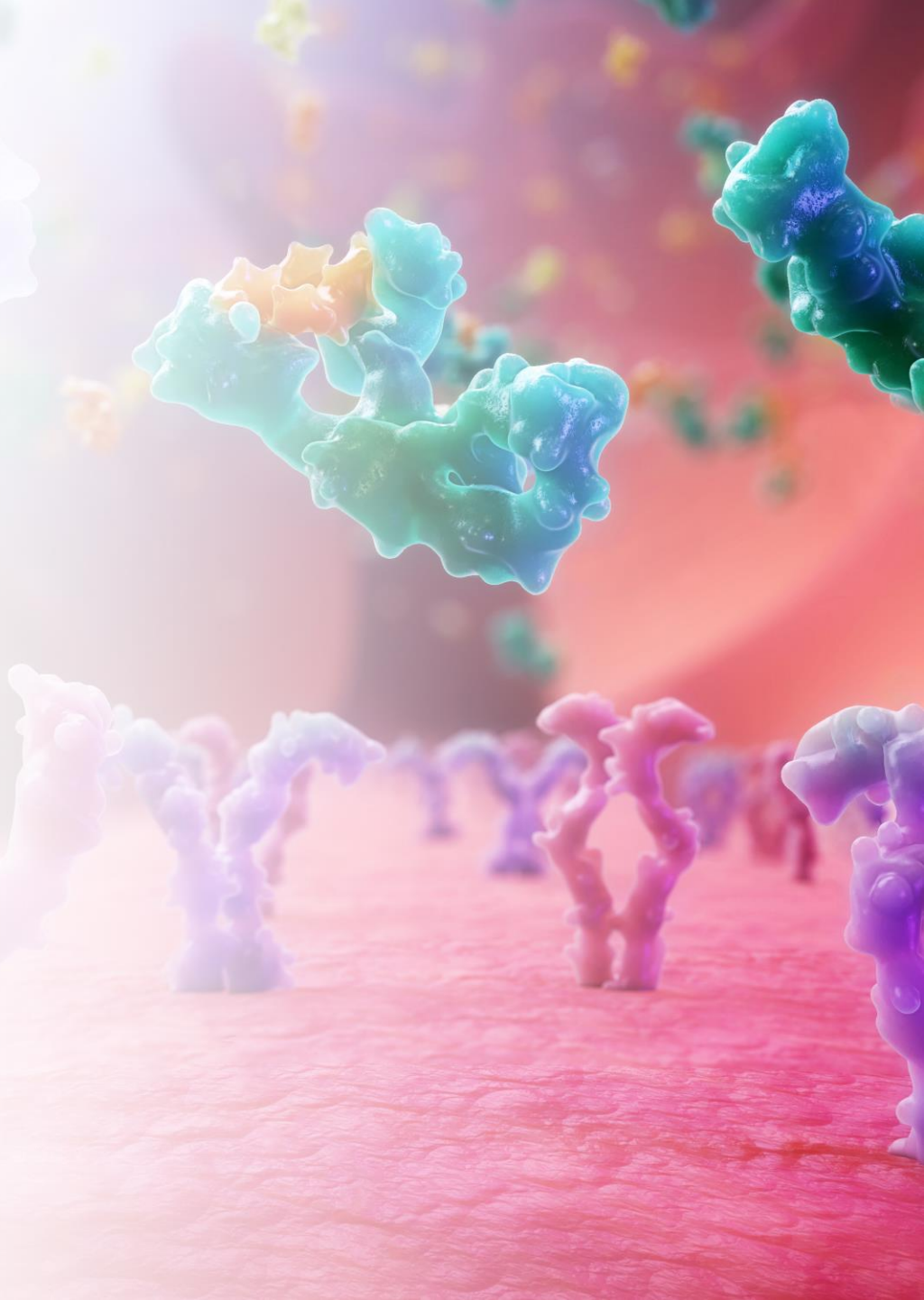
OPTHEA

Transforming Patient Outcomes with Superior Vision Gains



Corporate Presentation | August 2024

NASDAQ (OPT); ASX (OPT.AX)

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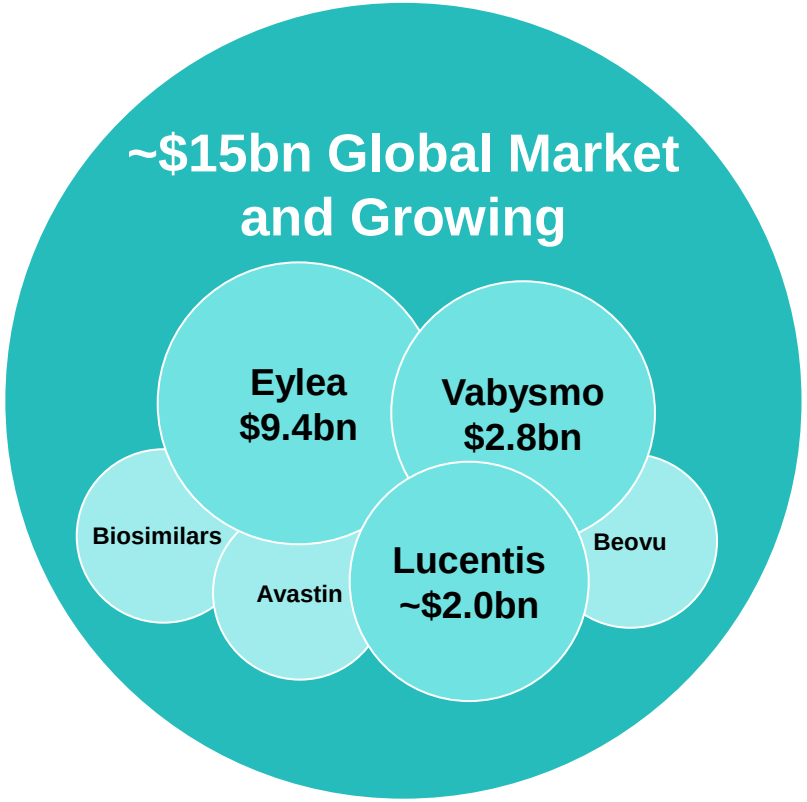
Sozinibercept Has the Potential to Be the First Product in More Than 15 Years to Improve Visual Outcomes

Addressing High Unmet Need	• Wet age-related macular degeneration (wet AMD) is the leading cause of vision loss in the elderly, impacting ~3.5 million patients in the US and Europe, despite wide use of anti-VEGF-A standard of care
Proprietary Technology	• First-in-class VEGF-C/D Trap 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
Enrollment Complete in Two Pivotal Trials	• COAST enrollment complete as of Feb 2024 (n=998); ShORe enrollment complete as of May 2024 (n=986) • Topline data anticipated for COAST in early 2Q CY2025 and ShORe in mid-CY2025
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

MOA – Mechanism of Action; SOC – Standard of care
*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:

<u>Targeting Improved Visual Function</u>

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 biosimiliars, 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

graybug vibrant.vision
NOVARTIS
Alcon

Peter Lang
Chief Financial Officer

aerie
HSBC
Bank of America Merrill Lynch
UBS

Megan Baldwin, PhD, MAICD
Founder, Chief Innovation Officer & Executive Director

Genentech

Judith Robertson
Chief Commercial Officer

aerie
janssen
Johnson & Johnson
Alcon

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

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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

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

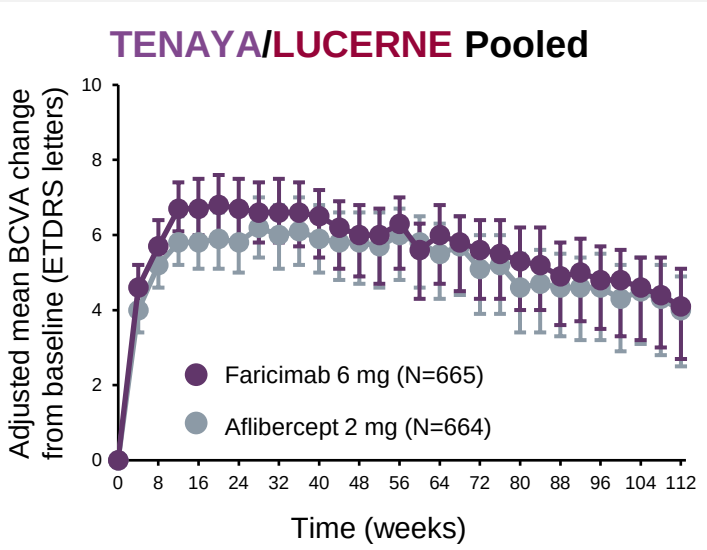
Most patients

cannot resume

routine daily activities, such as driving or reading

Unmet Needs in the Treatment of Wet AMD

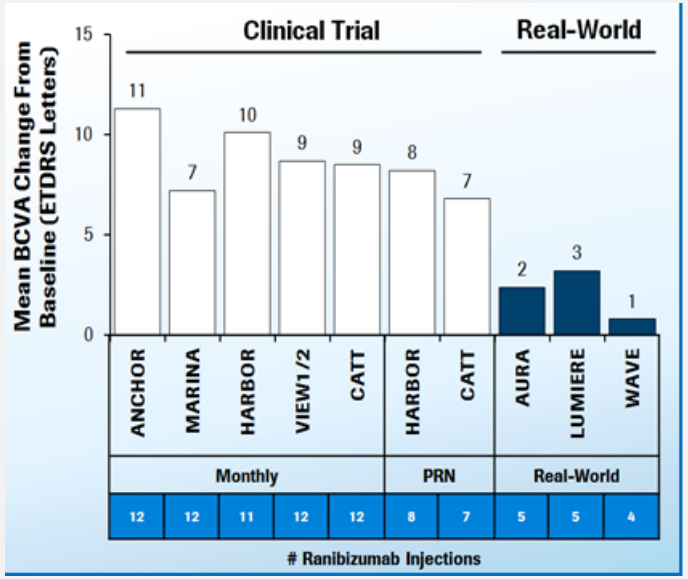
Efficacy



Faricimab trials in wet AMD – Year 1:

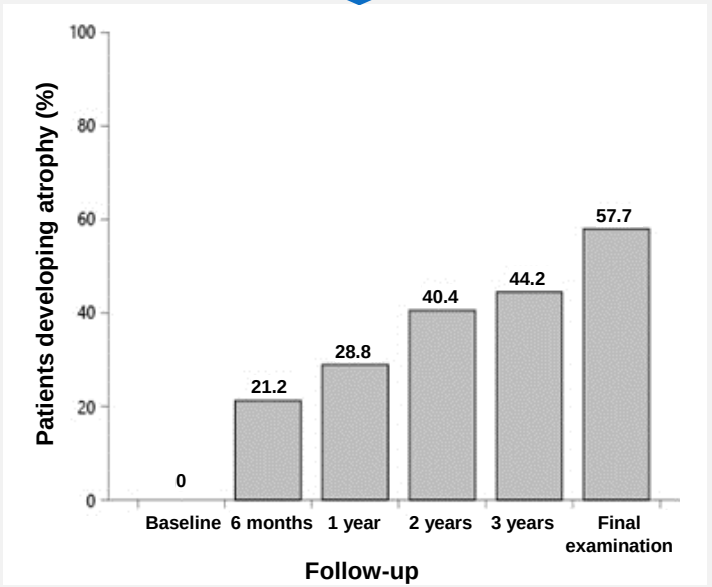
- 20%* gained ≥15 letters
- 57%† with ≥20/40 (driving vision)
- 9%† with vision ≤20/200

Durability



High treatment burden with frequent anti-VEGF-A injections leads to **sub-optimal vision** gains in the real world

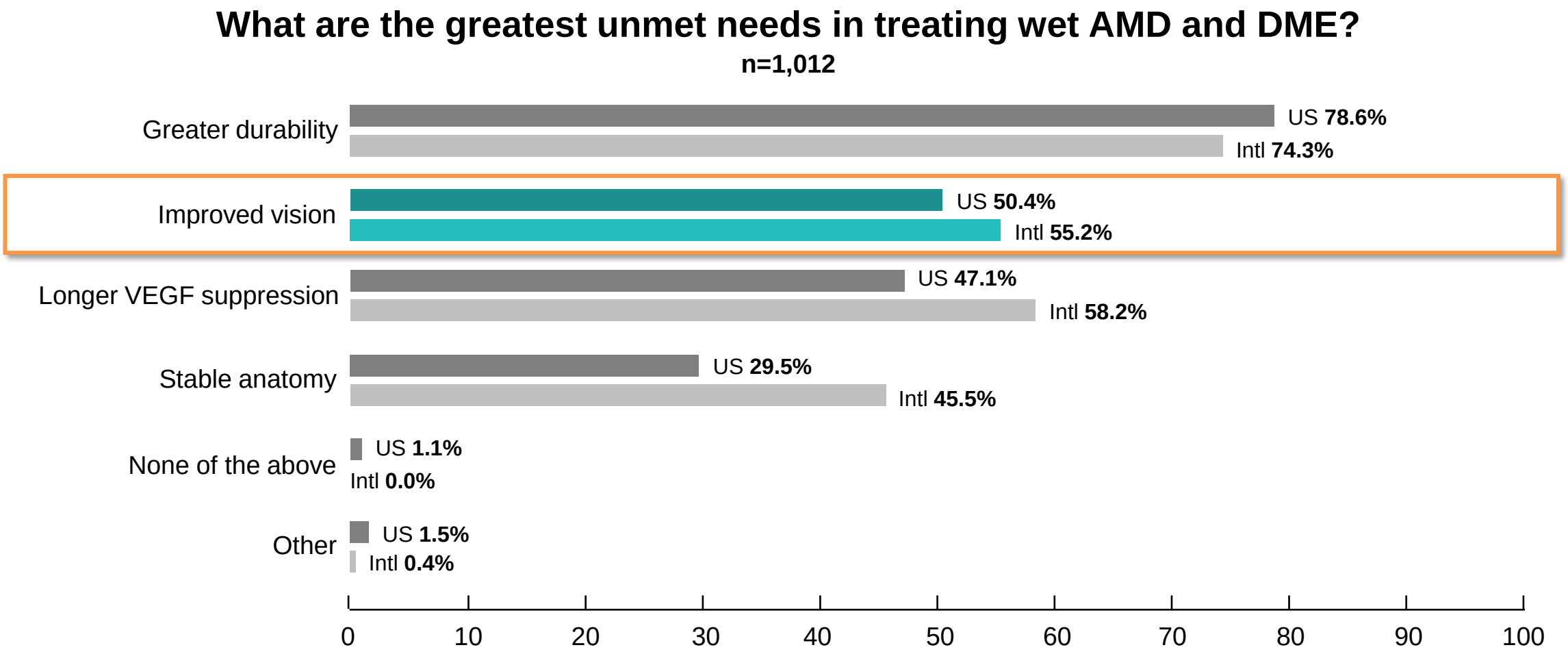
Disease Progression



Patients still develop **inflammation, fibrosis, atrophy,** and **ischemia** despite anti-VEGF-A therapy

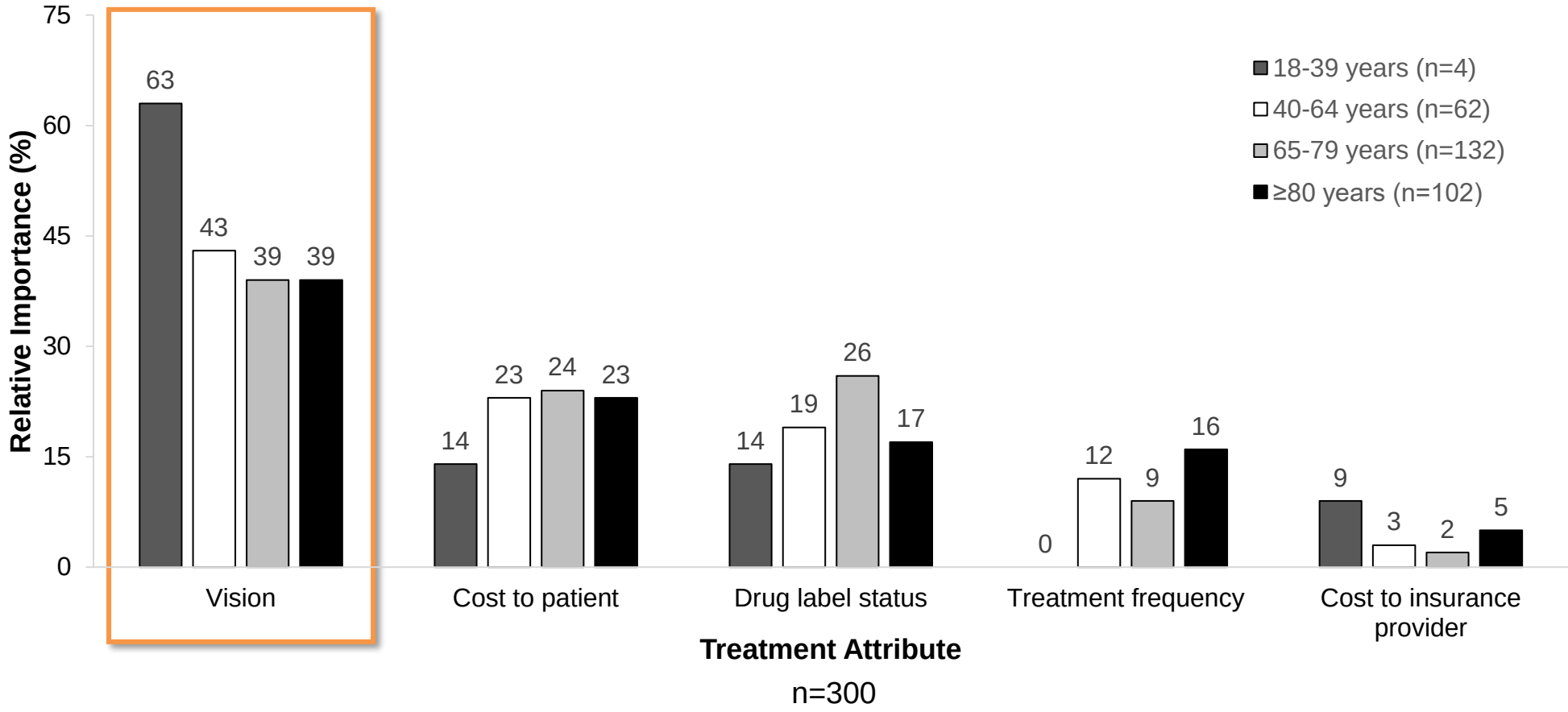
*Proportion averaged over Weeks 40, 44, and 48; †proportion at Week 48. BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; PRN, pro re nata (as needed); VEGF, vascular endothelial growth factor.

Improved Vision Is One of the Greatest Unmet Needs



AMD, age-related macular degeneration; DME, diabetic macular edema; Intl, international; US, United States of America; VEGF, vascular endothelial growth factor

Relative Importance of Treatment Attributes for Patients Receiving Anti-VEGF-A Monotherapy



Emerging Treatments for Wet AMD: Better Vision Outcomes or Durability

Sozinibercept is the only late-stage drug in development targeting **better vision outcomes**

Better Vision Outcomes

Sozinibercept (OPT-302)

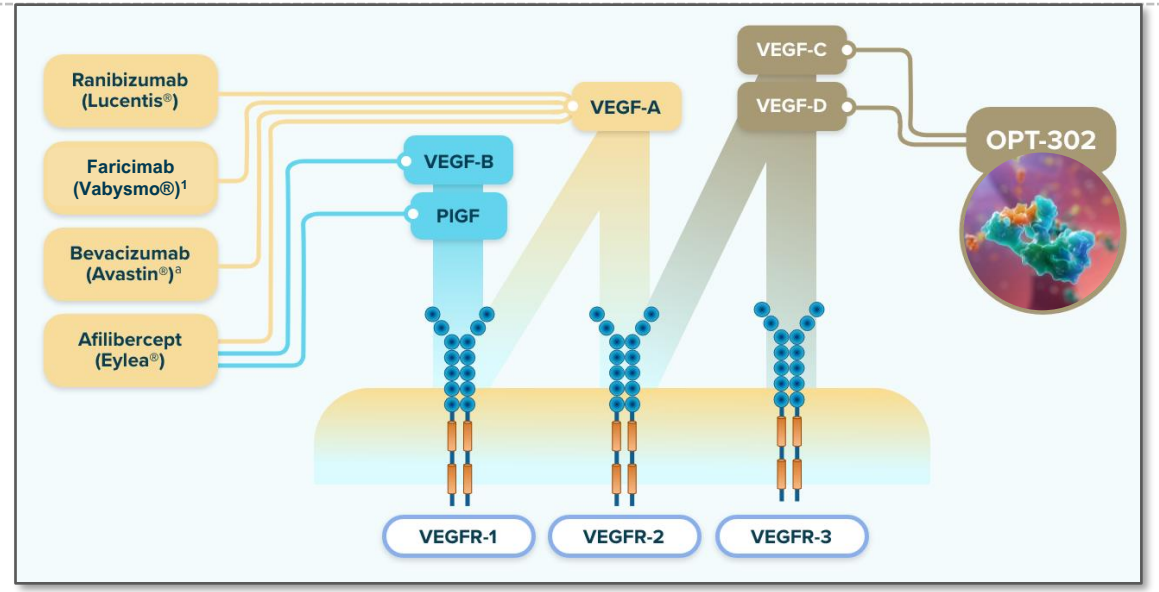
Better Durability

Tyrosine Kinase Inhibitors	Gene Therapy
OTX-TKI	RGX-314
CLS-AX	ADVM-022
EYP-1901	4D-150

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.



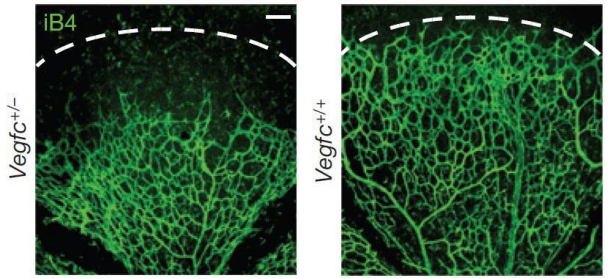
The Solution

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

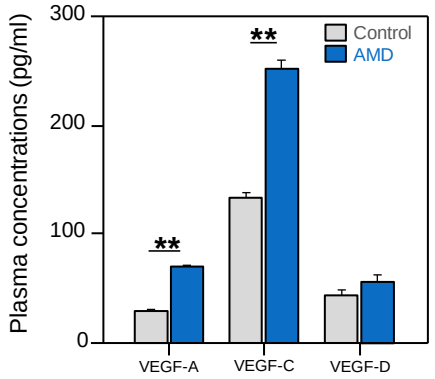
[1] Faricimab also has inhibitory effect on Ang-2.
[a] Bevacizumab is used ’off-label’ for the treatment of neovascular (wet) AMD

Published Evidence Supports Broader VEGF Pathway Inhibition with Sozinibercept

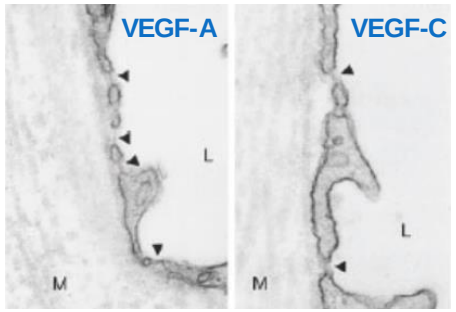
VEGF-C Stimulates Retinal Angiogenesis^



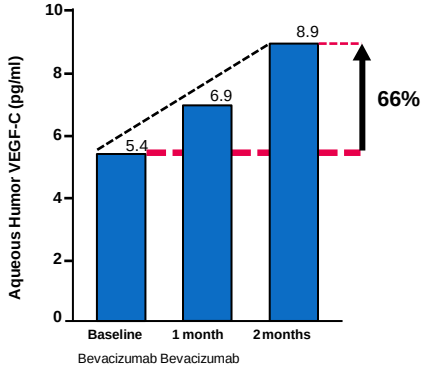
Circulating VEGF-C Levels Significantly Elevated in AMD Patients†



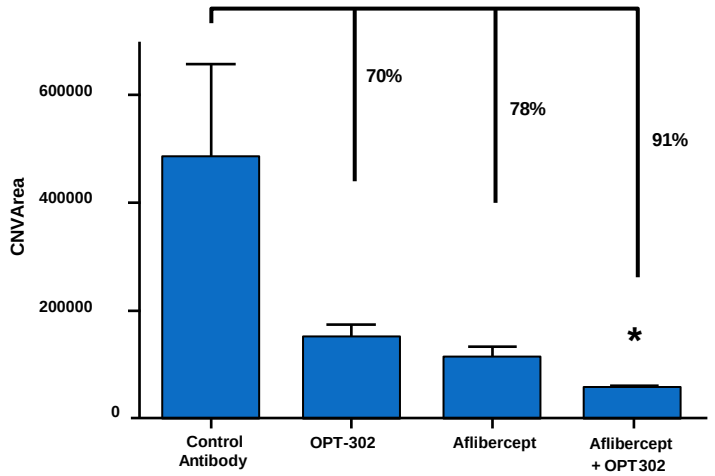
VEGF-A and VEGF-C Induce Vascular Leakage/permeability#



Elevated VEGF-C in Aqueous Humor Following Anti-VEGF-A therapy in Wet AMD Patients*

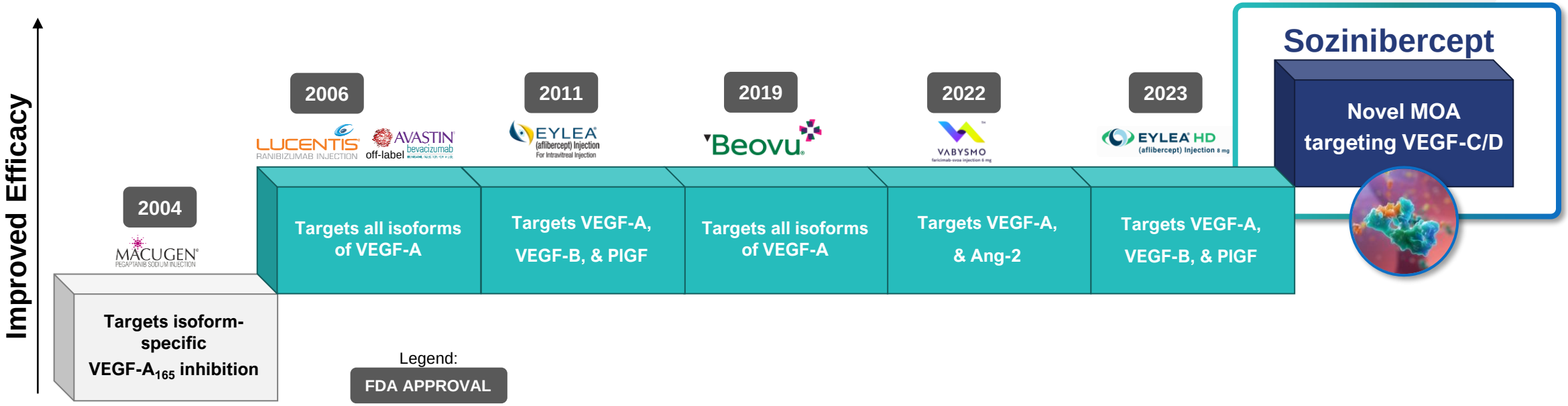


Additive Benefit of VEGF-A and VEGF-C/D Inhibition in Mouse Wet AMD Model



Sozinibercept Has the Potential to Be the First Therapy in More Than 15 Years to Improve Visual Outcomes in Patients with Wet AMD

Sozinibercept has demonstrated strong clinical evidence of superior patient visual outcomes



Sozinibercept 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

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)

Near-term Focus Is on Sozinibercept Phase 3 Execution

Pivotal Program Design Informed by Phase 2b and Optimized for Success

Completed Phase 1-2 Trials

Phase 2b (n=366)
Treatment **naïve** wet AMD

OPT-302: 6 x monthly dosing
Comparator: Ranibizumab (monthly)

Phase 1b/2a (n=153)
Prior-treated DME

OPT-302: 3 x monthly dosing
Comparator: Aflibercept (monthly)

Phase 1/2a: (n=51)
Treatment Naïve/Prior-treated wet AMD

OPT-302 + Ranibizumab:
3 x monthly dosing

Ongoing Phase 3 Trials

Topline data from both trials anticipated
for COAST (in early 2Q CY 2025) and ShORe (in mid-CY2025)

Enrollment Complete (Feb-24)

COAST

Phase 3 - wet AMD
(treatment naïve)
n=998

Comparator:

Aflibercept (Eylea®)
once every two months
after three monthly doses

Standard Dosing	Extended Dosing
OPT-302 once every month	OPT-302 once every two months after three monthly doses

Enrollment Complete (May-24)

ShORe

Phase 3 - wet AMD
(treatment naïve)
n=986

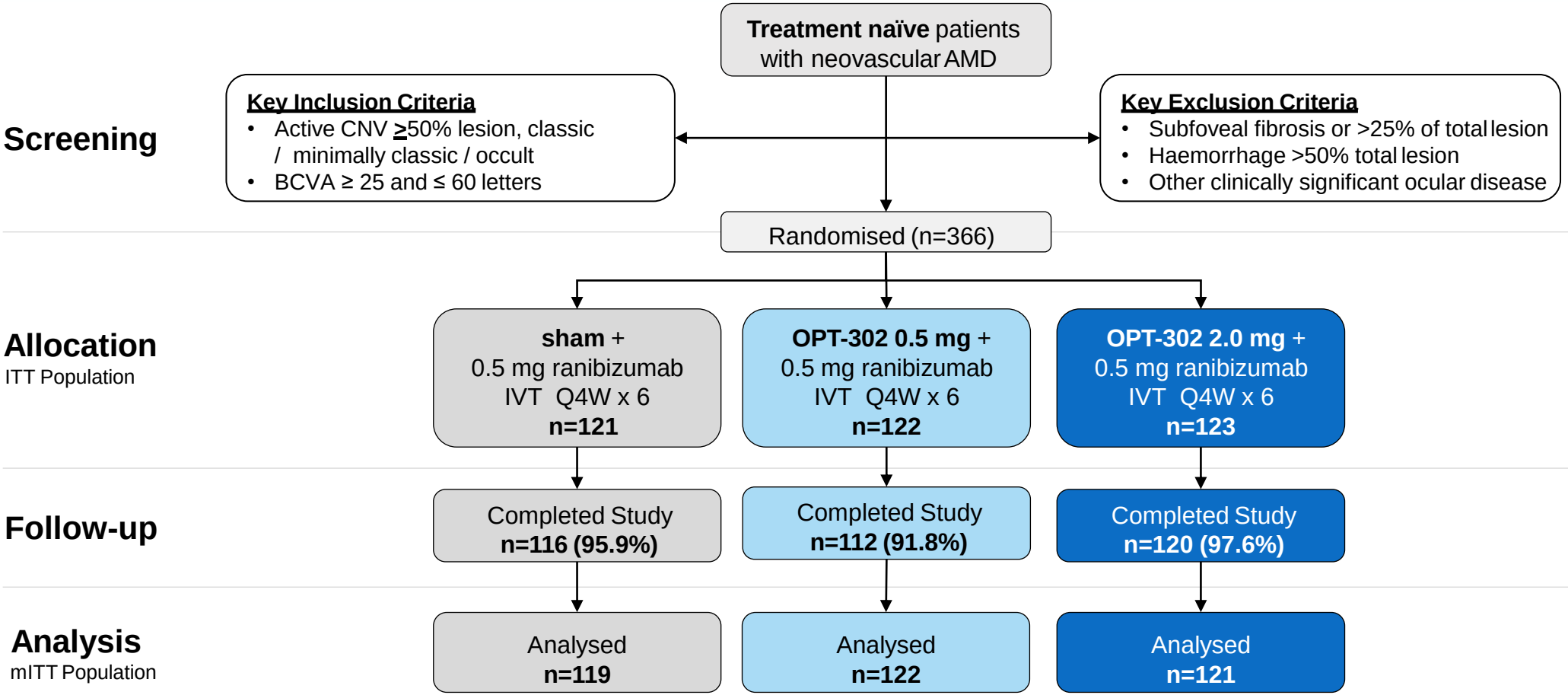
Comparator:

Ranibizumab (Lucentis®)
once every month

Standard Dosing	Extended Dosing
OPT-302 once every month	OPT-302 once every two months after three monthly doses

Ranibizumab (Lucentis®); Aflibercept (Eylea®)

Phase 2b Wet AMD Trial Overview



CNV – choroidal neovascularisation; IVT – intravitreal; Q4W – once very 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

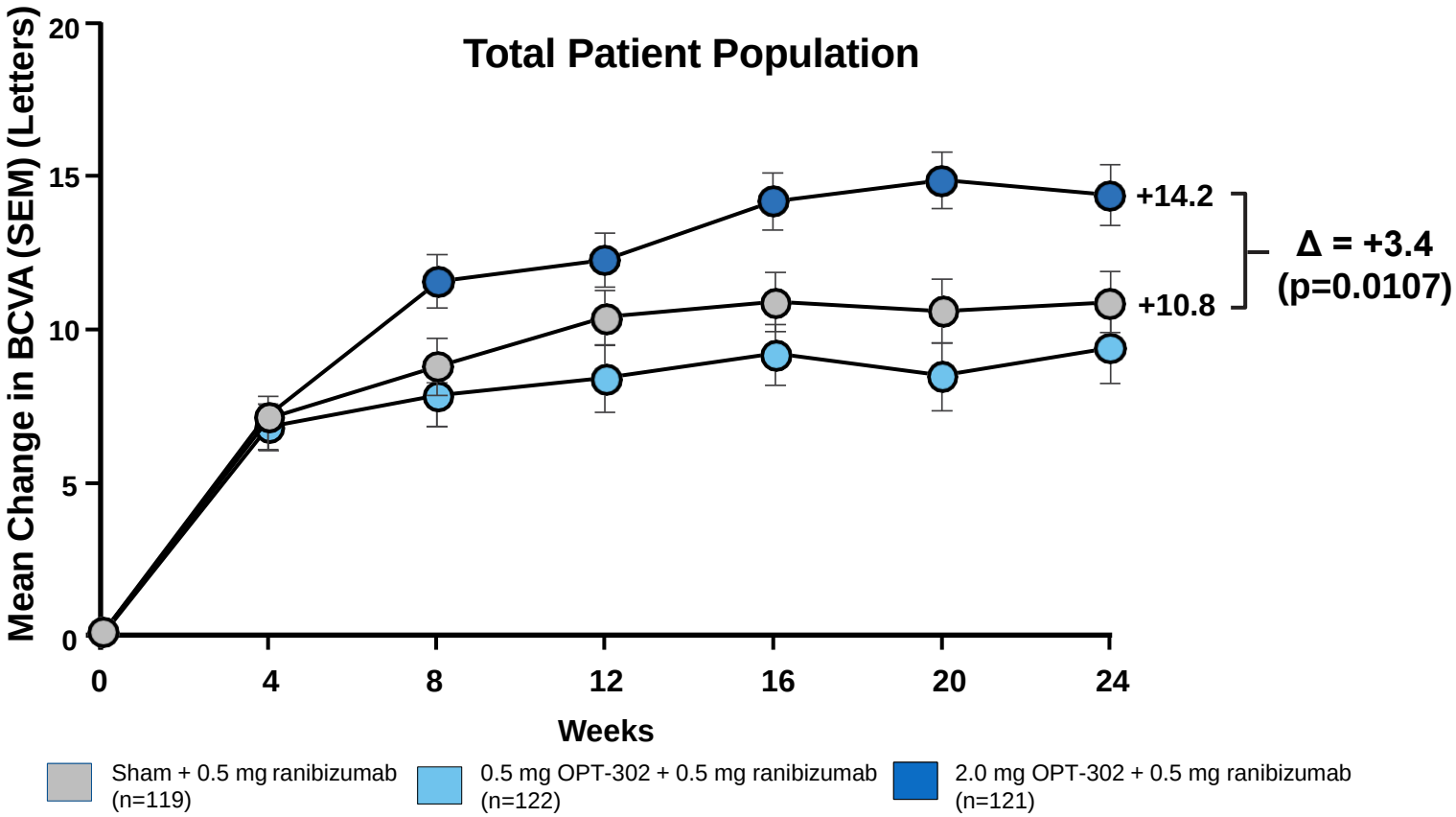
Phase 2b Trial Demographics and Baseline Characteristics

Demographic/Baseline Disease Characteristic		Sham + ranibizumab n=121	0.5 mg OPT-302 + ranibizumab n=122	2.0 mg OPT-302 + 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%)	45 (36.6%)
	Female	73 (60.3%)	73 (59.8%)	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 - mm² ± SD		6.08 ± 3.21	6.48 ± 3.30	6.62 ± 3.39
Lesion Type	Predominantly classic – n (%)	15 (12.4%)	15 (12.3%)	16 (13.0%)
	Minimally classic – n (%)	53 (43.8%)	51 (41.8%)	53 (43.1%)
	Occult - n (%)	53 (43.8%)	56 (45.9%)	54 (43.9%)
	PCV detected[1] – n (%)	20 (16.5%)	24 (19.7%)	22 (17.9%)
	RAP detected[2] – n (%)	15 (12.7%)	22 (18.5%)	14 (11.8%)
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%

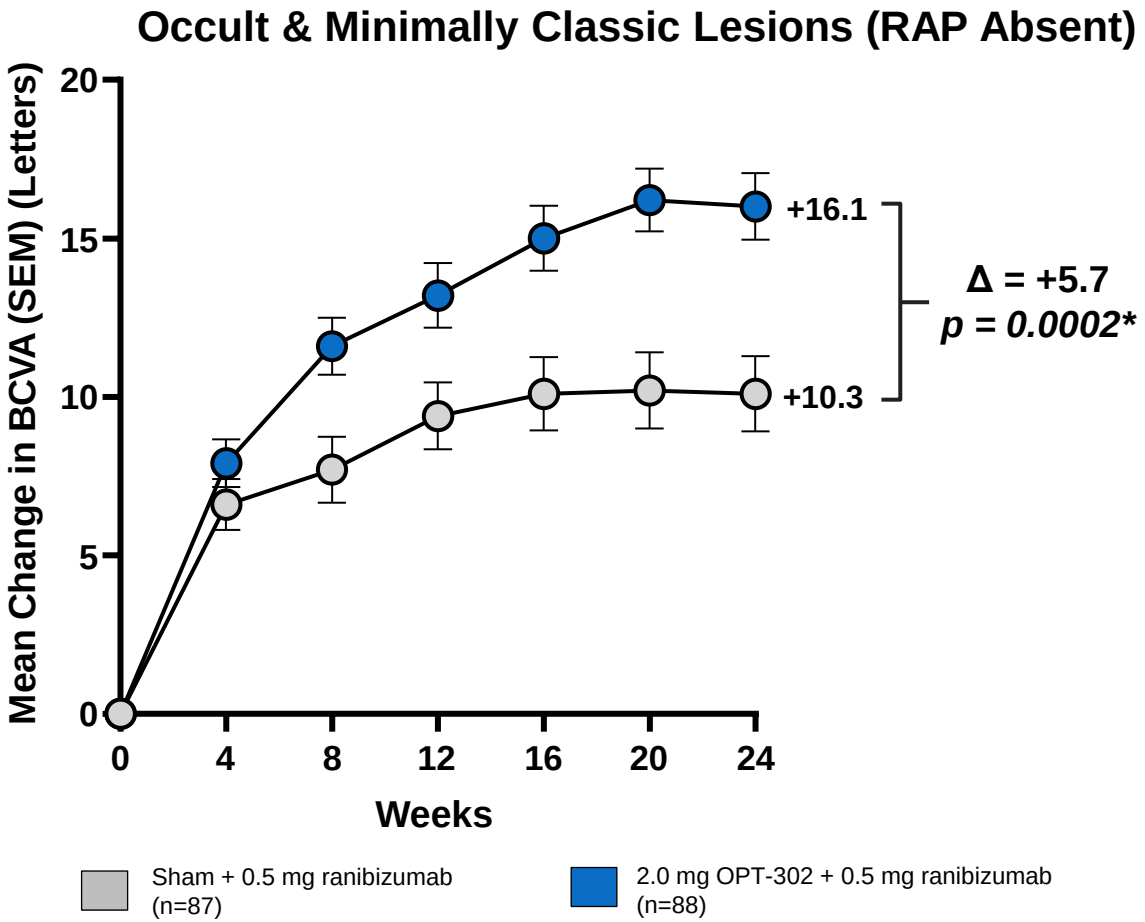
Intent-to-Treat (ITT) population; SD: standard deviation; BCVA: Best Corrected Visual Acuity. [1]PCV - polypoidal choroidal vasculopathy, detected by SD-OCT, FA and fundus photography. [2]RAP - retinal angiomatous proliferation, detected by SD-OCT, FA and fundus photography.

Sozinibercept 2.0 mg Combination Therapy Demonstrated Superiority in Visual Acuity over Ranibizumab Monotherapy

Phase 2b Primary Endpoint Achieved



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



Phase 2b demonstrated **superior efficacy** of **+5.7 letter gain over standard of care**, based on a **pre-specified analysis**

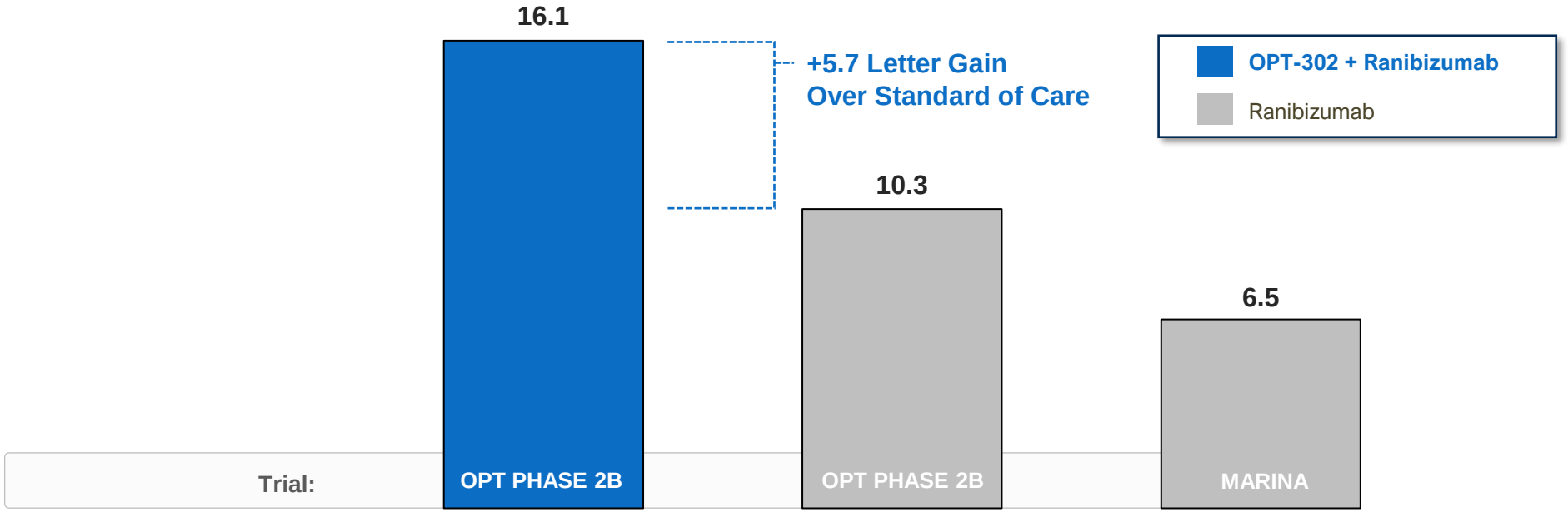
This patient population (minimally classic & occult) represents **~75% of wet AMD patients**

*Unadjusted p-value

Control Arm in Phase 2b Overperformed MARINA Trial at Week 24 in in Similar Lesion Type Patient Population

Mean Change in BCVA from Baseline at Week 24 – OPT-302 Phase 2b vs. MARINA Trial

Occult and Minimally Classic Lesions

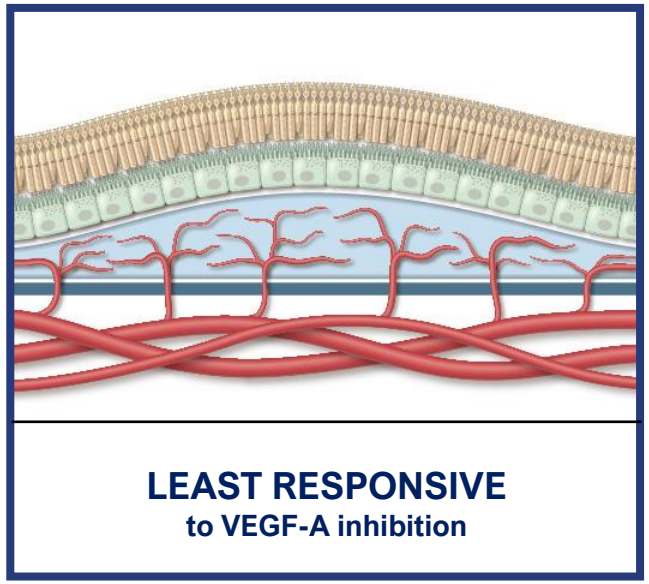


MARINA was a Phase 3 registrational trial. Baseline BCVA values across trials vary. Number of patients randomised to treatment group (n, bottom table). Mean change in Best Corrected Visual Acuity (BCVA) from baseline shown in ETDRS letters (top of bars).

Wet AMD Lesion Types

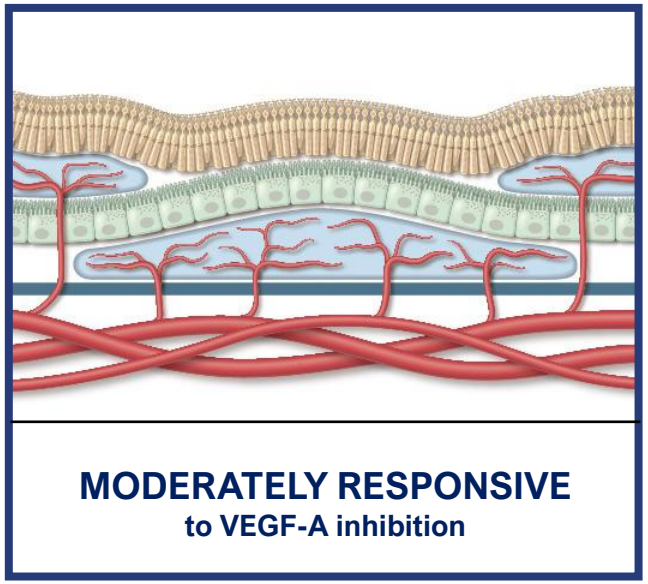
Differ in Vessel Location, Leakiness, and Responsiveness to VEGF-A Inhibitors

OCCULT



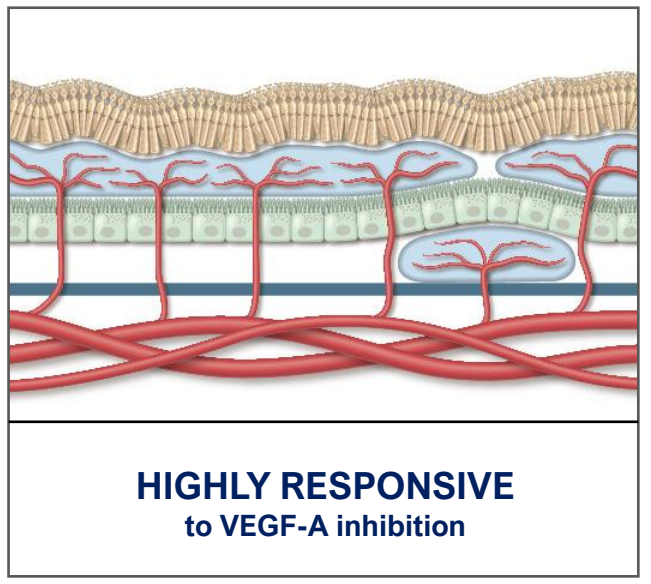
LEAST RESPONSIVE
to VEGF-A inhibition

MINIMALLY CLASSIC



MODERATELY RESPONSIVE
to VEGF-A inhibition

PREDOMINANTLY CLASSIC

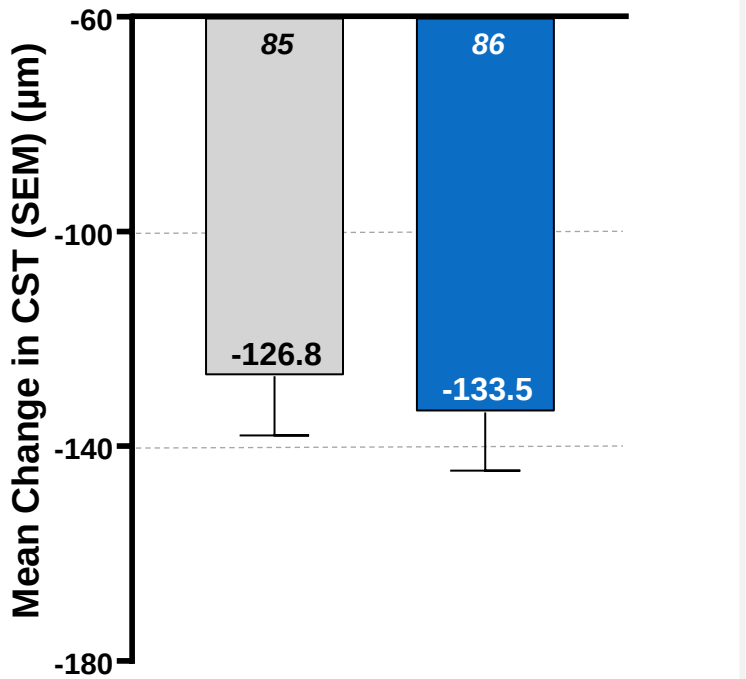


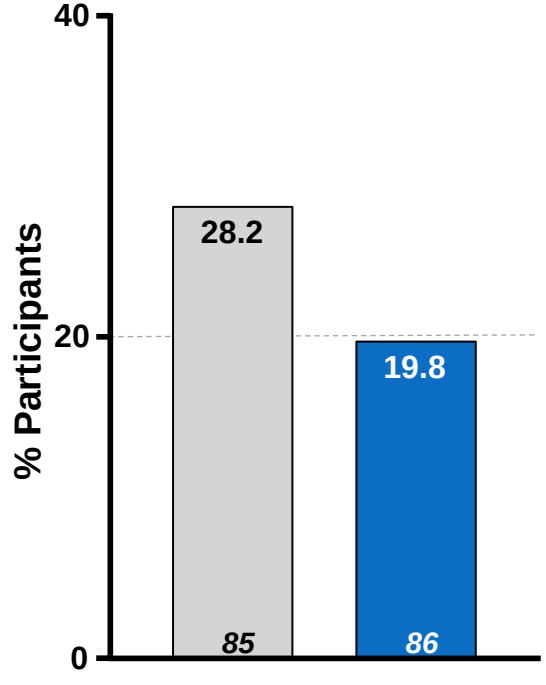
HIGHLY RESPONSIVE
to VEGF-A inhibition

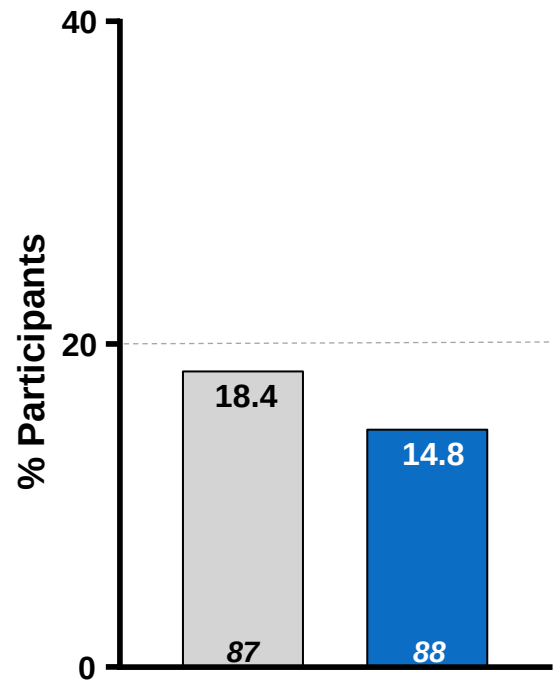
~75% of Wet AMD Patients Have Occult or Minimally Classic Lesions

Reduced Retinal Thickness and Better Retinal Drying

With Combination Therapy in Occult & Minimally Classic (RAP Absent) Patients







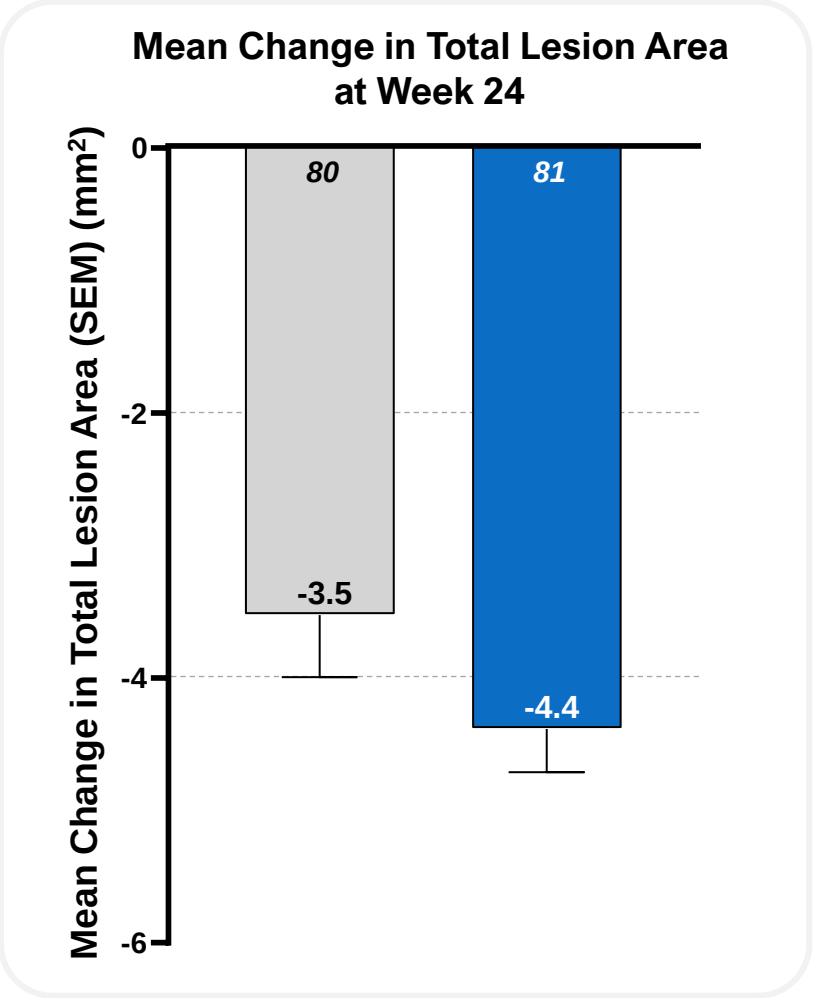
Sham + 0.5 mg ranibizumab

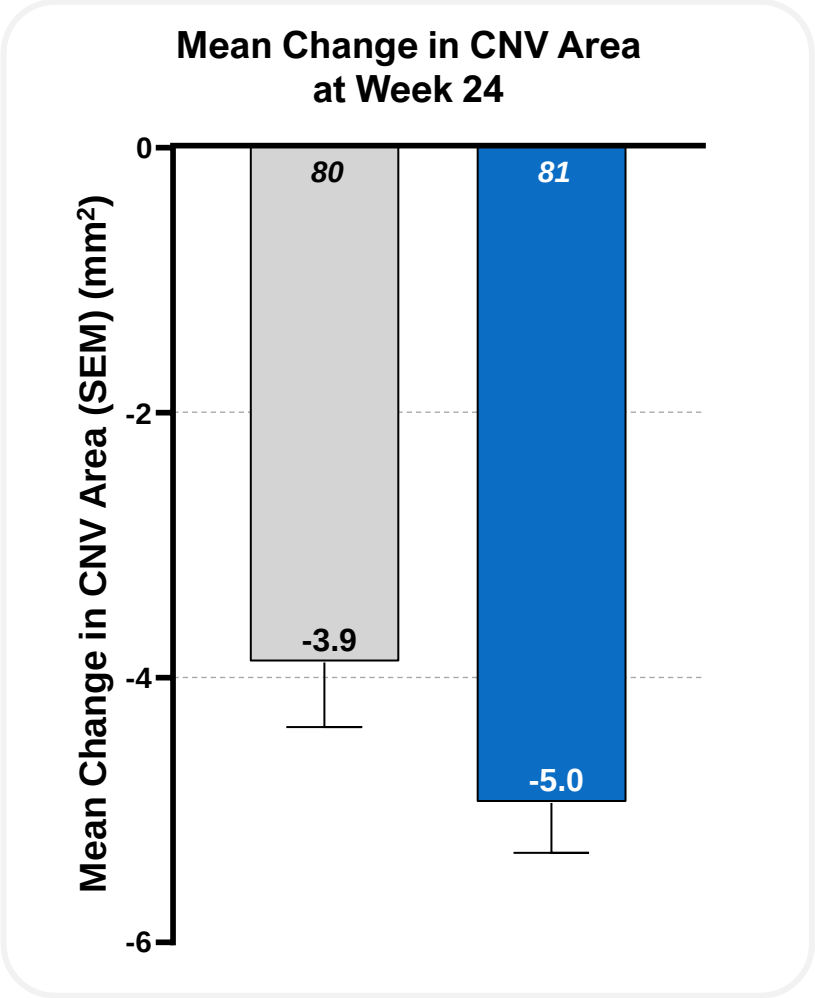
2.0 mg OPT-302 + 0.5 mg ranibizumab

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

Greater CNV and Lesion Regression

With Combination Therapy in Occult & Minimally Classic (RAP Absent) Patients



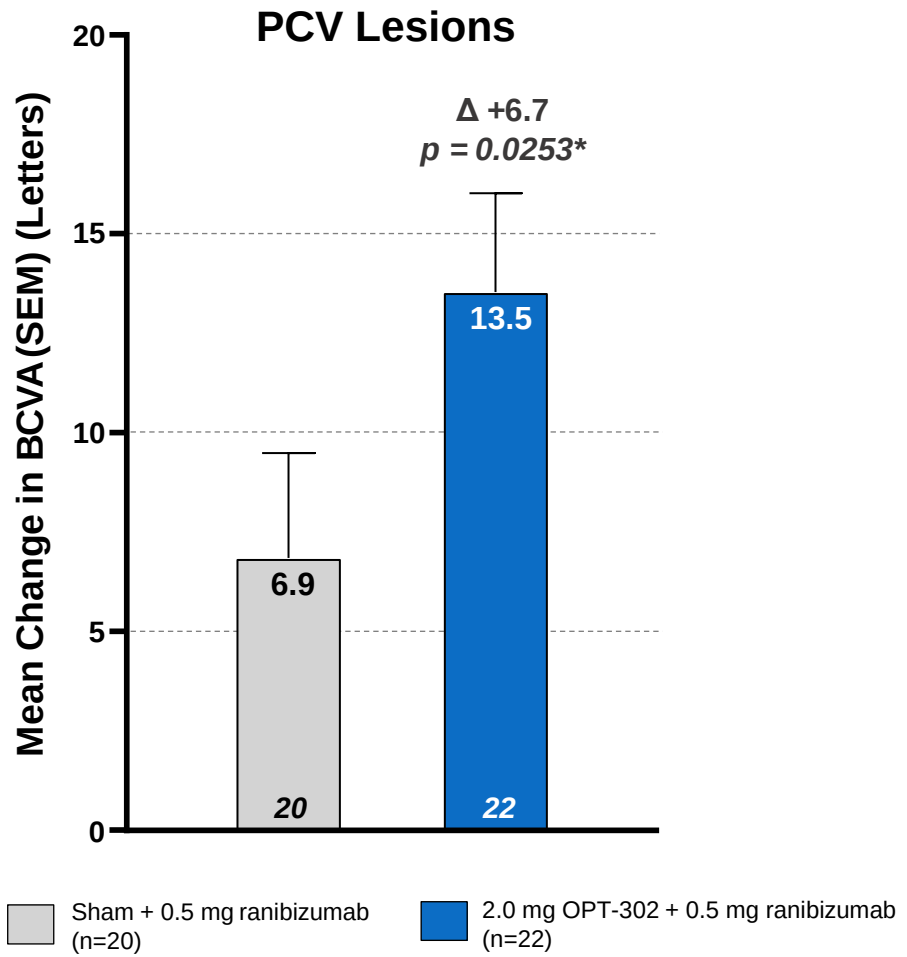


Sham + 0.5 mg ranibizumab (n=80)

2.0 mg OPT-302 + 0.5 mg ranibizumab (n=81)

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

Sozinibercept Further Demonstrated Superior Vision Gains in a Pre-Specified Subgroup of 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[1]

*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 OPT-302 Trials

Combination Therapy Well Tolerated and Comparable to Standard of Care Monotherapy

N Participants (%)	OPT-302 Any dose* N=399 (N=1,842 injections)	OPT-302 2.0 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 OPT-302 trials
- Data Monitoring Committee (“DMC”) regularly reviews data from ongoing Phase 3 COAST and ShORe studies
- Safety data from our completed OPT-302 trials show OPT-302 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**

[1]Transient anterior chamber cell (trace 1-4 cells); [2] SAE of endophthalmitis, with AE’s of hypopyon and anterior chamber cell (n=1; 0.5 mg); [3] SAE of vitritis (n=1; 0.5 mg); [4]Non-fatal myocardial infarction; [5]Cerebrovascular accident; [6]Enteritis; [7]Abdominal pain; [8]Increased IOP; [9] Non-fatal angina pectoris; [10]Fatal congestive heart failure/myocardial infarction; [11]Non-fatal arterial embolism; [12]Embolic stroke; [13]Metatstaic ovarian cancer; [14] Pneumonia; [15] infective endocarditis.
*Any dose (OPT-302 0.3 mg, 0.5 mg, 1 mg or 2 mg)
**Masked data represent pooled data from both OPT-302 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 OPT-302 from the Phase 3 clinical trial, if completed, will be consistent with results from masked data available to date.

Very Low Intraocular Inflammation Observed in Combination Therapy Study Eye Across Completed OPT-302 Trials

N Participants (%)	OPT-302 Any dose* N=399 (N=1,842 injections)	OPT-302 2.0 mg N=263 (N=1,121 injections)	Sham + anti-VEGF-A control N=170 (N=854 injections)
Intraocular Inflammation[1]	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
[1]AEs observations considered to be indicative of intraocular inflammation, defined prior to database lock
[a]Observed during ophthalmic examination, but not reported as TEAEs
[b]Considered associated with lens extraction and not reported as TEAEs

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

- **Hierarchical primary analysis first conducted in the high-responding occult and minimally classic population (RAP absent)**, 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

1,984 Patients Enrolled in Phase 3 Program |
Topline Data for COAST (anticipated in early 2Q CY 2025) and for ShORe (anticipated in mid-CY2025)

Design	• Multi-center, double-masked, randomized (1:1:1), sham control • Treatment naïve wet AMD patients
Sample Size	• COAST n=998; ShORe n=986
Comparators	• 2 mg Eylea® q8w (COAST) & 0.5 mg Lucentis® q4w (ShORe)
Regulatory Quality	• ~90% power, 5% type I error rate

Phase 3 Primary and Secondary Endpoints

Primary Efficacy Endpoint at Week 52 to Support BLA Submission

Primary Endpoint

Mean change from baseline in BCVA at week 52

Key Secondary Endpoints (Baseline to Week 52)

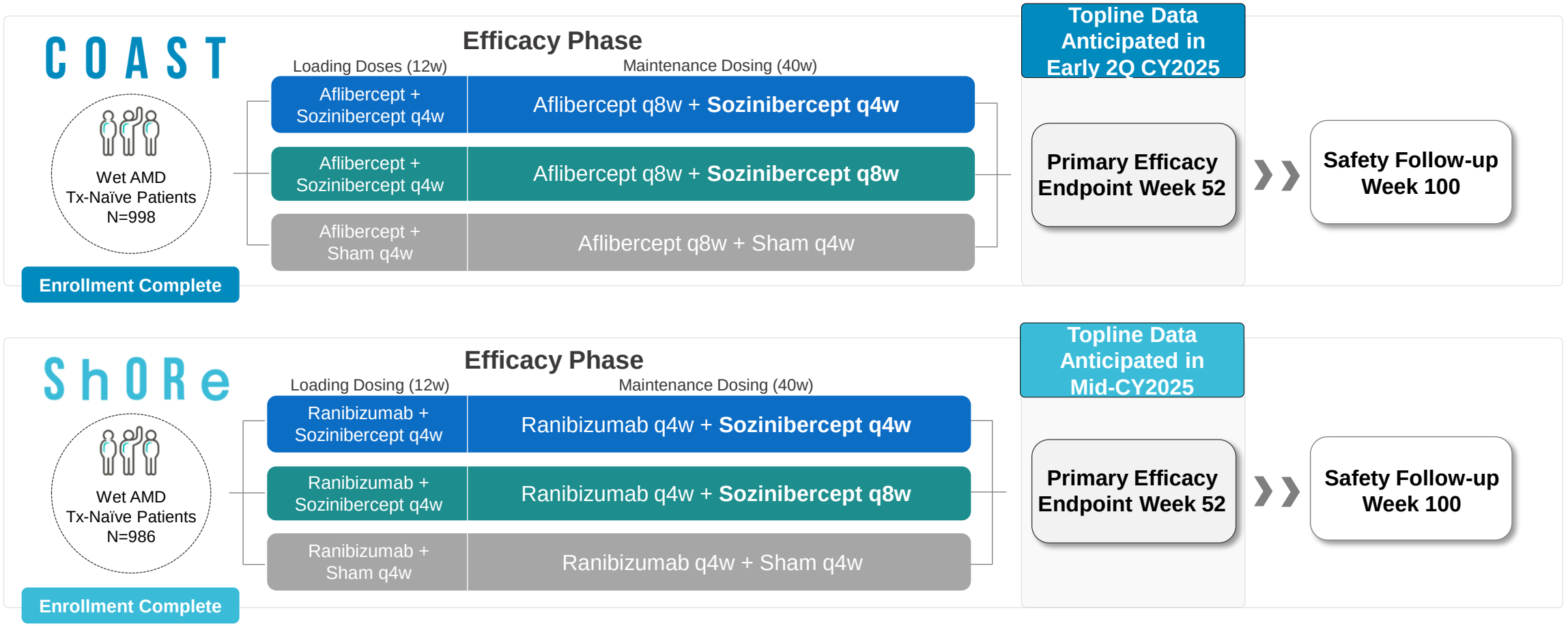
Proportion of participants gaining ≥15 letters

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

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



Standard of care administered according to approved dosing schedule: **aflibercept** (2.0 mg IVT q8w after 3 loading doses) and **ranibizumab** (0.5 mg IVT q4w after 3 loading doses). Sozinibercept dosed at 2.0 mg. Note that Sham administered at visits when sozinibercept is not administered. Maintenance dosing continued through end of the safety follow-up.

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	• Production of 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

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

MOA – Mechanism of Action