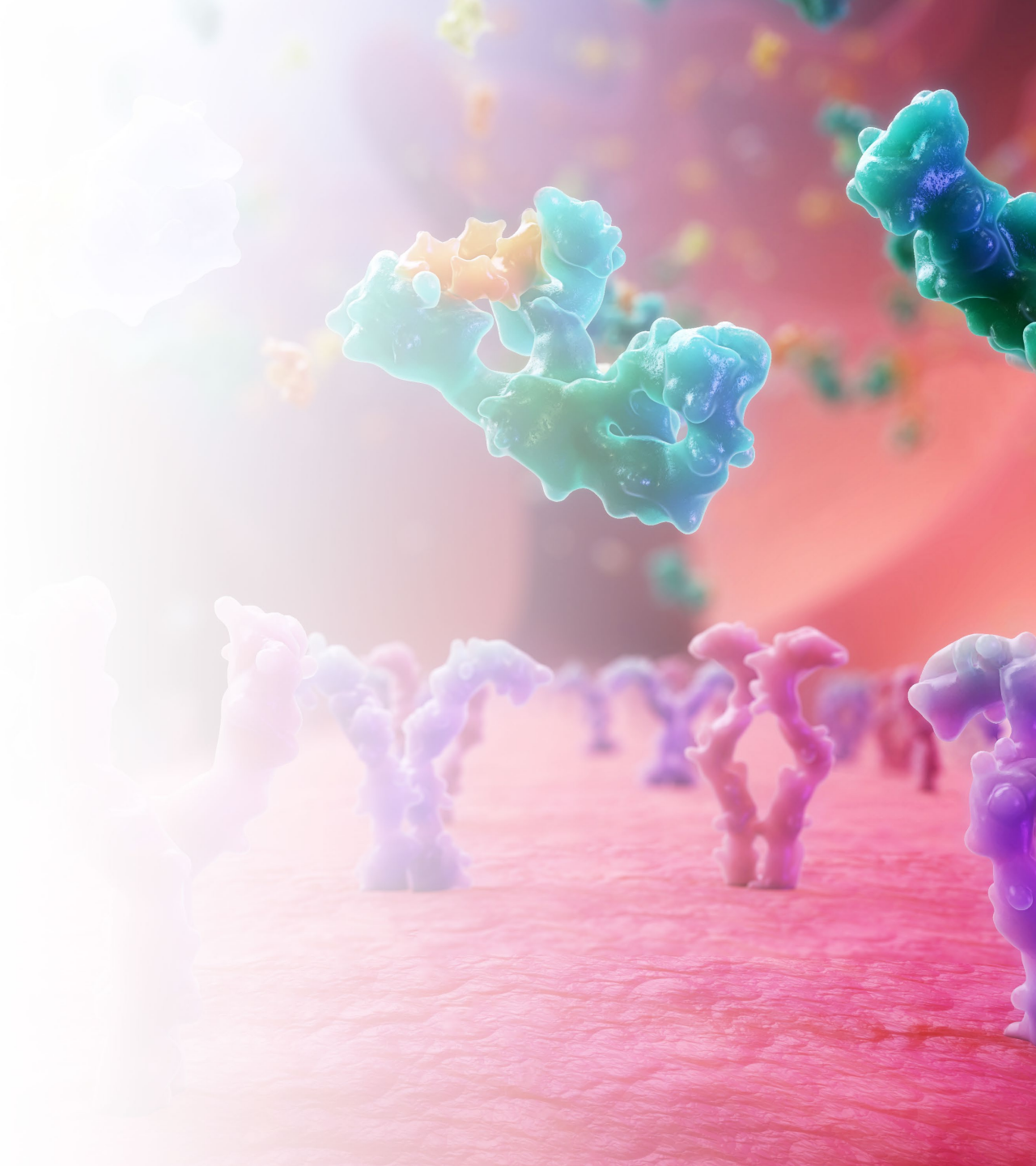
OPTHEA

Transforming Patient Outcomes with Superior Vision Gains



Corporate Presentation | March 2024

NASDAQ (OPT); ASX (OPT.AX)

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Opthea: Transforming Patient Outcomes with Superior Vision Gains

Our Vision

Advancing **bold therapeutic innovation** and **inspiring transformation** in the global retinal community.

Our Mission

Dedicated to **improving and protecting vision** in people with retinal diseases.

Investment Highlights

Potential to be the first product in more than 15 years to improve vision loss

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
Two Large Pivotal Trials Ongoing	• Phase 3 trials **near completion of enrollment**: COAST (enrolled Feb 2024); ShORe (estimated 2Q CY2024) • **Topline data** from both trials **expected mid-CY 2025**
Substantial Market Opportunity	• **Multibillion dollar commercial opportunity** in a **growing market** with an **established clinical practice** • Sozinibercept used **in combination with any anti-VEGF-A,** not competing with any approved drug

MOA = Mechanism of Action; SOC = Standard of care

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

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 Associate Professor at the University of Nevada, Reno School of Medicine

Clinical Advisory Board

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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

Better Vision Gains is an Unmet Medical Need in Wet AMD

The Leading Cause of Irreversible Blindness, Impacting ~3.5M Patients in the US & EU

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[1] of patients **fail to achieve**

20/40 vision

Most patients

cannot resume

routine daily activities, such as driving or reading

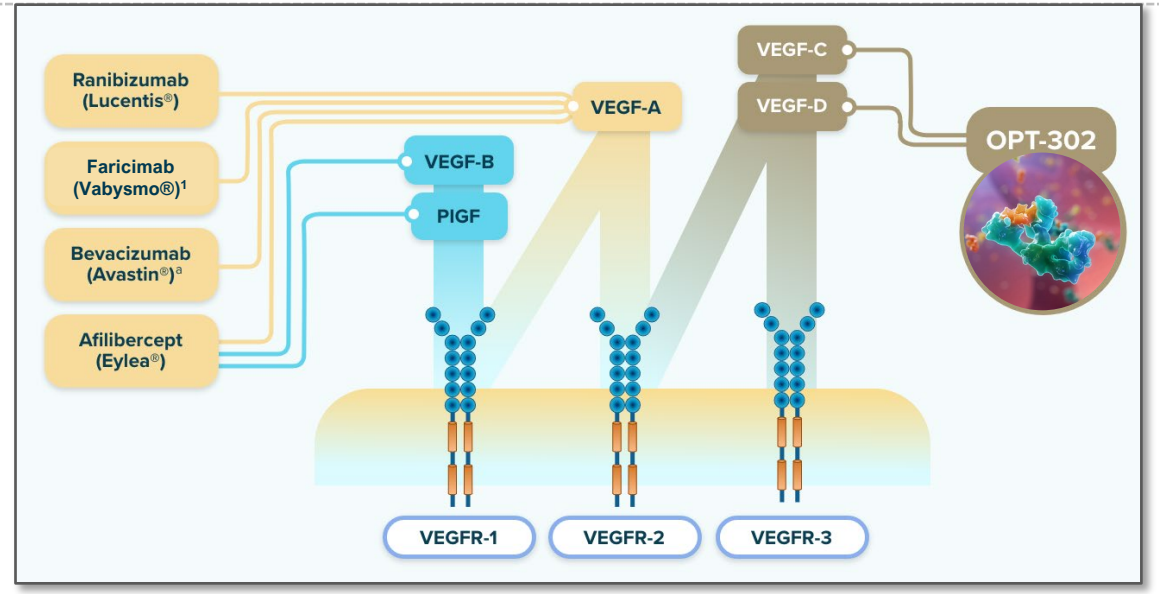
*Based on randomised, controlled clinical trial data; >45% fail to achieve ≥ 2 lines improvement in Best Corrected Visual Acuity (BCVA); Persisting fluid: SD-OCT CST ≥ 300 µM or Time-Domain OCT CST ≥ 250 µM

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

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.



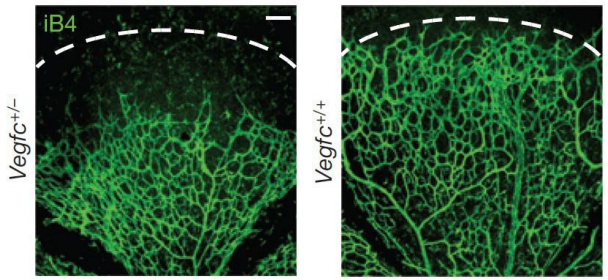
The Solution

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

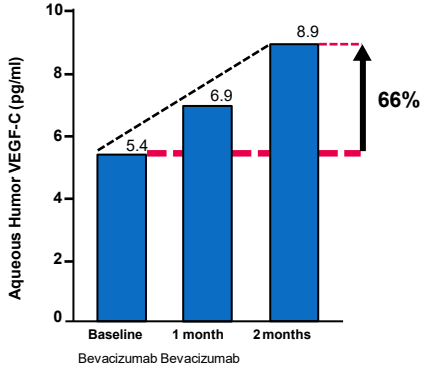
[1] Faricimab also has inhibitory effect on Ang-2.
[a] Bevacizumab is used ’off-label’ for the treatment of neovascular (wet) AMD

Published Evidence Supports Broader VEGF Pathway Inhibition with Sozinibercept

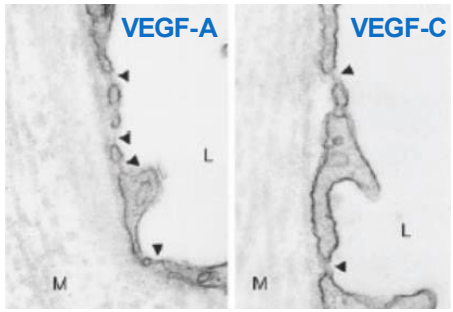
VEGF-C Stimulates Retinal Angiogenesis^



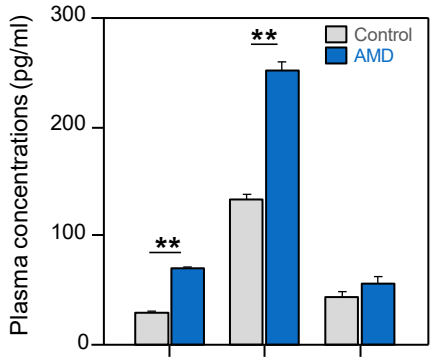
Elevated VEGF-C in Aqueous Humor Following Anti-VEGF-A therapy in Wet AMD Patients*



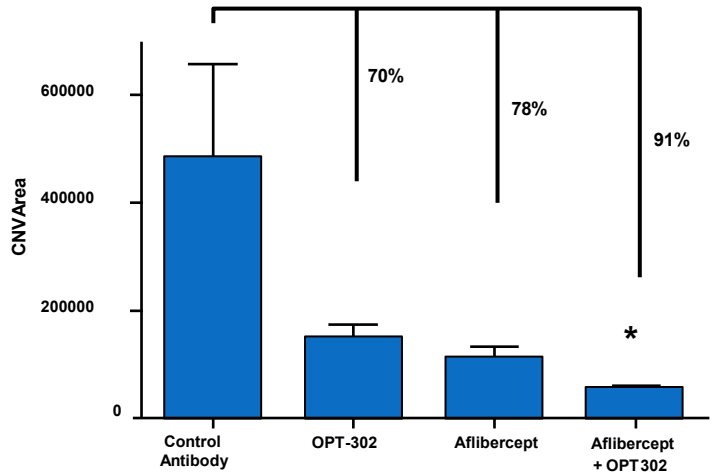
VEGF-A and VEGF-C Induce Vascular Leakage/permeability#



Circulating VEGF-C Levels Significantly Elevated in AMD Patients†



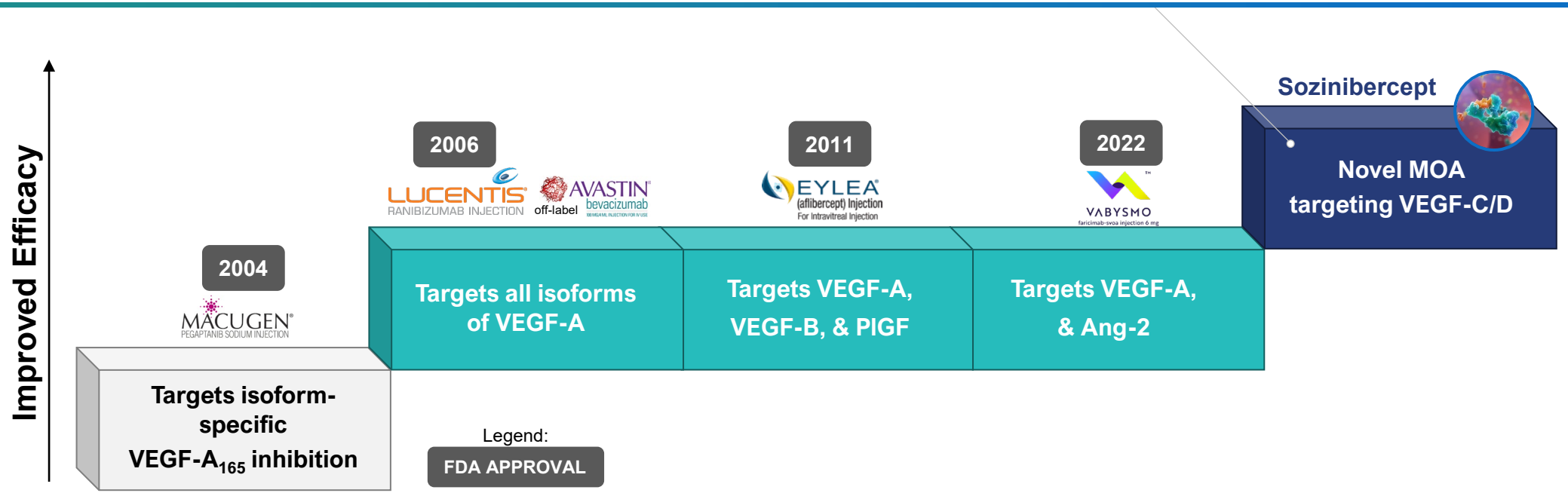
Additive Benefit of VEGF-A and VEGF-C/D Inhibition in Mouse Wet AMD model



^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 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**



MOA = Mechanism of Action

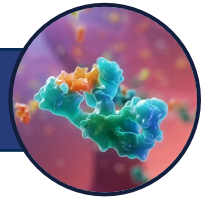
Sozinibercept is Being Developed to Tap into the Entire VEGF-A Inhibitor Market

Branded VEGF-A Inhibitors

~$9B

Global wAMD Revenues of Anti-VEGF-A Inhibitors

Sozinibercept



~$14B

Branded VEGF-A Inhibitors

Biosimilars / Off-label

Potential Addressable wAMD Market

Biosimilar / Off-label

~$5B*

~35% of patients receive off-label AVASTIN®

**potential market size assuming branded pricing*

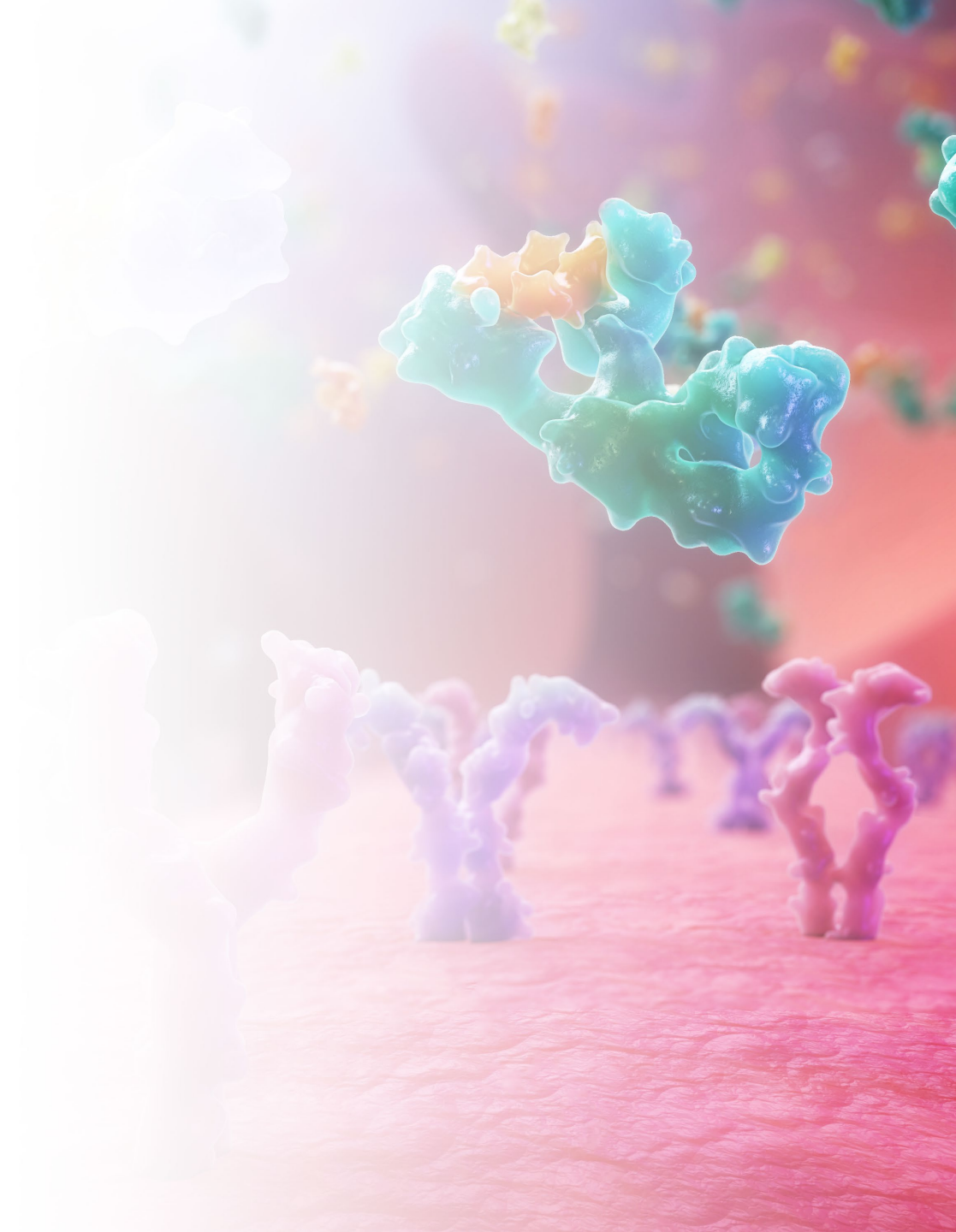
Long-term Value Opportunities for Sozinibercept

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					**Complete enrollment** of pivotal trials: Q2 CY 2024 **Topline data:** mid-CY 2025
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)

Sozinibercept Wet AMD Clinical Summary



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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 in mid-CY 2025

Enrollment Complete

COAST
Phase 3 - wet AMD
(treatment naïve)
n=~990

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

Anticipated CY 2Q 2024

ShORe
Phase 3 - wet AMD
(treatment naïve)
n=~990

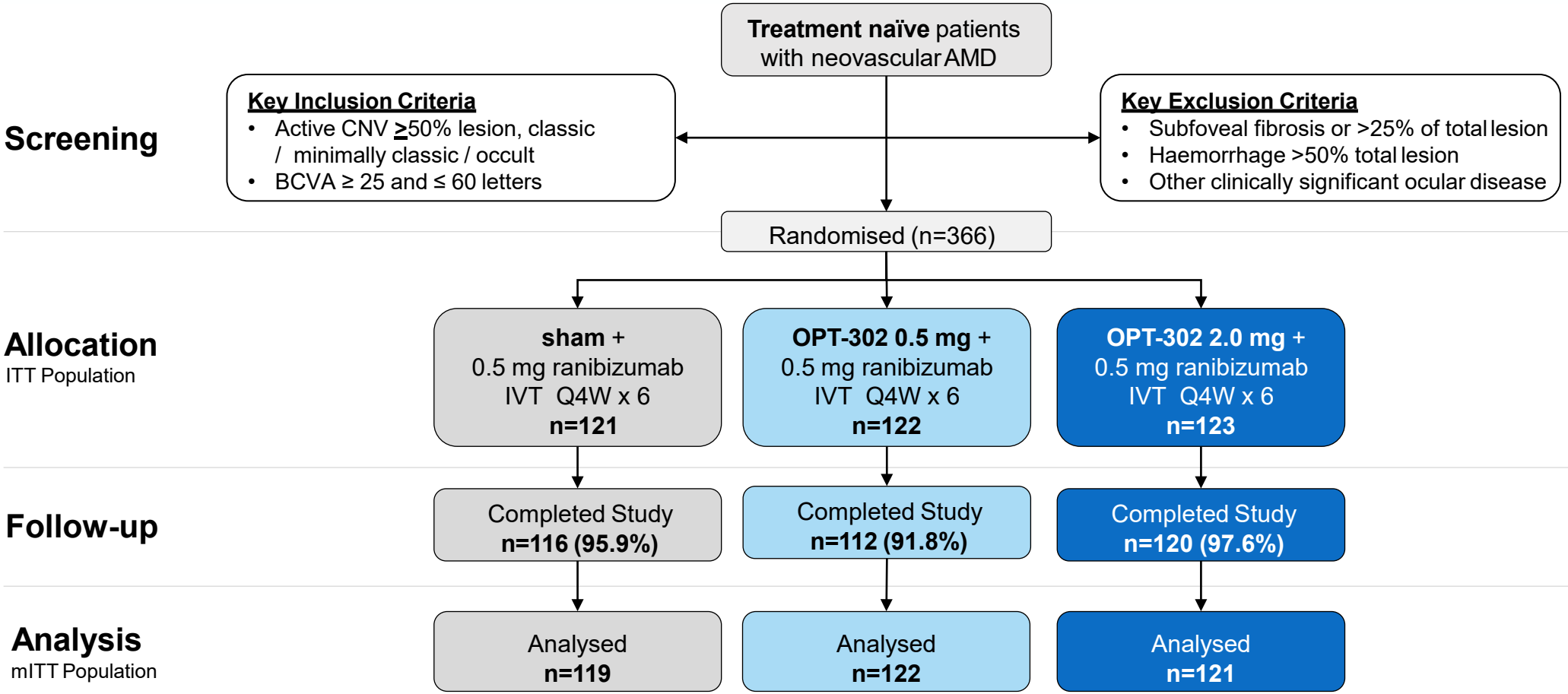
Comparator:

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 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

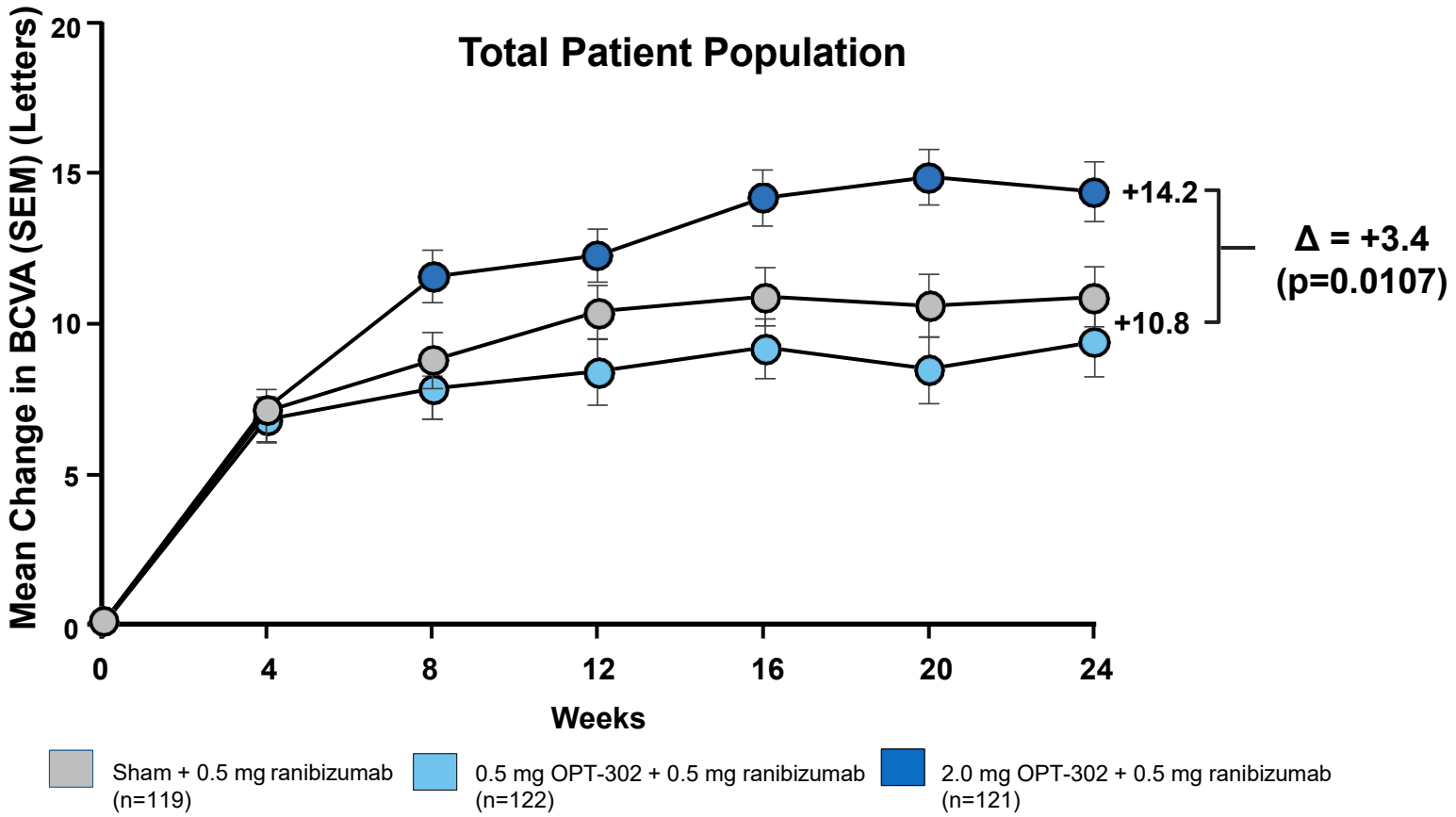
Phase 2b Trial Demographics and Baseline Characteristics

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.

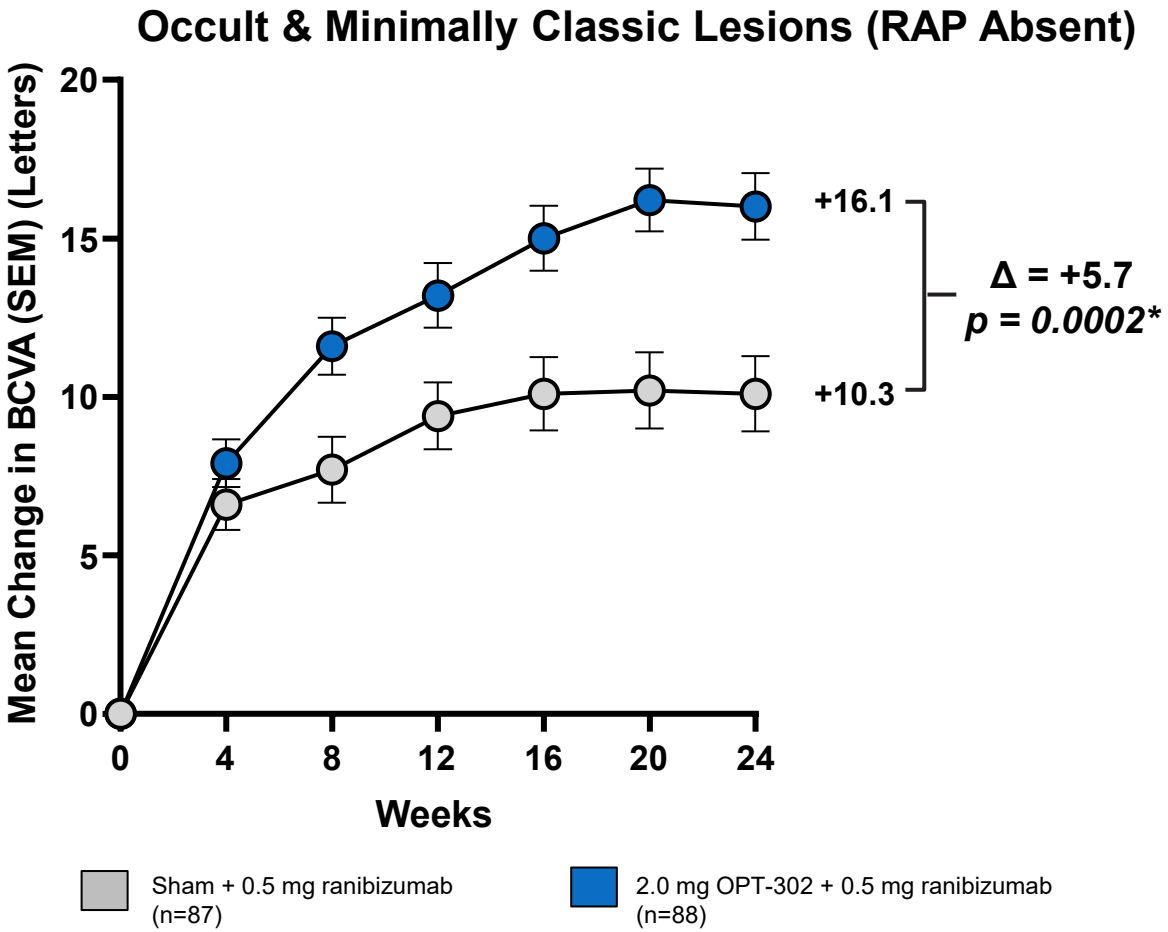
Sozinibercept 2.0 mg Combination Therapy Demonstrated Superiority in Visual Acuity over Ranibizumab Monotherapy

Phase 2b Primary Endpoint Achieved



mITT; BCVA – Best Corrected Visual Acuity.
Left: Difference in Least Square Means, using Model for Repeated Measures (MRM) analysis. Right: Graph represents "as observed" data and SEM.

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-determined analysis**

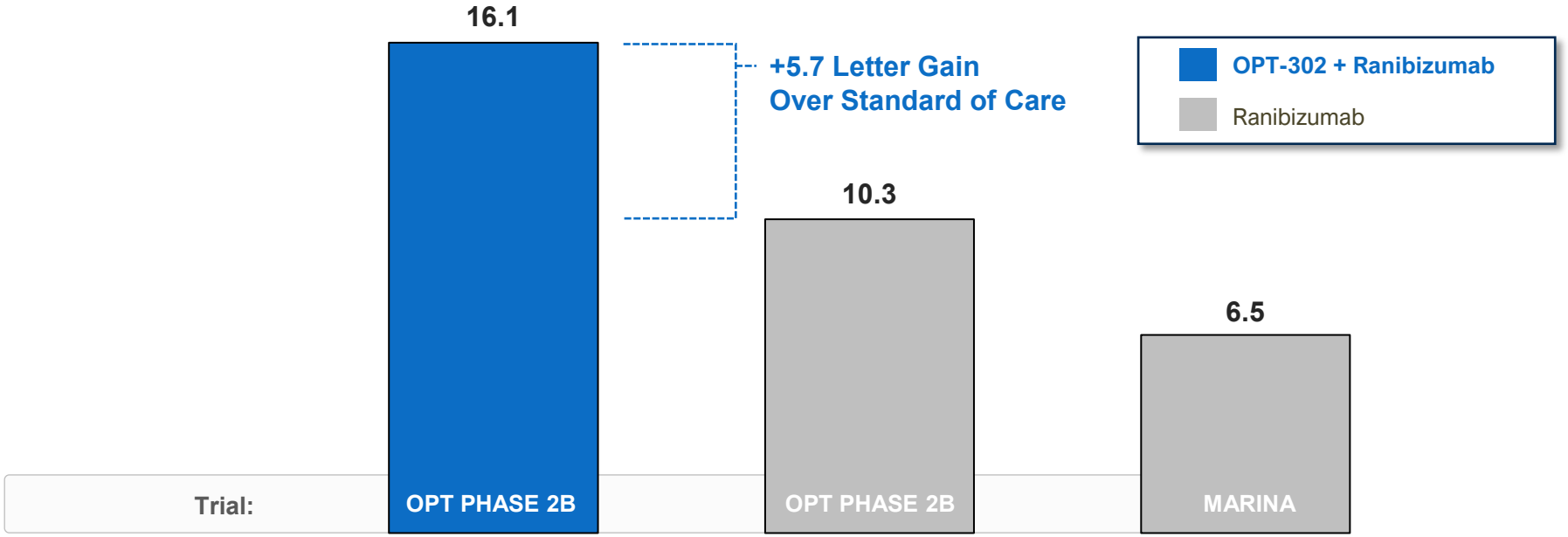
This patient population (minimally classic & occult) represents **~75% of Wet AMD patients**

*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

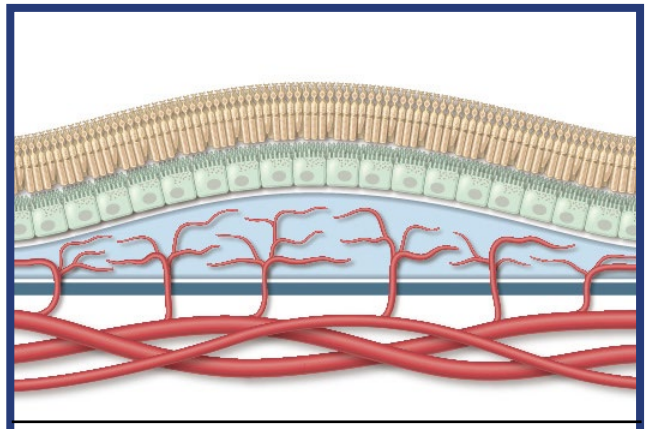


MARINA was a Phase 3 registrational trial. Baseline BCVA values across trials vary. Number of patients randomised to treatment group (n, bottom table). Mean change in Best Corrected Visual Acuity (BCVA) from baseline shown in ETDRS letters (top of bars).

Wet AMD Lesion Types

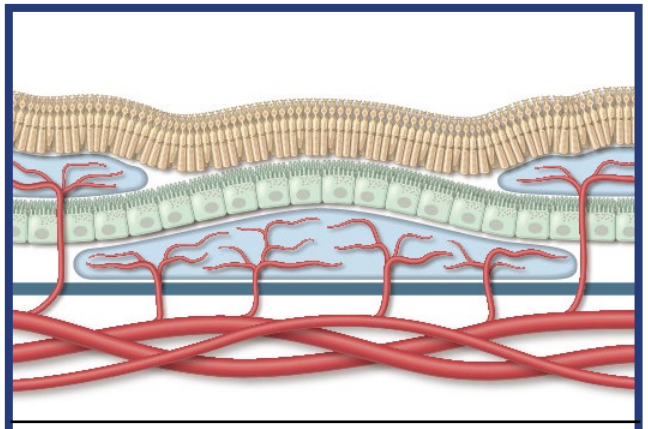
Differ in Vessel Location, Leakiness, and Responsiveness to VEGF-A Inhibitors

OCCULT



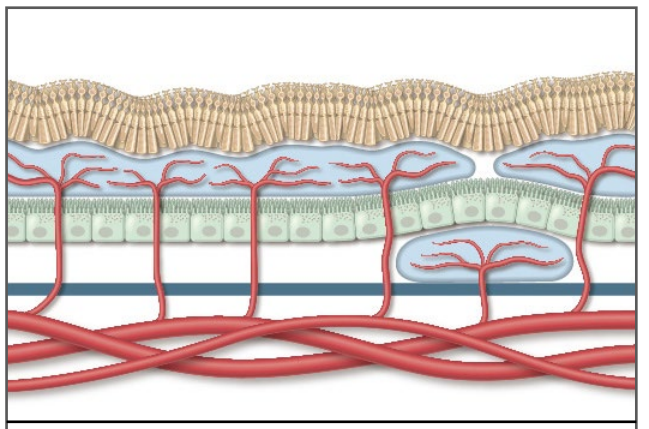
LEAST RESPONSIVE
to VEGF-A inhibition

MINIMALLY CLASSIC



MODERATELY RESPONSIVE
to VEGF-A inhibition

PREDOMINANTLY CLASSIC

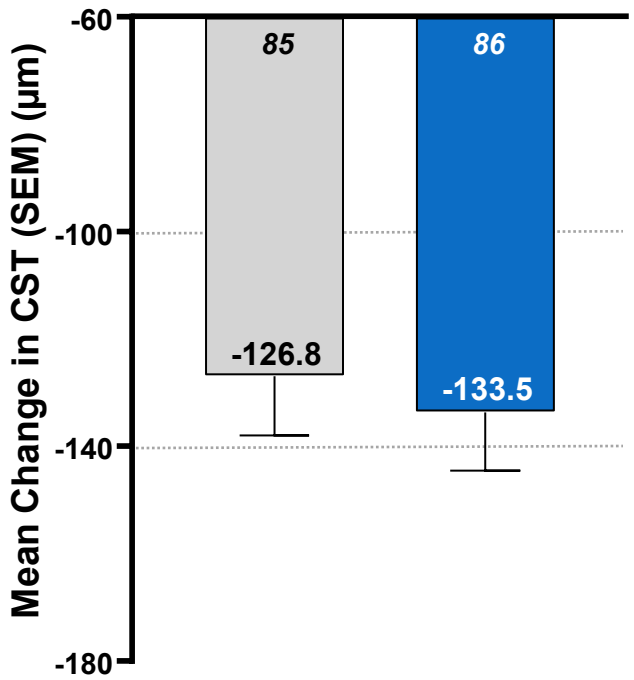


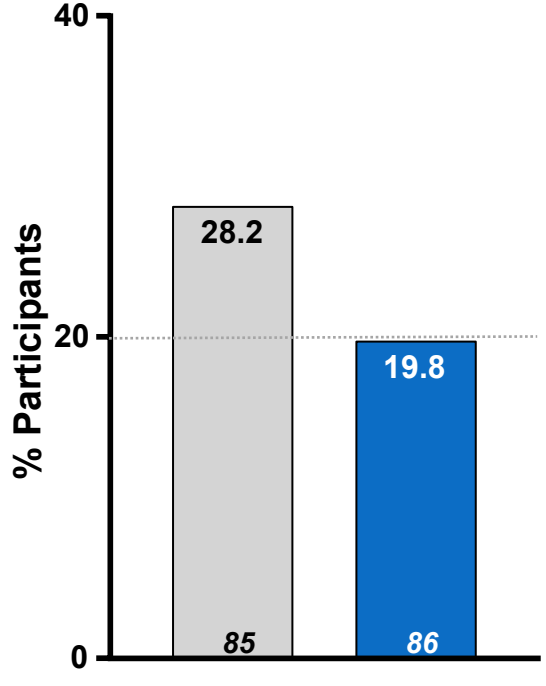
HIGHLY RESPONSIVE
to VEGF-A inhibition

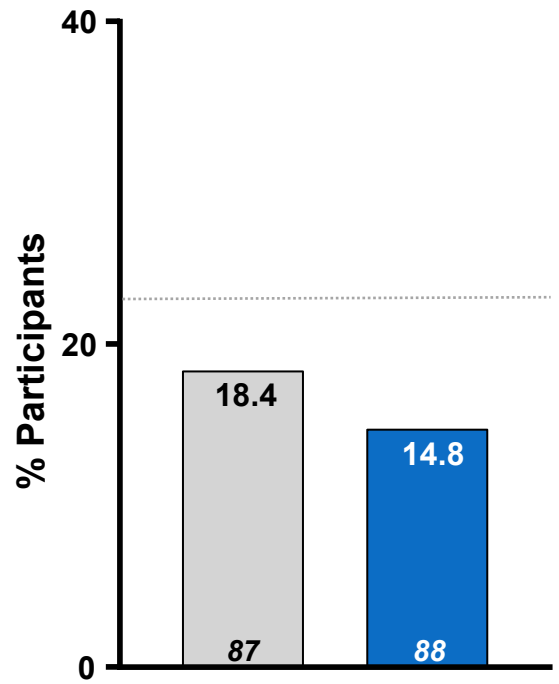
~75% of Wet AMD Patients have Occult or Minimally Classic Lesions

Reduced Retinal Thickness and Better Retinal Drying

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







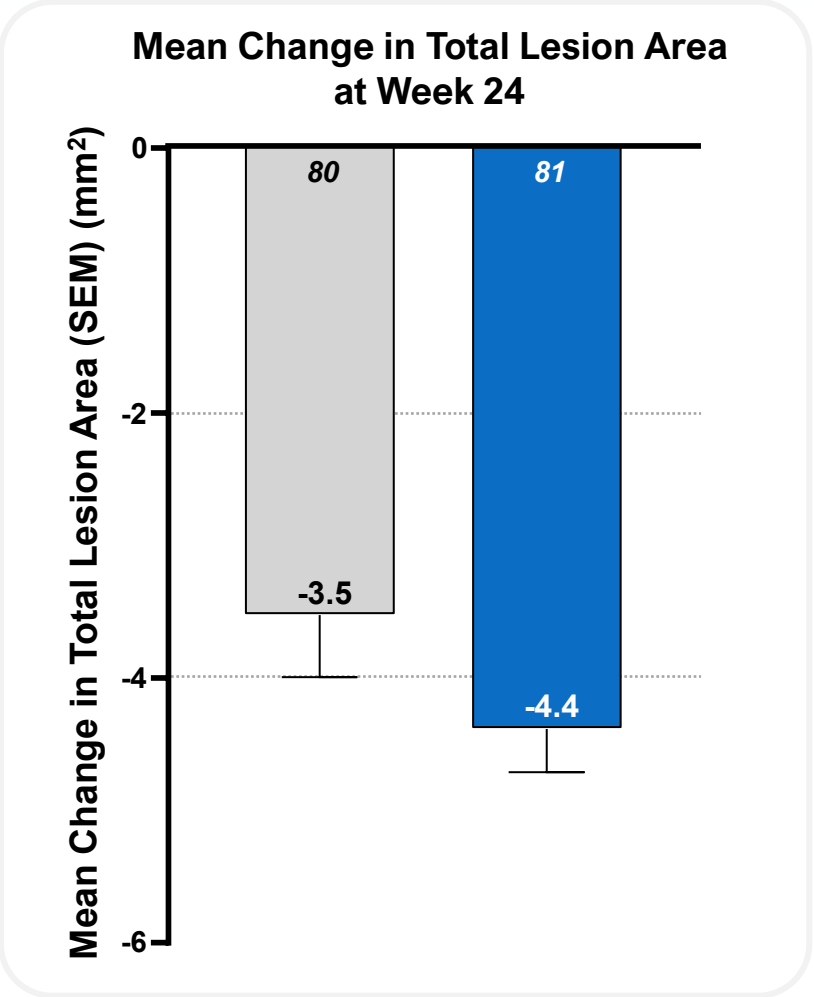
Sham + 0.5 mg ranibizumab

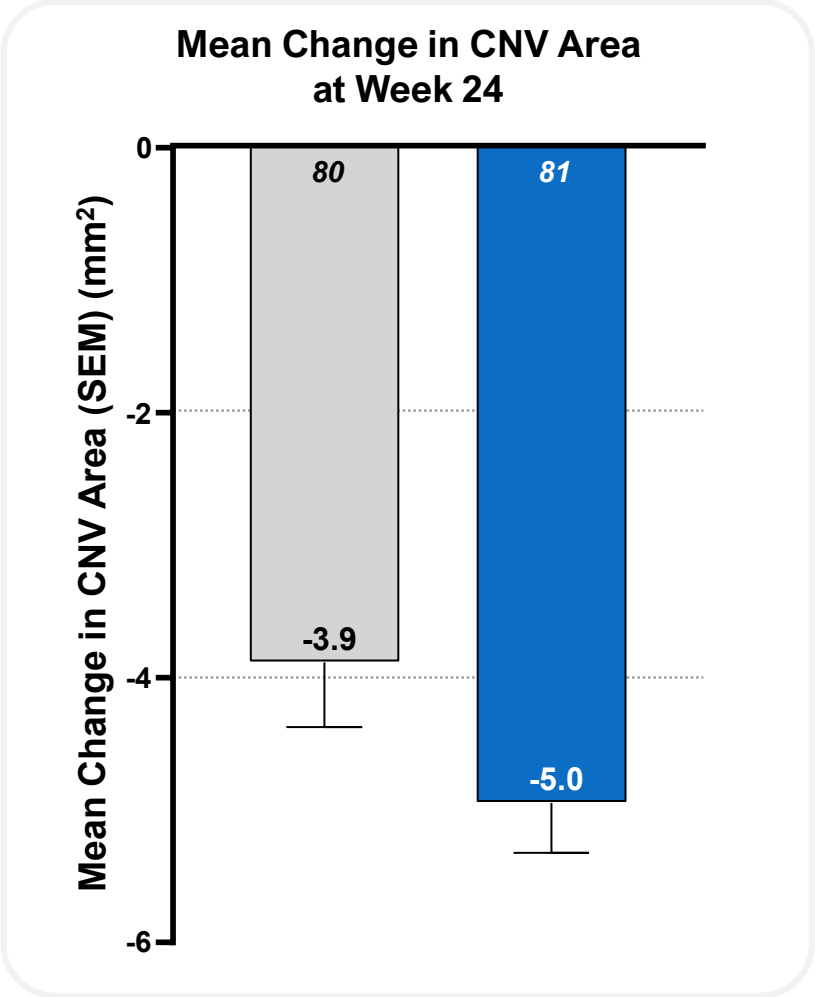
2.0 mg OPT-302 + 0.5 mg ranibizumab

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



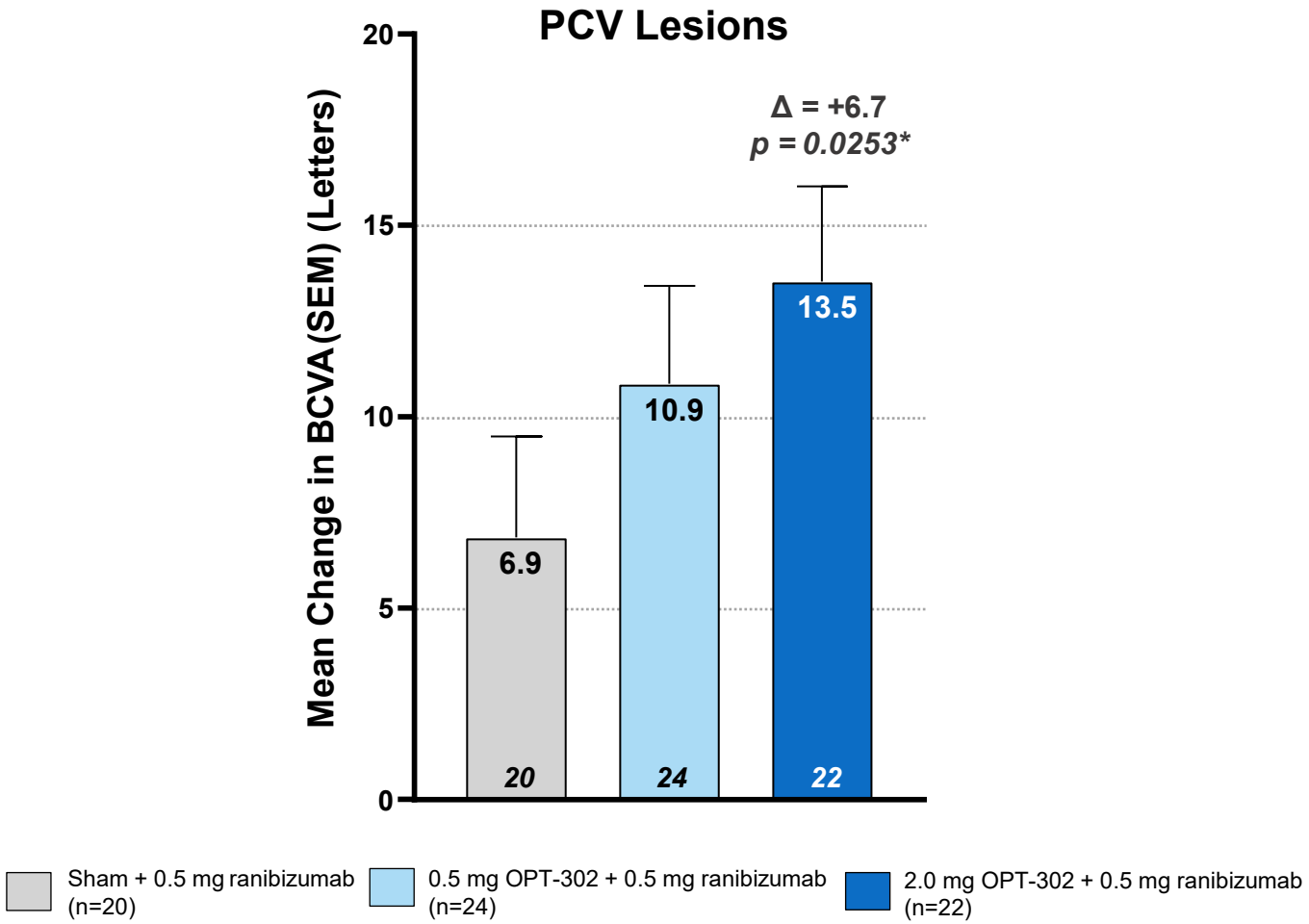


Sham + 0.5 mg ranibizumab

2.0 mg OPT-302 + 0.5 mg ranibizumab

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

Sozinibercept Further Demonstrated Superior Vision Gains in a Pre-Specified Sub-group 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% prevalent in Caucasians

Phase 3 ShORe and COAST trials enrolled patients with PCV[1]

*Unadjusted p-value

[1] Evaluated by color, FP, FA and 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=169 (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%)

[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, 1 mg or 2 mg)

Phase 3 Enrollment Expected to Complete in Q2 CY2024

Trial Highlights Potential to Use Sozinibercept in Combination With Any Anti-VEGF-A Therapy

Trials in **Treatment Naïve** Wet AMD Patients

Efficacy Phase

3x Loading Doses (12w) | OPT-302 dosing every 4 and 8 weeks (40w)

COAST

Combination OPT-302 with Aflibercept Study

Aflibercept + OPT-302 q4w	**Aflibercept q8w + OPT-302 q4w**
Aflibercept + OPT-302 q4w	**Aflibercept q8w + OPT-302 q8w**
Aflibercept + Sham q4w	**Aflibercept q8w + Sham q8w**

ShORe

Study of OPT-302 in combination with Ranibizumab

Ranibizumab + OPT-302 q4w	**Ranibizumab q4w + OPT-302 q4w**
Ranibizumab + OPT-302 q4w	**Ranibizumab q4w + OPT-302 q8w**
Ranibizumab + OPT-302 q4w	**Ranibizumab q4w + Sham q4w**

Primary efficacy endpoint to support BLA Submission

Primary Efficacy Endpoint Week 52 ›› **Safety Follow–up Week 100**

Primary Efficacy Endpoint Week 52 ›› **Safety Follow–up Week 100**

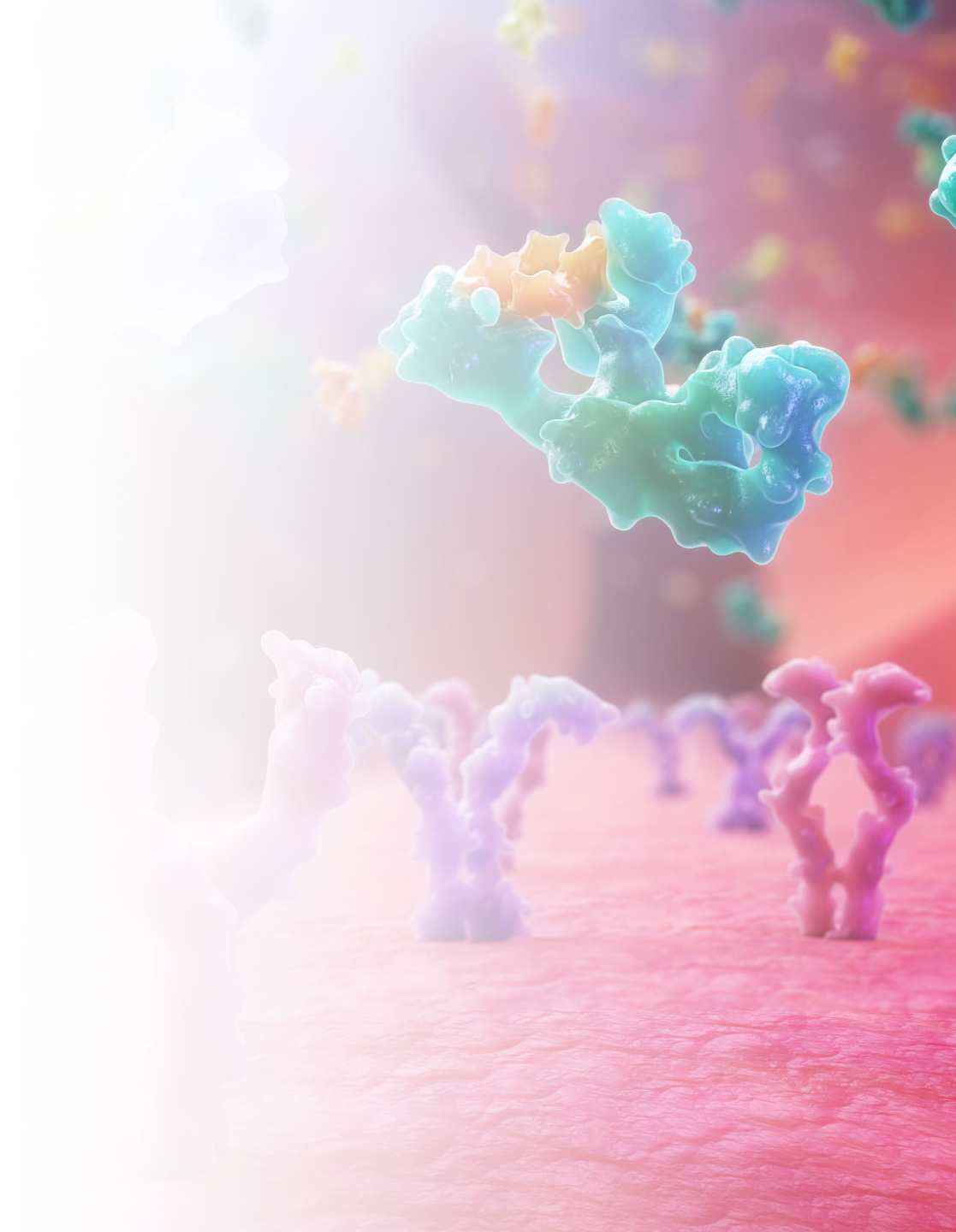
- **Design:** Multi-center, double-masked, randomized (1:1:1), sham control
- **Regulatory quality:** 90% power, 5% type I error rate
- **Sample size:** ~330 patients per arm, ~990 per trial
- **Primary Objective:** Mean change from Baseline in BCVA at Week 52

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). OPT-302 dosed at 2.0 mg. Note that Sham administered at visits when OPT-302 is not administered

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**, followed by total patient population
- Phase 3 designed to support label for use in **combination with any VEGF-A inhibitor for all wet AMD patients** (treatment naïve and prior treated)
- Sozinibercept granted **Fast Track designation** by FDA

Corporate Activities Summary and Financial Snapshot



OPTHEA

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

We are dedicated to advancing sozinibercept to **improve and protect patients' vision**

Next Steps

Clinical Milestones	• Complete enrollment in 2nd Phase 3 trial (ShORe) in Q2 CY2024 • Mid-CY2025 topline data from both pivotal Phase 3 studies
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

Financial Snapshot & Corporate Activities

Financial Overview	
Ticker	OPT (ASX/NASDAQ)
Shares Outstanding[1]	662.8M (Ordinary)/ 82.9M (ADSs equivalents)
Cash/Cash Equivalents[1]	US$157.1M
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 split between fixed payments and variable payments at 7% of revenues, capped at 4x investment
- No amounts owed if the clinical trials do not meet the primary endpoint or if regulatory approval is not received

[1] As of December 31, 2023

Investment Highlights

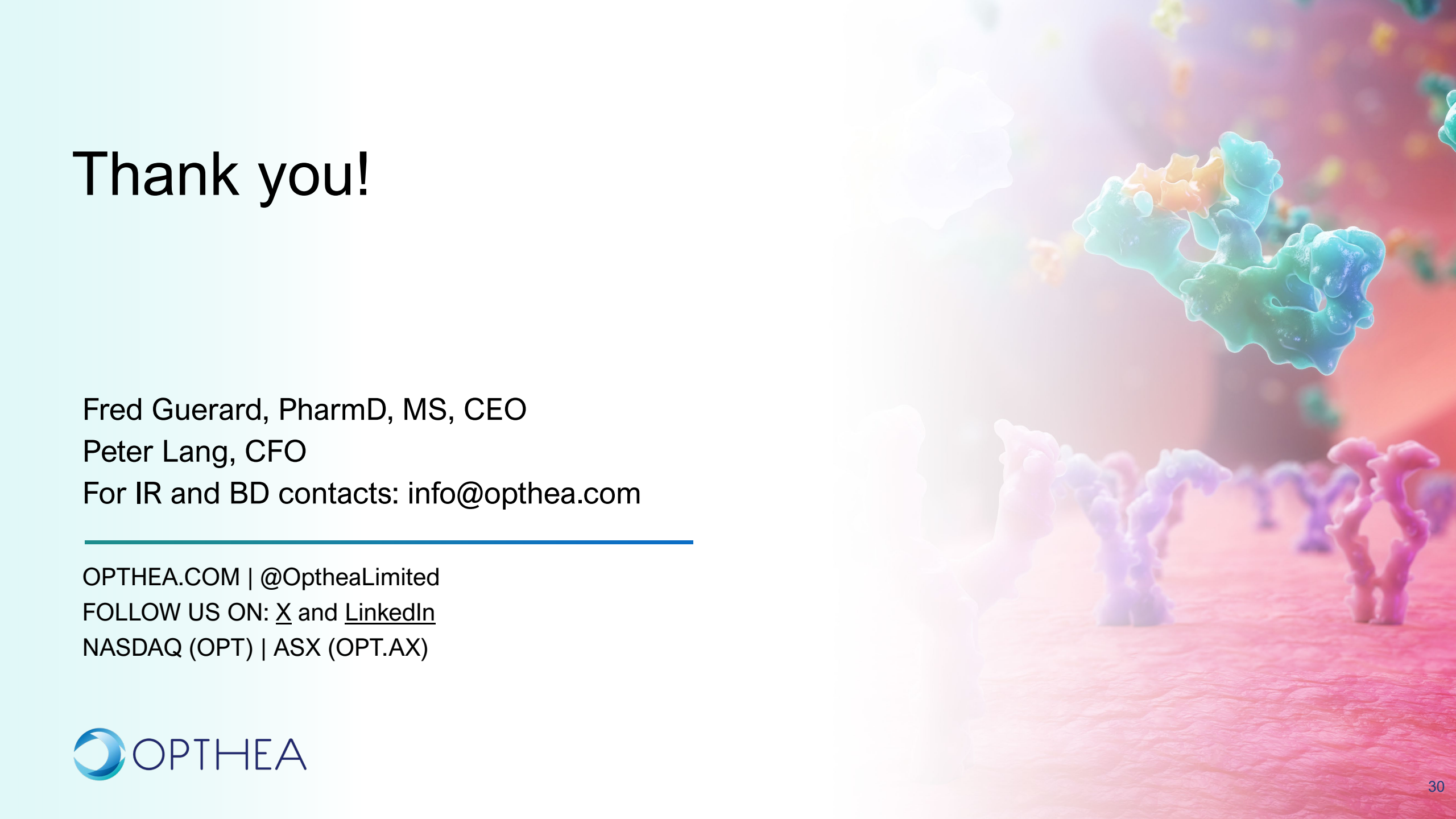
Potential to be the first product in more than 15 years to improve vision loss

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
Two Large Pivotal Trials Ongoing	• Phase 3 trials **near completion of enrollment**: COAST (enrolled Feb 2024); ShORe (estimated 2Q CY2024) • **Topline data** from both trials **expected mid-CY2025**
Substantial Market Opportunity	• **Multibillion dollar commercial opportunity** in a **growing market** with an **established clinical practice** • Sozinibercept used **in combination with any anti-VEGF-A,** not competing with any approved drug

MOA = Mechanism of Action; SOC = Standard of care

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

Thank you!



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