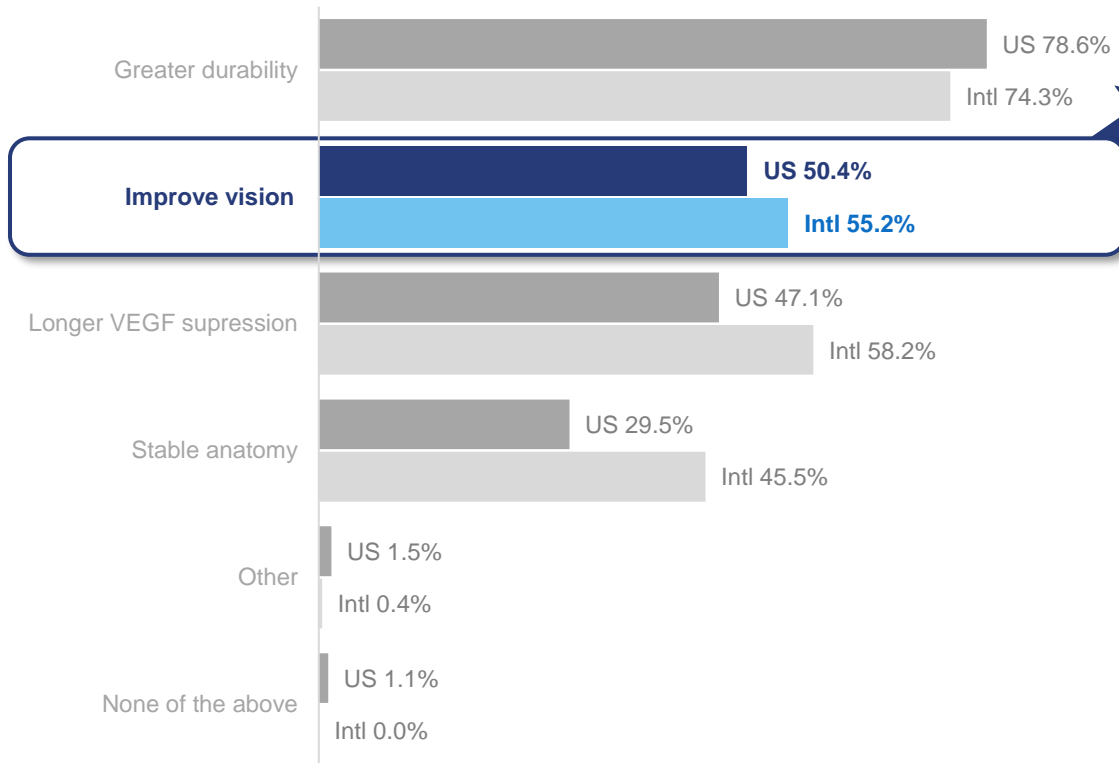


Jason Slakter, MD
Clinical Profession at New York University School of Medicine and partner at Vitreous Retina Macula Consultants of New York

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

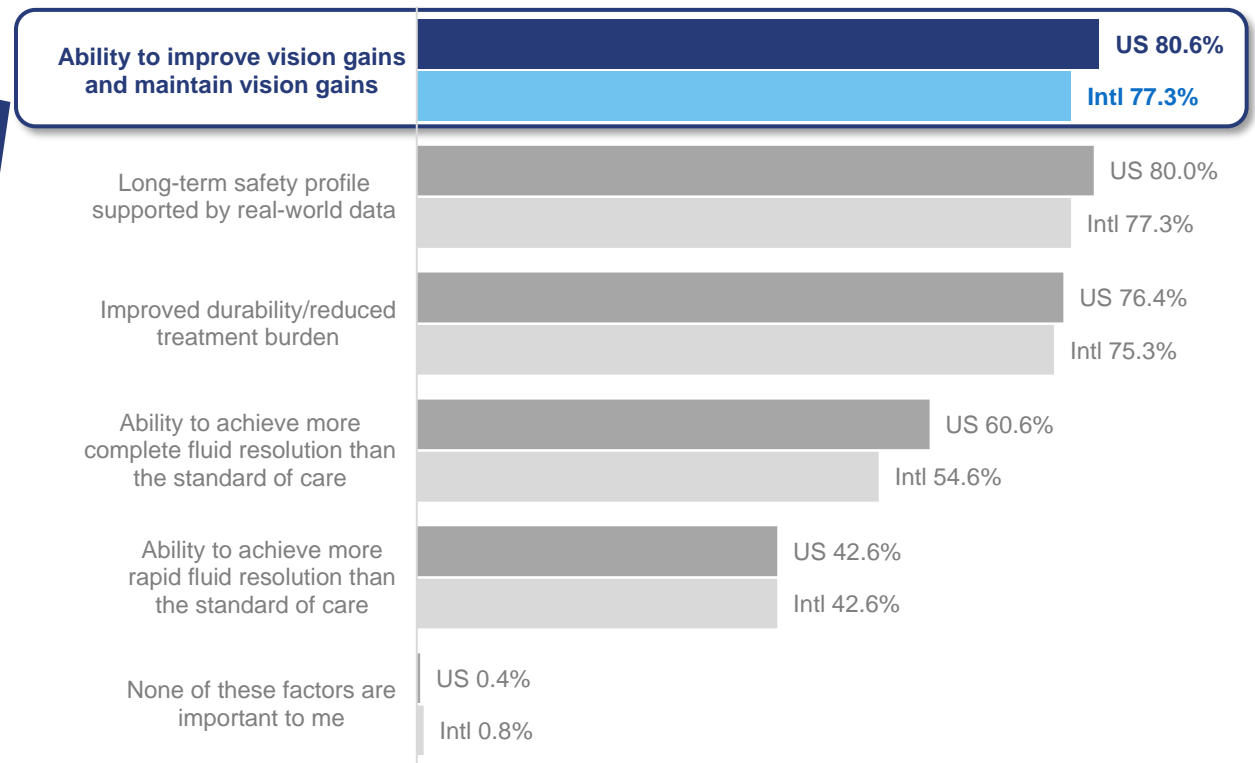
ASRS PAT Survey 2023

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



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 vision¹



Suboptimal vision is associated with decrease in Instrumental Activities of Daily Living (IADL) skills²

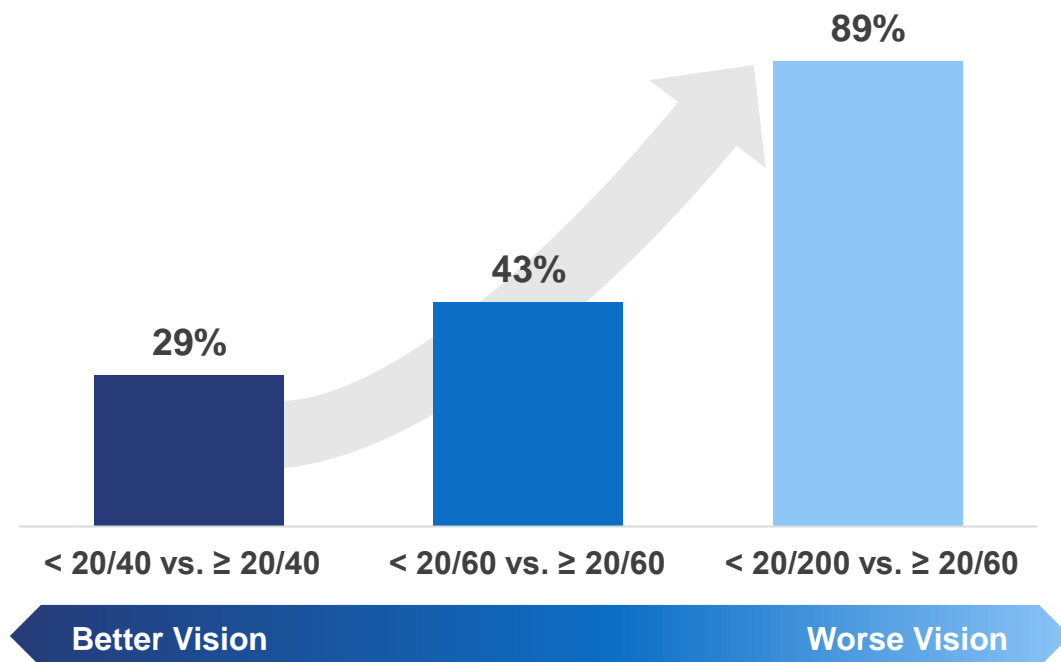
*Based on randomised, controlled clinical trial data; >45% fail to achieve ≥ 2 lines improvement in Best Corrected Visual Acuity (BCVA); Persisting fluid: SD-OCT CST ≥ 300 μM or Time-Domain OCT CST ≥ 250 μM
IADL: Instrumental activities of daily living (complex activities related to the ability to live independently)

¹Mettu PS, et al. Prog Retin Eye Res. 2021

²Hochberg C, et al. Invest Ophthalmol Vis Sci. 2012 May 31.

Every Letter Counts When Loss of Vision Potentially Leads to Increased Mortality Risk

Hazard for All-cause Mortality¹ Higher in People with Vision Impairment



**Decrease of 1 ETDRS letter per year
increases mortality risk by 16%²
associated exclusively with IADL levels**

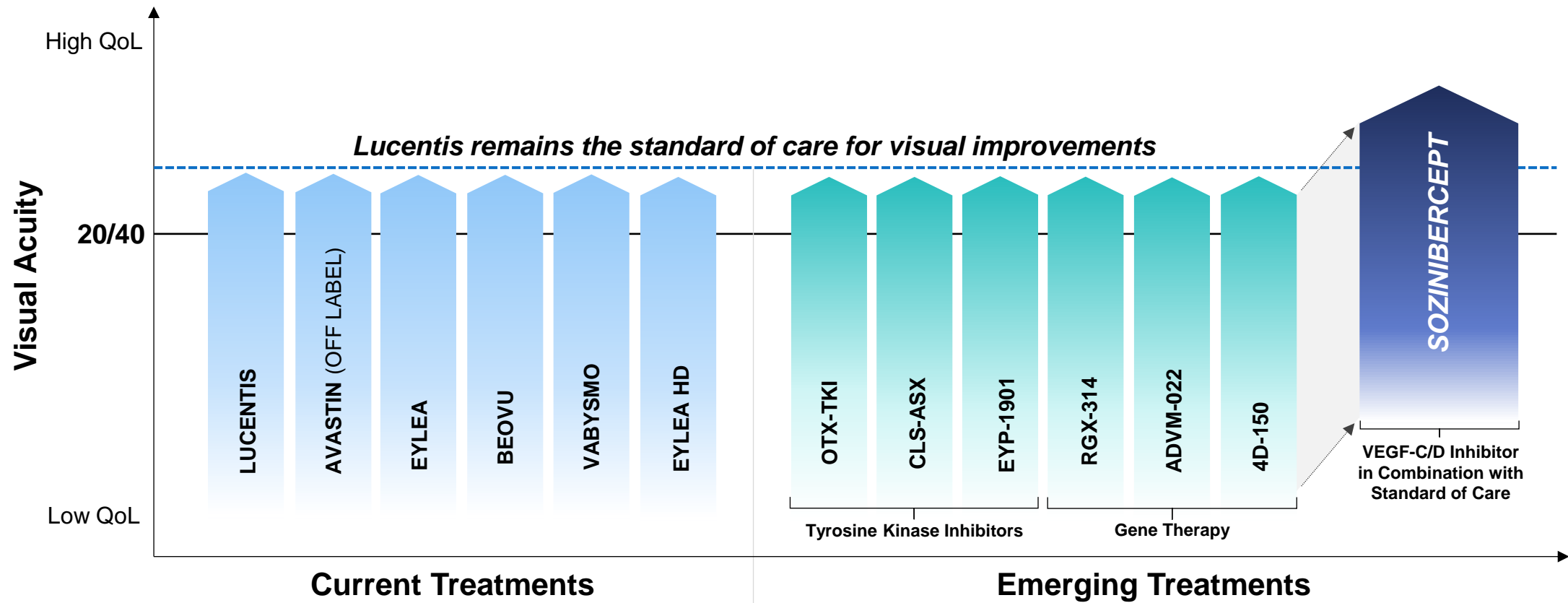
IADL – Instrumental activities of daily living; ETDRS – Early Treatment Diabetic Retinopathy Study chart

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

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

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

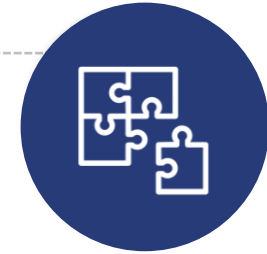
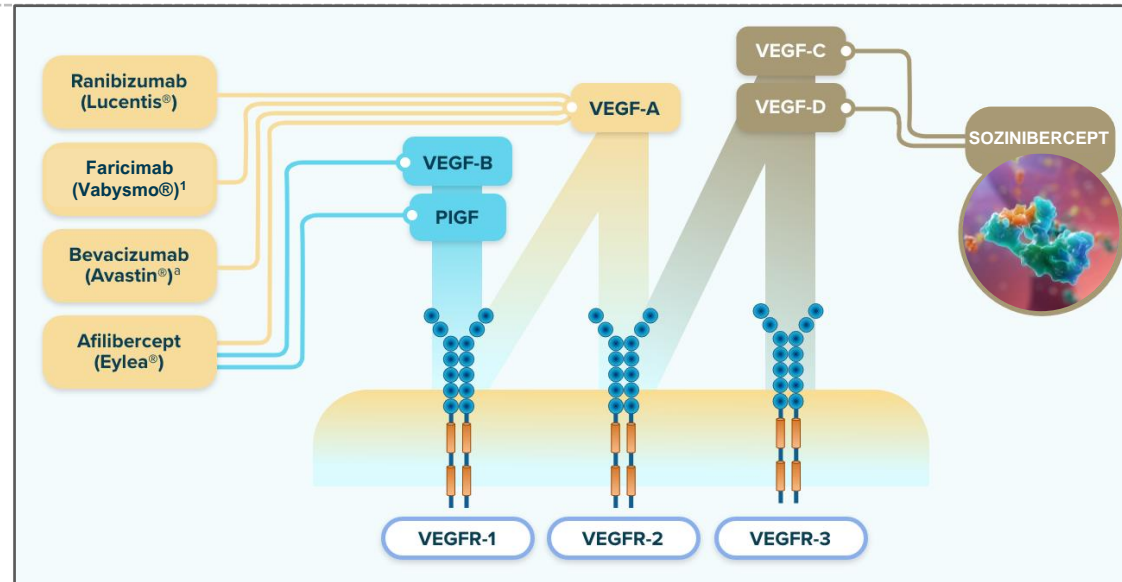


Sozinibercept, a Proprietary VEGF-C/D “Trap” Inhibitor, Has the Potential to Address the Limitations of Anti-VEGF-A Therapies



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

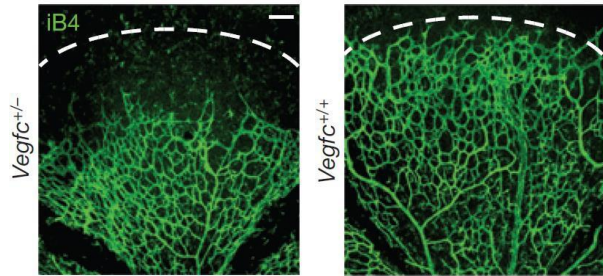
When used in combination with any VEGF-A inhibitor, **sozinibercept completely blocks VEGFR-2 and VEGFR-3 signaling**.

¹ Faricimab also has inhibitory effect on Ang-2.

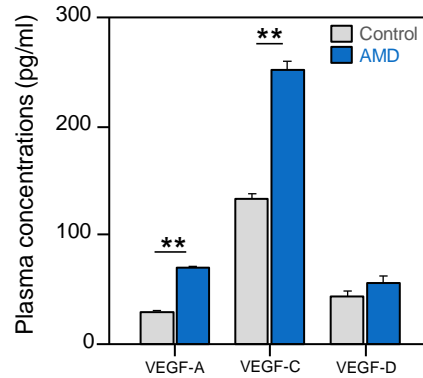
^a Bevacizumab is used 'off-label' for the treatment of neovascular (wet) AMD

Published Evidence Supports Broader VEGF Pathway Inhibition with Sozinibercept

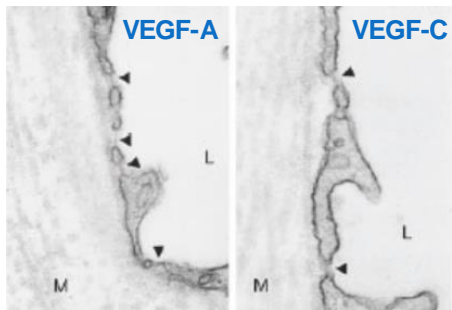
VEGF-C Stimulates Retinal Angiogenesis[^]



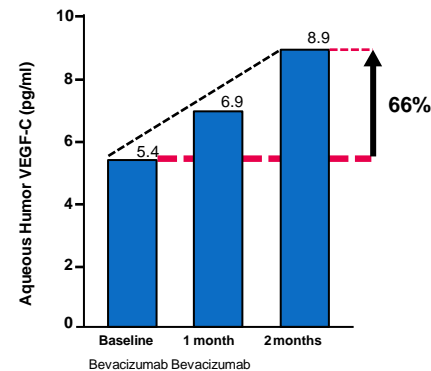
Circulating VEGF-C Levels Significantly Elevated in AMD Patients[†]



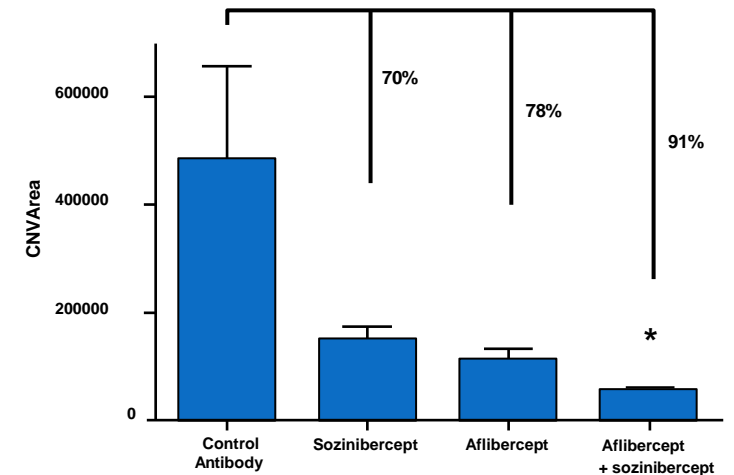
VEGF-A and VEGF-C Induce Vascular Leakage/permeability[#]



Elevated VEGF-C in Aqueous Humor Following Anti-VEGF-Atherapy in Wet AMD Patients^{*}



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



[^]Tammela et al., Nature Cell Biology, 2011; [#]Zhou et al. BMC Ophthalmology (2020) 20:15; [#]Cao et al., Circ Res., 2004; [†]Lashkari et al, 2013 ARVO Annual Meeting, 4999-A0128; ^{*}Cabral et al., 2018 Ophthalmology Retina (2018).

Sozinibercept Is Designed to Integrate into Current Anti-VEGF-A Clinical Practice



Patients

- Superior visual outcomes meaningfully improves patients' lives
- Intended to be administered at same anti-VEGF-A visit



Retina Specialists

- Better vision outcomes is a high unmet medical need
- Designed to be agnostic to anti-VEGF-A treatment type, including biosimilars

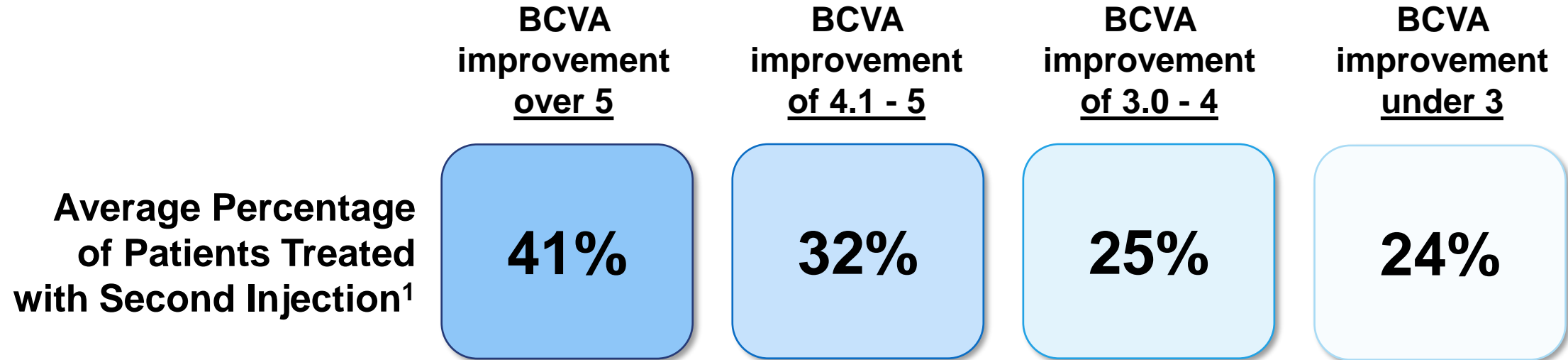


Payors / Insurance Companies

- Better clinical outcomes represent better health economics
- Visual benefits a key driver in reimbursement

Concentrated prescriptions in U.S. enables potential self-commercialization opportunity with lean and targeted organization

Physicians Willing to Administer Second Injection to up to 41% of Their Patients for Additional BCVA Improvement



What percentage of your Wet AMD patients would you use a second injection (anti-VEGF C/D) immediately after an anti-VEGF-A injection at various levels of BCVA improvement of the combination over SoC? (Among Total Respondents, Avg. % of Patients, n=125)*

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

TAM – Total Addressable Market

¹Source: InCrowd Awareness Trial and Usage (ATU) Report, June 2024

*Averages calculated using the midpoints of each % prescribing allocation group. Callouts indicate statistical significance between groups at 90% CI.

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	
Wet Age-Related Macular Degeneration (Wet AMD)					
Sozinibercept For use in combination with anti-VEGF-A therapies					Topline data: COAST (in early 2Q CY2025) ShORe (in mid-CY2025)
Diabetic Macular Edema (DME)					
Sozinibercept For use in combination with anti-VEGF-A therapies					Phase 3 ready
Co-formulation (Sozinibercept + VEGF-A Inhibitor)					
Sozinibercept 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

Clinical Milestones

- Phase 3 program enrolled 1,984 patients across COAST and ShORe
- Topline data anticipated for COAST in early 2Q CY2025 and ShORe in mid-CY2025

Manufacturing Scale-up

- DS PPQ campaign completed Sep-2024; update on DP PPQ in early CY2025
- PPQ validation batches supportive of BLA filing and launch

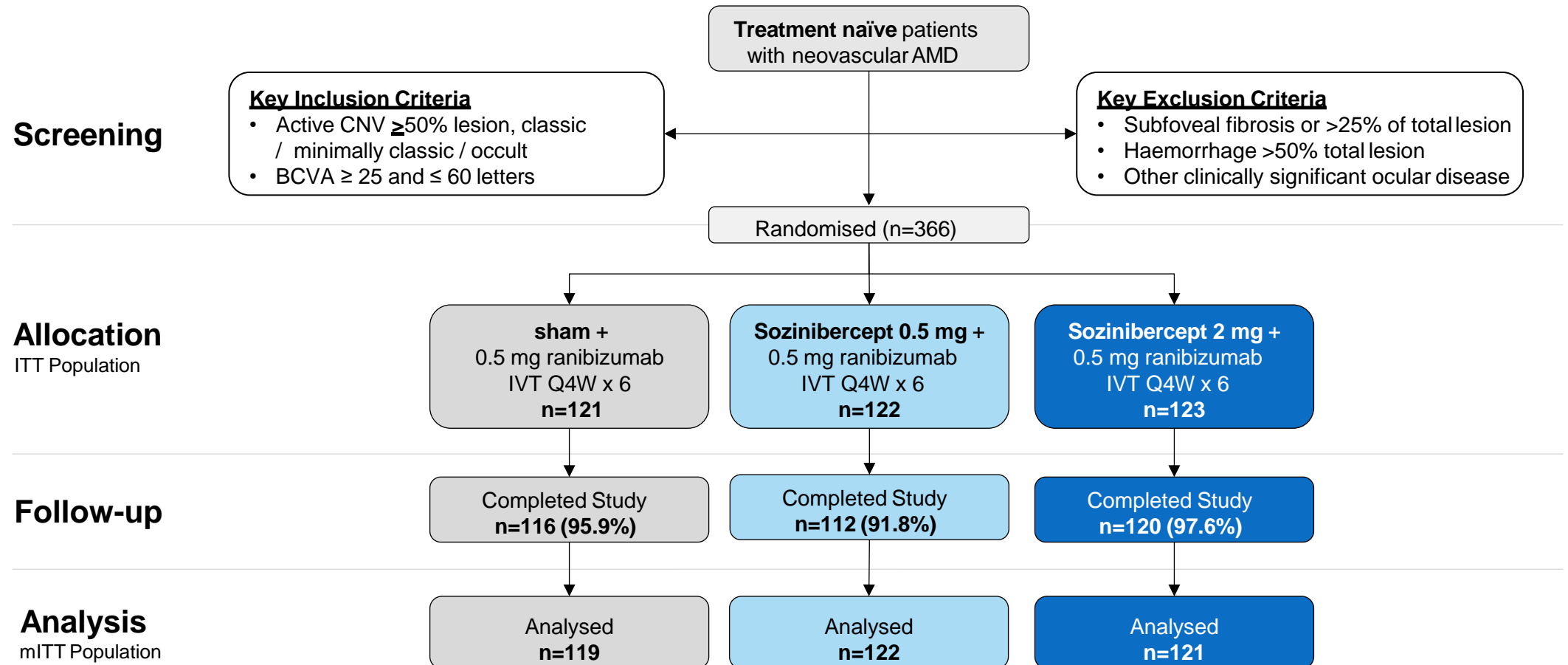
Regulatory Preparations

- FDA Fast Track designation allows rolling submission of completed BLA modules

Commercial Readiness

- Strengthen medical expert engagement and develop market access strategy
- Complete development of product launch plan

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

Primary Endpoint

Mean change from baseline in BCVA at week 24

Key Secondary Endpoints

Proportion of patients gaining ≥ 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

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%)	45 (36.6%)
	Female	73 (60.3%)	78 (63.4%)
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 ² ± 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 ¹ – n (%)	20 (16.5%)	24 (19.7%)
	RAP detected ² – 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%

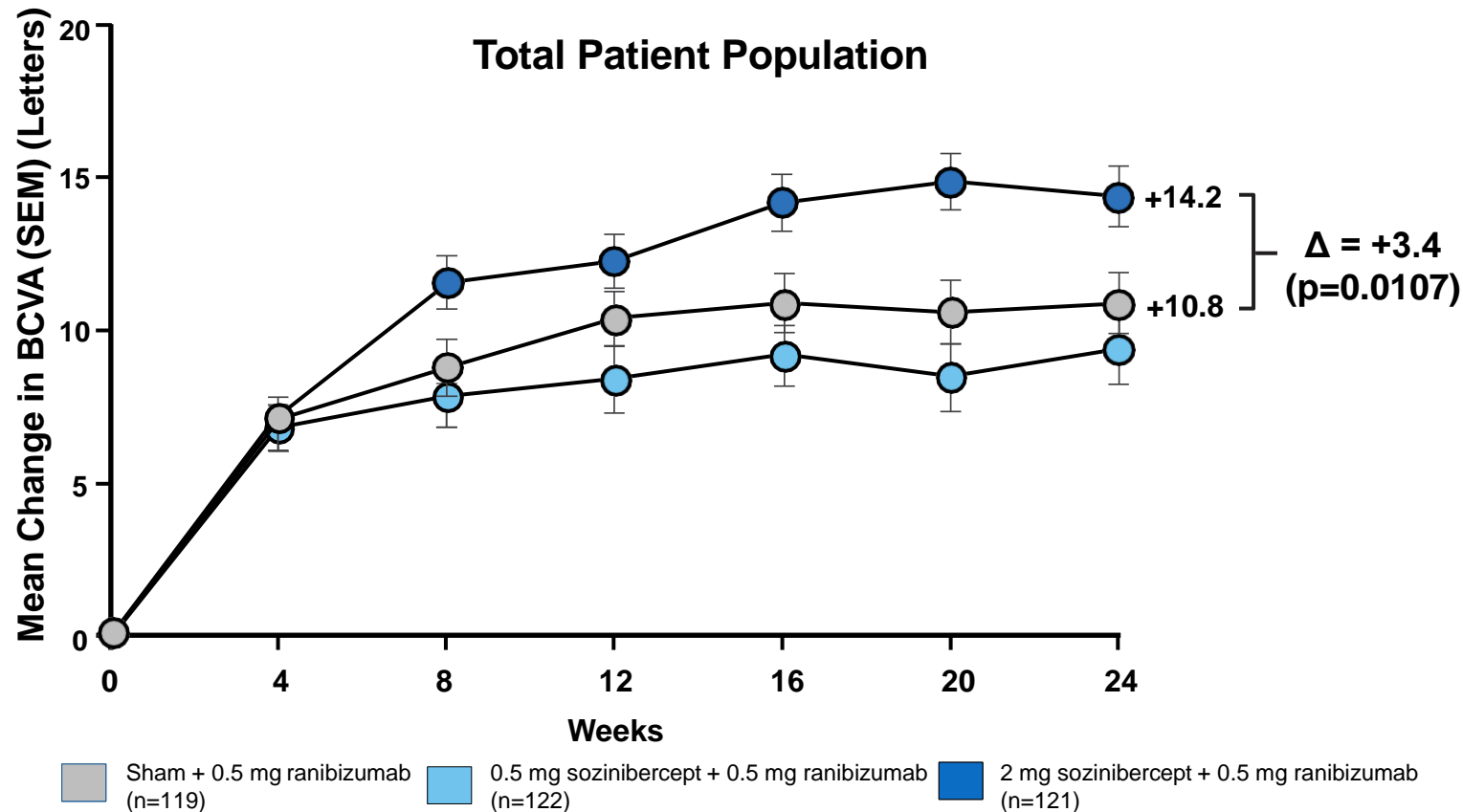
Intent-to-Treat (ITT) population; SD – standard deviation; BCVA – Best Corrected Visual Acuity

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

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

Sozinibercept 2 mg Combination Therapy Demonstrated Superiority in Visual Acuity over Ranibizumab Monotherapy

Phase 2b Primary Endpoint Achieved

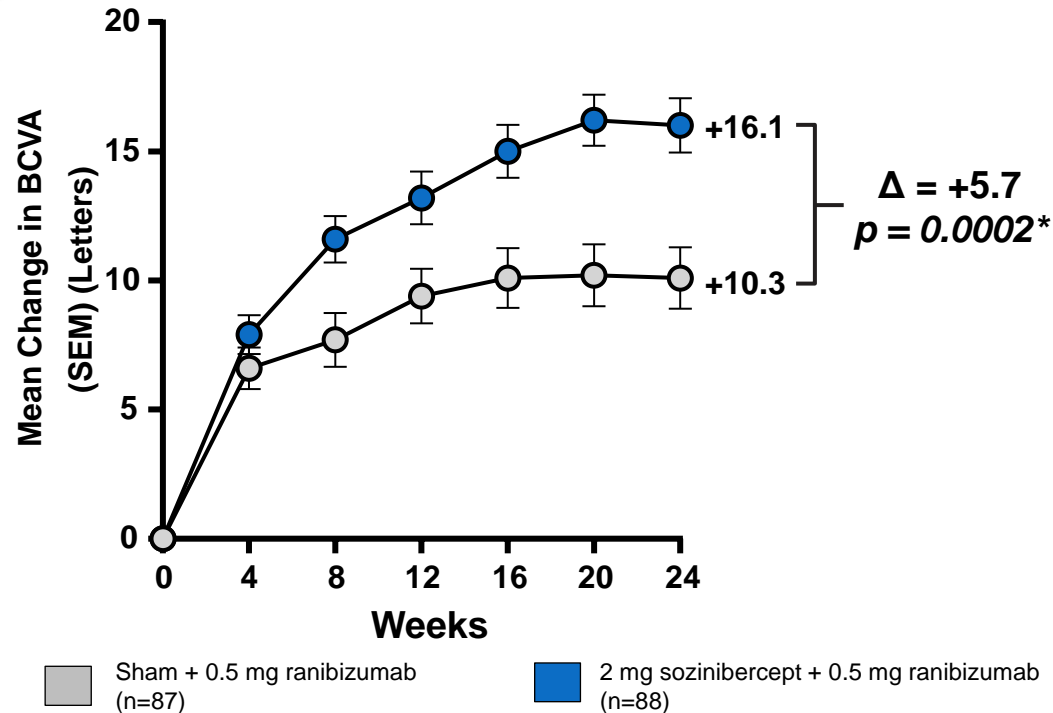


To Maximize Probability of Success, Best Responding Phase 2b Patients Represents Primary Analysis Population in the Pivotal Phase 3 Trials

Phase 3 Hierarchical Primary Analysis Testing Order Informed by Pre-Specified Phase 2b Subgroups

1st

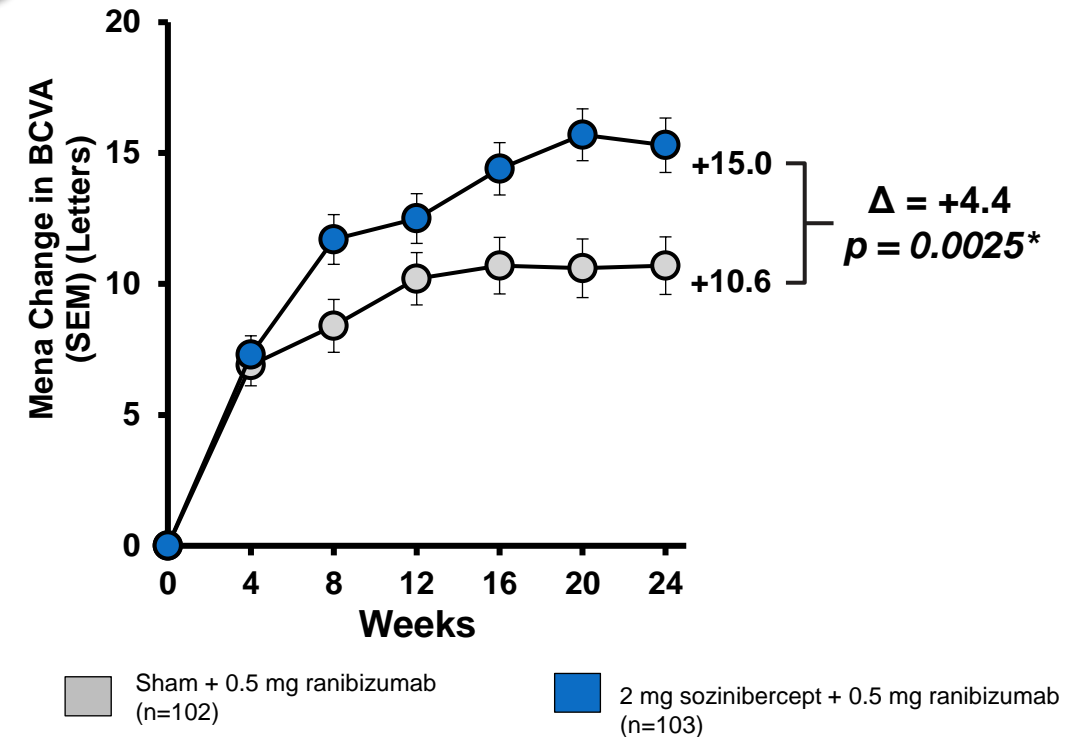
Occult & Minimally Classic Lesions (RAP Absent)



Represents ~75%¹ of wet AMD patients

2nd

Total Patient Population (RAP Absent)



Represents ~90%² of wet AMD patients

*Unadjusted p-values

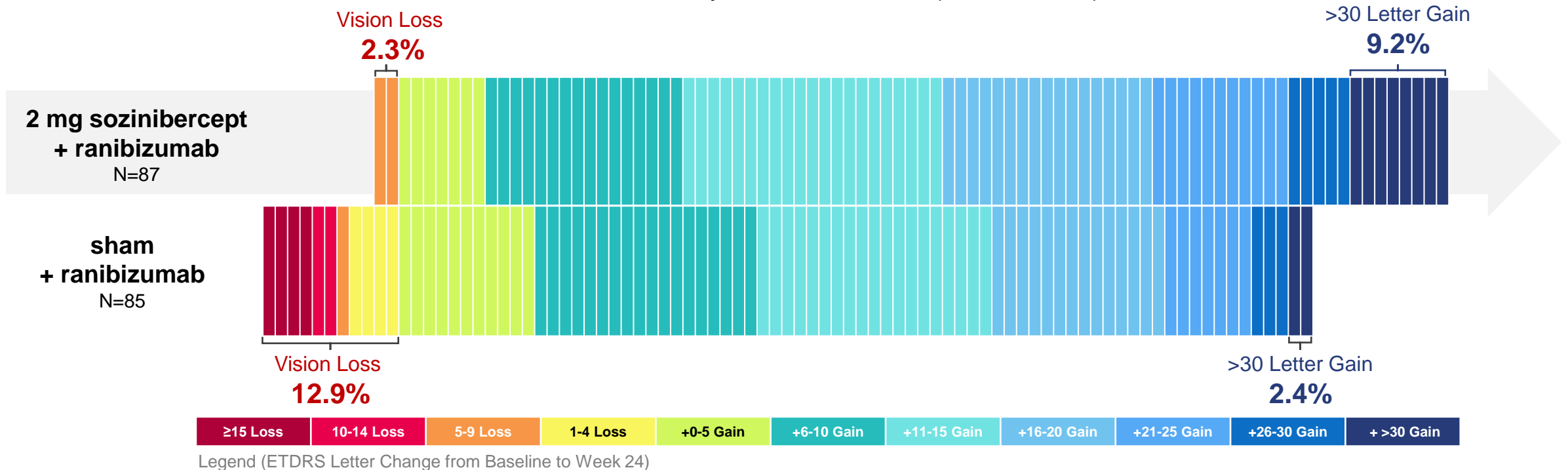
¹Olsen, Timothy W et al. Fluorescein angiographic lesion type frequency in neovascular Age-Related macular degeneration. Ophthalmology, 111(2), 250 – 255.

²Daniel, 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.

In a Disease Where Every Letter Counts, a Greater Proportion of Sozinibercept Patients Gained Substantial Vision and Fewer Experienced Vision Loss

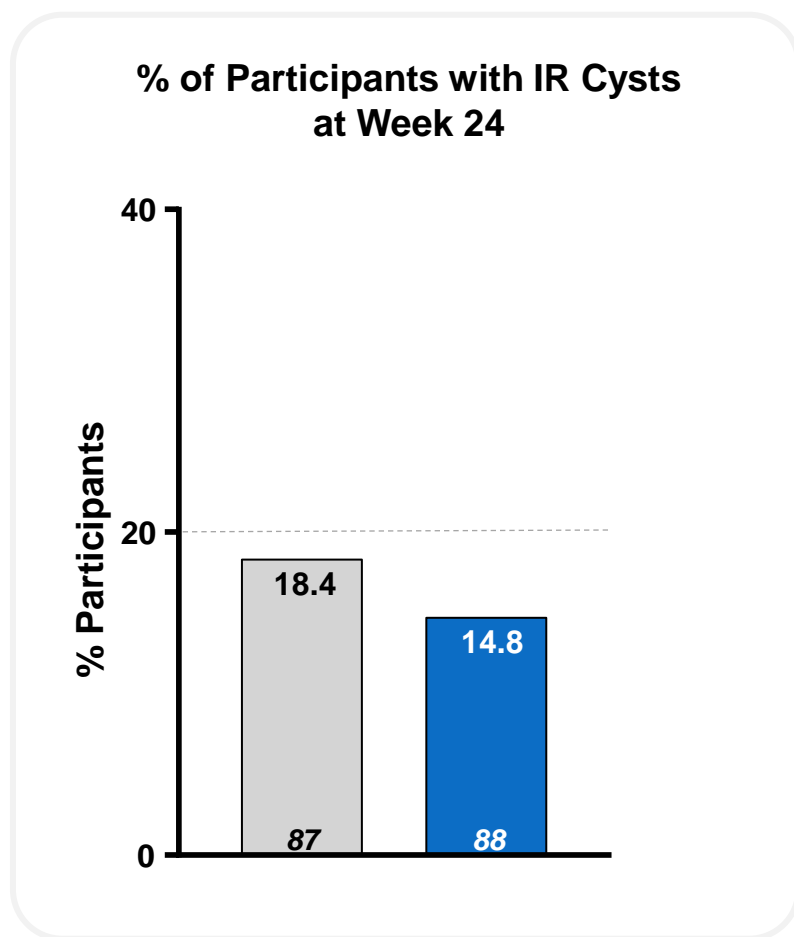
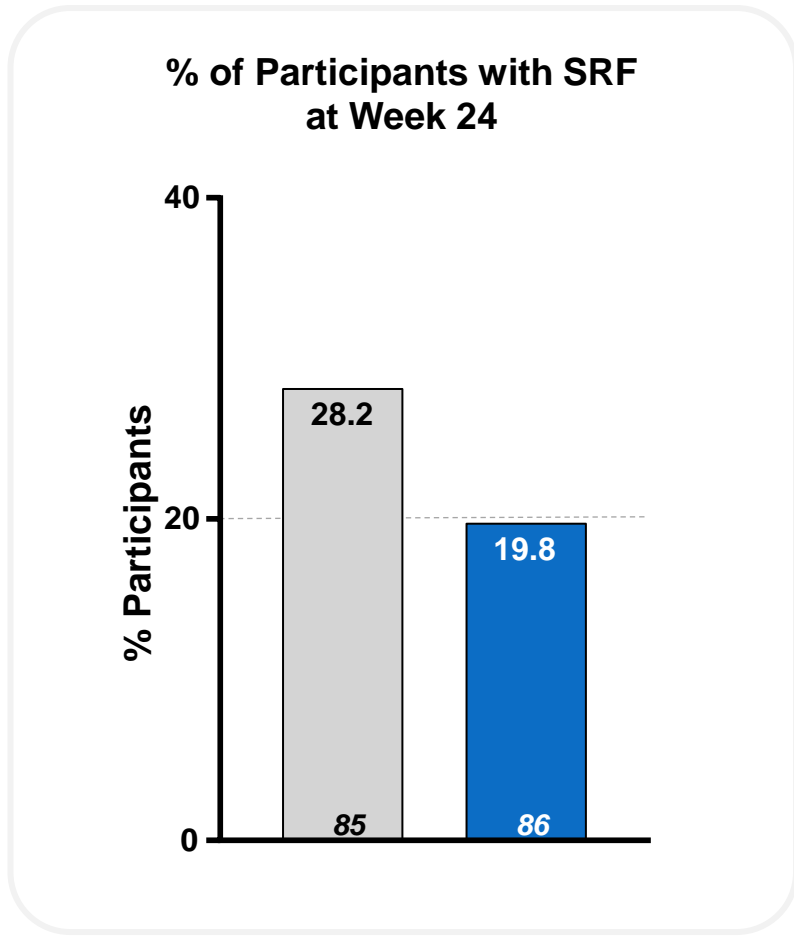
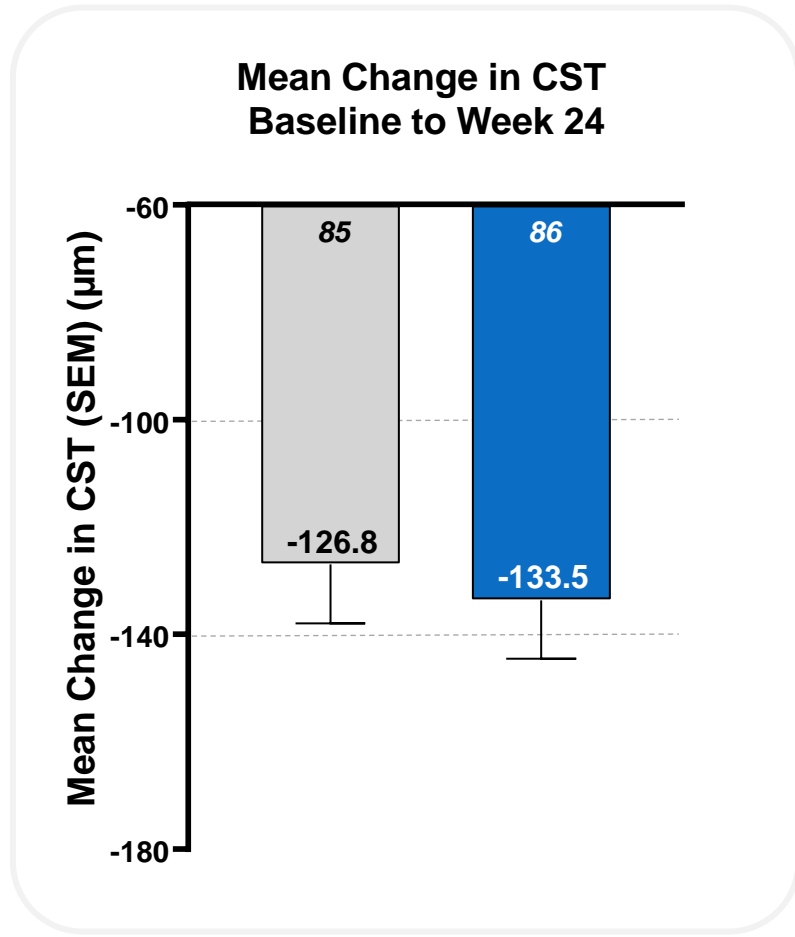
Change from Baseline to Week 24 (ETDRS Letters, Individual Participants)

Occult and Minimally Classic Lesions (RAP Absent)



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

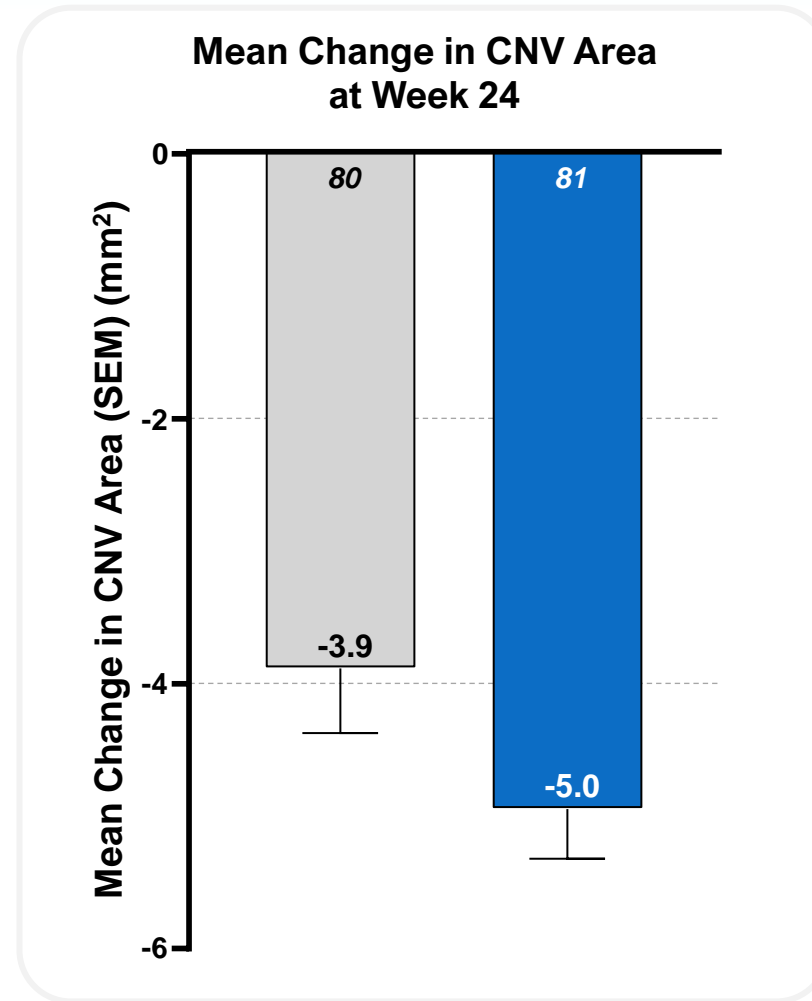
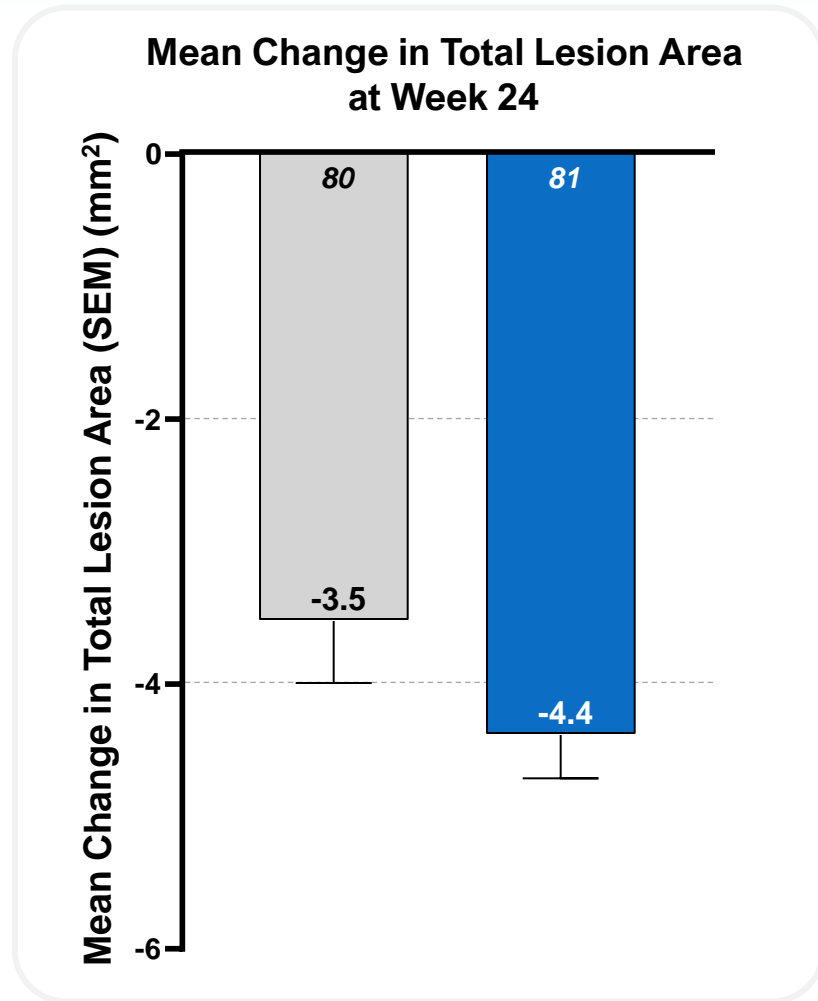
Sozinibercept Reduced Retinal Thickness and Dried the Retina Better With Combination Therapy in Occult & Minimally Classic (RAP Absent) Patients



Sham + 0.5 mg ranibizumab 2 mg sozinibercept + 0.5 mg ranibizumab

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

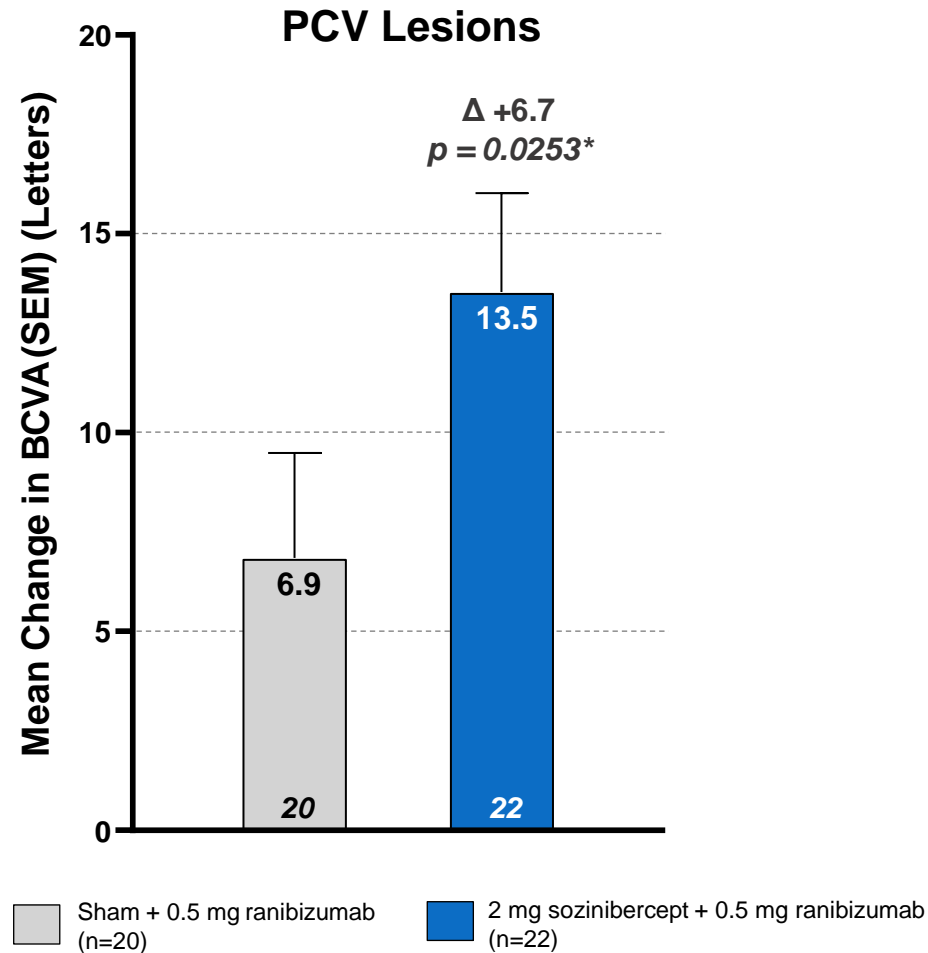
Sozinibercept Demonstrated Greater CNV and Lesion Regression With Combination Therapy in Occult & Minimally Classic (RAP Absent) Patients



Sham + 0.5 mg ranibizumab (n=80)

2 mg sozinibercept + 0.5 mg ranibizumab (n=81)

Sozinibercept Demonstrated Superior Vision Gains in a Pre-Specified Subgroup of 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 PCV¹

*Unadjusted p-value

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

Pooled Safety for Completed Sozinibercept Trials

Combination Therapy Well Tolerated and 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 ^{1,2,3} (1.8%)	3 ¹ (1.1%)	3 ¹ (1.8%)
Participants with AEs leading to treatment discontinuation	4 ^{2,4-6} (1.0%)	1 ⁴ (0.4%)	2 ^{7,8} (1.2%)
Any APTC event	4 ^{4,5,9,10} (1.0%)	3 ^{5,9,10} (1.1%)	2 ^{11,12} (1.2%)
Deaths	2 ^{10,13} (0.5%)	2 ^{10,13} (0.8%)	2 ^{14,15} (1.2%)

- Pooled safety analysis of 399 patients for completed sozinibercept trials
- Data Monitoring Committee (“DMC”) regularly reviews data from ongoing Phase 3 COAST and ShORe studies
- Safety data from our completed sozinibercept trials show sozinibercept combination therapy has a safety and tolerability profile comparable to standard of care anti-VEGF-A monotherapy.
- Masked data from patients that have completed the week 52 visit in the ongoing Phase 3 clinical trials show greater mean BCVA increases from baseline than results with standard of care anti-VEGF-A monotherapy from Opthea’s Phase 2b study**

¹Transient anterior chamber cell (trace 1-4 cells); ²SAE of endophthalmitis, with AE’s of hypopyon and anterior chamber cell (n=1; 0.5 mg); ³SAE of vitritis (n=1; 0.5 mg); ⁴Non-fatal myocardial infarction; ⁵Cerebrovascular accident; ⁶Enteritis; ⁷Abdominal pain;

⁸Increased IOP; ⁹Non-fatal angina pectoris; ¹⁰Fatal congestive heart failure/myocardial infarction; ¹¹Non-fatal arterial embolism; ¹²Embolic stroke; ¹³Metastatic ovarian cancer; ¹⁴Pneumonia; ¹⁵infective endocarditis.

*Any dose (sozinibercept 0.3 mg, 0.5 mg, 1 mg or 2 mg)

**Masked data represent pooled data from both sozinibercept combination and standard of care monotherapy treatment arms. The Phase 3 clinical trial masked data are incomplete and subject to additional analysis once unmasked. There is no assurance that standard of care monotherapy in our Phase 3 clinical trials will yield similar results to our prior clinical trials or previously published clinical trials with anti-VEGF-A monotherapies. As a result, there can be no assurance that topline results for sozinibercept from the Phase 3 clinical trial, if completed, will be consistent with results from masked data available to date.

Intraocular Inflammation Observed in Combination Therapy Across Completed Sozinibercept Trials Similar to Standard of Care

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)
Intraocular Inflammation¹	7 (1.8%)	3 (1.1%)	3 (1.8%)
OPT-302-1001 (Phase 1/2a wet AMD)	2	0	0
Uveitis with anterior chamber cell 1+	1	0	0
Uveitis with anterior chamber cell 2+	1	0	0
OPT-302-1002 (Phase 2b wet AMD)	3	1	2 ^a
Endophthalmitis with anterior chamber 1+ and hypopyon	1	0	0
Vitritis	1	0	0
Anterior chamber cell, trace	1	1	2 ^a
OPT-302-1003 (Phase 1b/2a DME)	2 ^b	2 ^b	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 ^b	1 ^b	0

Safety population

¹AEs observations considered to be indicative of intraocular inflammation, defined prior to database lock

^aObserved during ophthalmic examination, but not reported as TEAEs

^bConsidered 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)

Phase 3 Wet AMD Trials COAST and ShORe Are Well Advanced

Phase 3 Trial Design Supports Potential Broad Label for Use With Any Anti-VEGF-A Therapy

Trial Design

- Multi-center, double-masked, randomized (1:1:1), sham control
- ~90% power, 5% type I error rate

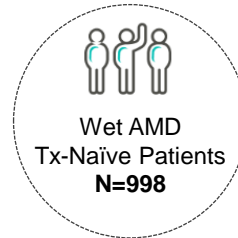
Primary Endpoint

- Mean change in BCVA from baseline to week 52

Key Secondary Endpoints (Baseline to Week 52)

- Proportion of participants gaining ≥ 15 letters
- Proportion of participants gaining ≥ 10 letters
- Change in choroidal neovascularization area
- Proportion of participants with absence of both sub-retinal fluid and intra-retinal cysts

COAST

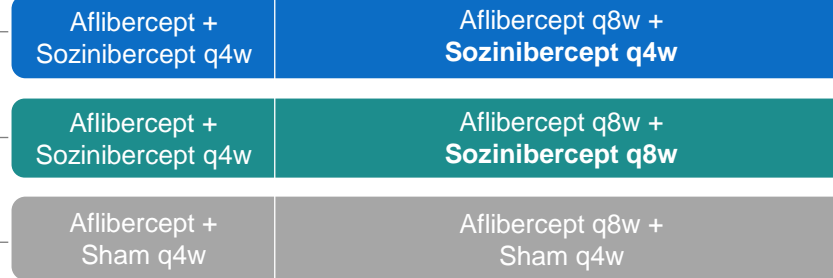


Enrollment Complete

Efficacy Phase

Loading Doses (12w)

Maintenance Dosing (40w)

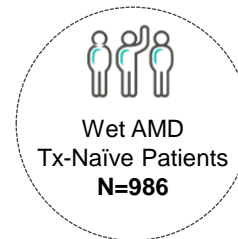


Topline Data Anticipated in Early 2Q CY2025

Primary Efficacy Endpoint Week 52

Safety Follow-up Week 100

ShORe

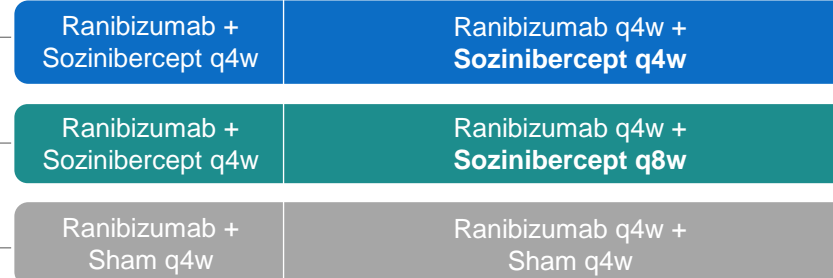


Enrollment Complete

Efficacy Phase

Loading Doses (12w)

Maintenance Dosing (40w)



Topline Data Anticipated in Mid-CY2025

Primary Efficacy Endpoint Week 52

Safety Follow-up Week 100

Recent Financings Anticipated to Provide Cash Runway Through Both Pivotal Topline Data Readouts

Financial Overview

Ticker	OPT (ASX/NASDAQ)
Shares Outstanding¹	Ordinary Shares: 1,231.1M ADS equivalents: 153.9M
Cash/Cash Equivalents²	US\$167.5M
Offices	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 received³

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

²As of September 30, 2024

³In 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 Development Funding Agreement ("DFA"). As a result of obligations under the DFA and applicable law regarding liquidity, the Company expects to raise or obtain additional capital in one or more transactions, earlier than 3Q CY 2025 or anticipated topline data readout dates.

Sozinibercept Will Not Compete Head-to-Head with Anti-VEGF-A

Differentiated Combination Approach Targeting Better Visual Outcomes Drives Commercial Value

1

Addressing unmet medical need of improved efficacy in large wet AMD patient population in a potential ~\$15B market

2

First and only therapy to have demonstrated superior visual outcomes over anti-VEGF-A therapy with a novel and highly differentiated MOA

3

Only asset in near or long-term pipeline with potential to disrupt treatment paradigm on basis of efficacy in wet AMD

4

Concentrated prescriptions in U.S. enables potential self-commercialization opportunity with lean and targeted organization