Sozinibercept (OPT-302) for Wet AMD

Transforming Patient Outcomes by Improving Vision

Corporate Presentation | January 2024

OPTHEA.COM | @OptheaLimited | NASDAQ (OPT); ASX (OPT.AX)

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Sozinibercept has the potential to improve vision for millions of patients with wet AMD

We are developing sozinibercept, a first-in-class VEGF-C/D ‘trap’, to be used in combination with standard of care anti-VEGF-A therapies

Potential to be the first therapy to demonstrate visual acuity superiority in combination over standard of care in wet AMD

- Wet AMD is the **leading cause of vision loss** in the elderly, impacting **~3.5 million patients** in the US and Europe
- Sozinibercept is the **first and only drug** with strong clinical evidence demonstrating **visual acuity superiority** in combination with standard of care anti-VEGF-A therapy for wet AMD, with **well tolerated safety profile**
- Pivotal Phase 3 trials ongoing, **enrollment completion anticipated in 1H CY24**
  - Phase 3 clinical trials **~90% enrolled** at the beginning of January 2024
  - Anticipated patient enrollment: COAST 1Q CY2024 | ShORe 2Q CY2024
  - Topline data expected mid-CY2025
- FDA granted **Fast Track designation** based on superior Phase 2b results
- Sozinibercept represents a **multibillion-dollar** commercial opportunity, with potential **rapid adoption** by patients, physicians and payers globally due to:
  - High unmet need with current standard-of-care
  - Growing wet AMD market and established clinical practice
  - Favorable physician economics
- **Long-term value** opportunity:
  - Composition of Matter and Methods of Use Patents through 2034
  - Further opportunity for Patent Term Extension, Data and Market Exclusivity periods beyond 2034
  - Expansion into DME additional upside opportunity

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Better Vision Gains is an Unmet Medical Need in Wet AMD

Wet AMD is the leading cause of irreversible blindness:

- Impacts ~3.5M patients[1]
- ~1.6M patients in the U.S.
- ~200,000 new patients each year in the U.S.

Established clinical practice:

- 80% of patients are diagnosed
- 80% of diagnosed patients are treated
- 99% receive anti-VEGF-A therapy

WET AMD UNMET MEDICAL NEED

Despite treatment with anti-VEGF-A therapy[2]:

>45%	Do not achieve significant vision gains
>60%	Will have persisting macular fluid
25%	Will have further vision loss at 12 months & beyond

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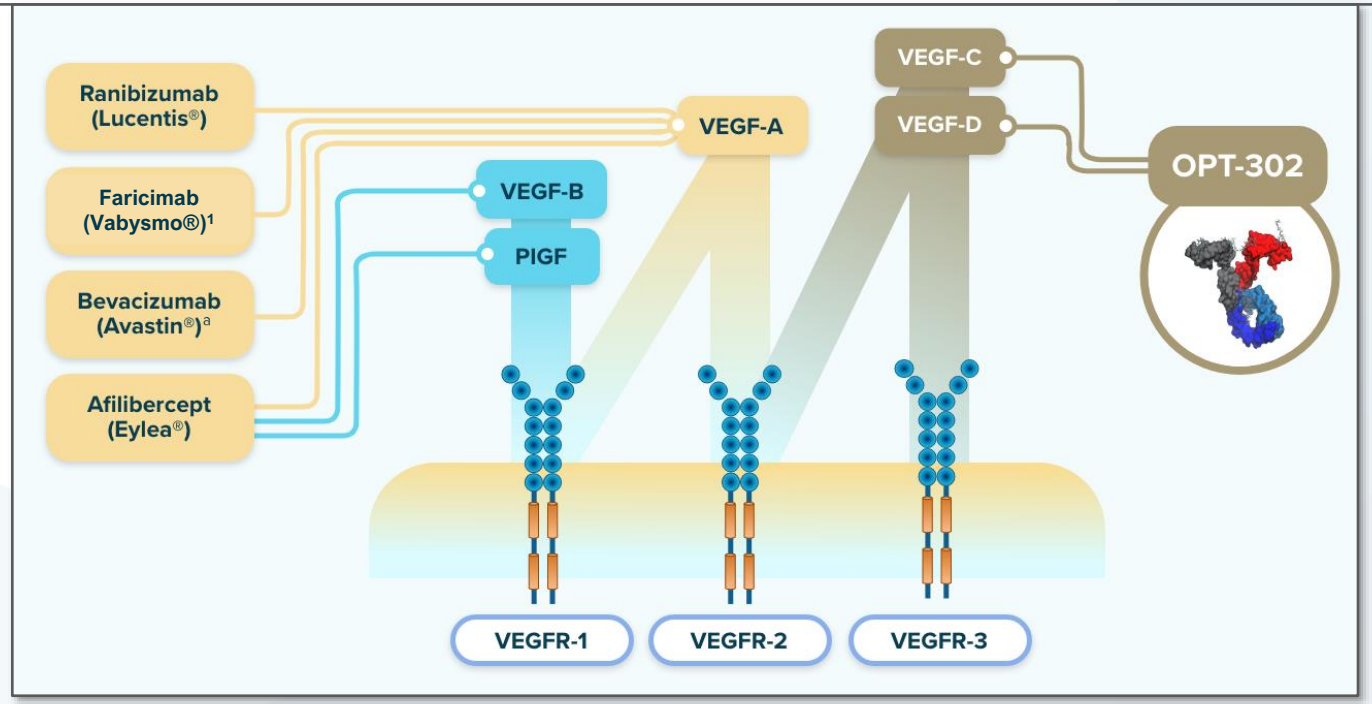
[1]U.S., EU. [2] Based on randomised, controlled clinical trial data; >45% Fail to achieve ≥ 2 lines improvement in Best Corrected Visual Acuity (BCVA); Persisting fluid: SD-OCT CST ≥ 300 µM or Time-Domain OCT CST ≥ 250 µM

Sozinibercept has the Potential to be the Next Transformative Step in the Treatment of Wet AMD

THE PROBLEM

Wet AMD is a **multi-factorial disease**.

VEGF-C and **VEGF-D** activate validated wet AMD disease pathways, 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.

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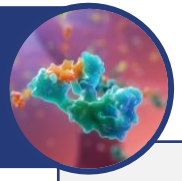
Faricimab also has an inhibitory effect on Ang-2.

Large & Growing Market Opportunity in Wet AMD

Sozinibercept could be combined with any anti-VEGF-A

Sozinibercept is positioned to tap into the entire VEGF-A inhibitor market



~US$8B+

~50% treated patients receive branded products

LUCENTIS RANIBIZUMAB INJECTION

EYLEA (aflibercept) Injection For Intravitreal Injection

VABYSMO faricimab-svoa injection 6 mg

Wet AMD Total Global Revenue

~US$16B+

~50% treated patients receive Avastin®

LUCENTIS RANIBIZUMAB INJECTION

EYLEA (aflibercept) Injection For Intravitreal Injection

VABYSMO faricimab-svoa injection 6 mg

AVASTIN bevacizumab

Off-label use

Implied Total Addressable Market for Sozinibercept

Captures Lucentis, Eylea, Vabysmo, and Avastin or biosimilar-treated patients worldwide

Wet AMD Potential Addressable Market

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Near-term Focus is on Sozinibercept Phase 3 Execution

BLA preparations and pre-commercial activities continue

Completed
Phase 1/2a
wet AMD
(n=51)

Comparator

Ranibizumab
once every month

OPT-302
once every month

3 x monthly dosing

Treatment naïve / Prior-treated

Completed
Phase 1b/2a
DME
(n=153)

Comparator

Aflibercept
once every month

OPT-302
once every month

3 x monthly dosing

Prior-treated

Completed
Phase 2b
wet AMD
(n=366)

Comparator

Ranibizumab
once every month

OPT-302
once every month

6 x monthly dosing

Treatment naïve

Enrollment Completion Anticipated in 1H CY24

ShORe
Phase 3
wet AMD
(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
Monthly dosing	Every two months dosing

Treatment naïve patients

COAST
Phase 3
wet AMD
(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
Monthly dosing	Every two months dosing

Treatment naïve patients

OPT-302 pivotal registrational Phase 3 wet AMD program designed to maximize outcomes with flexible standard of care dosing regimens

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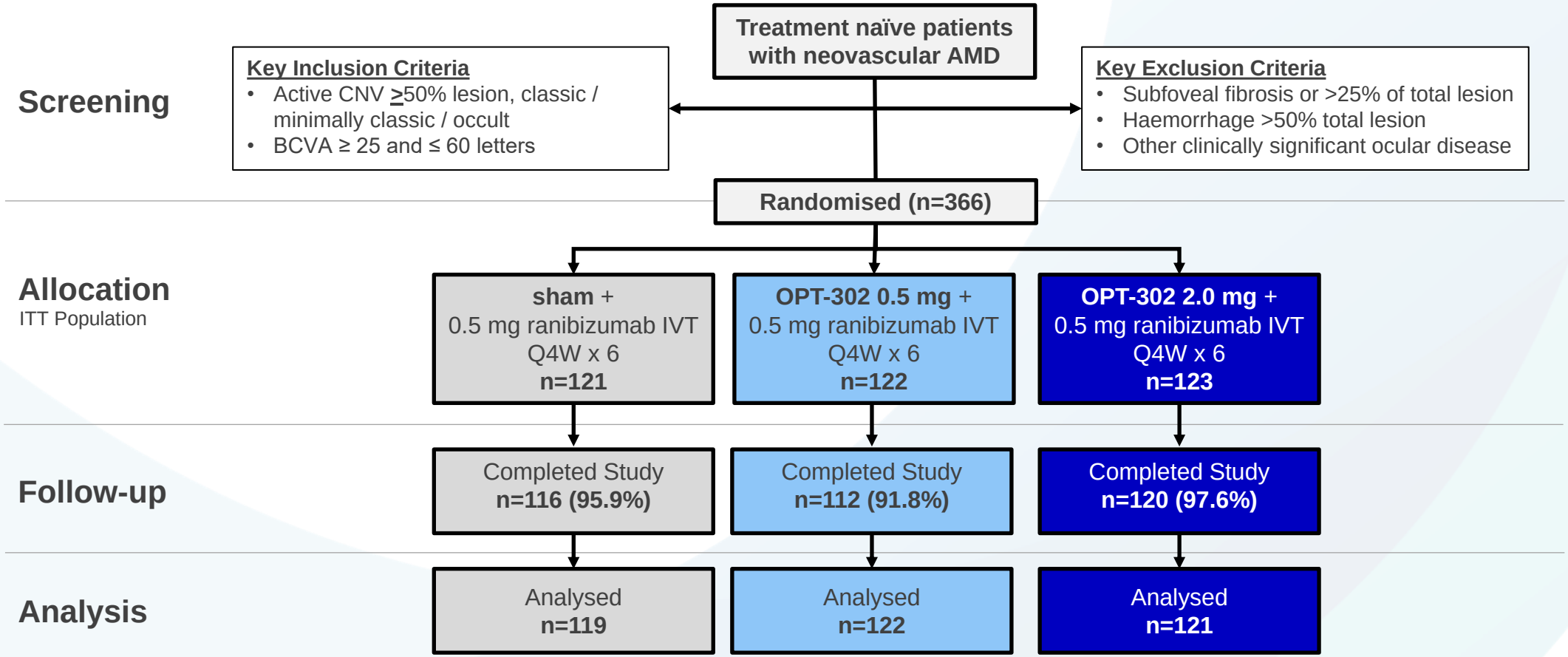
Ranibizumab (Lucentis®); Aflibercept (Eylea®)

Phase 2b Trial



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 Visual Acuity score and/or any participant who did not return for at least one post-baseline visit

Phase 2b 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%

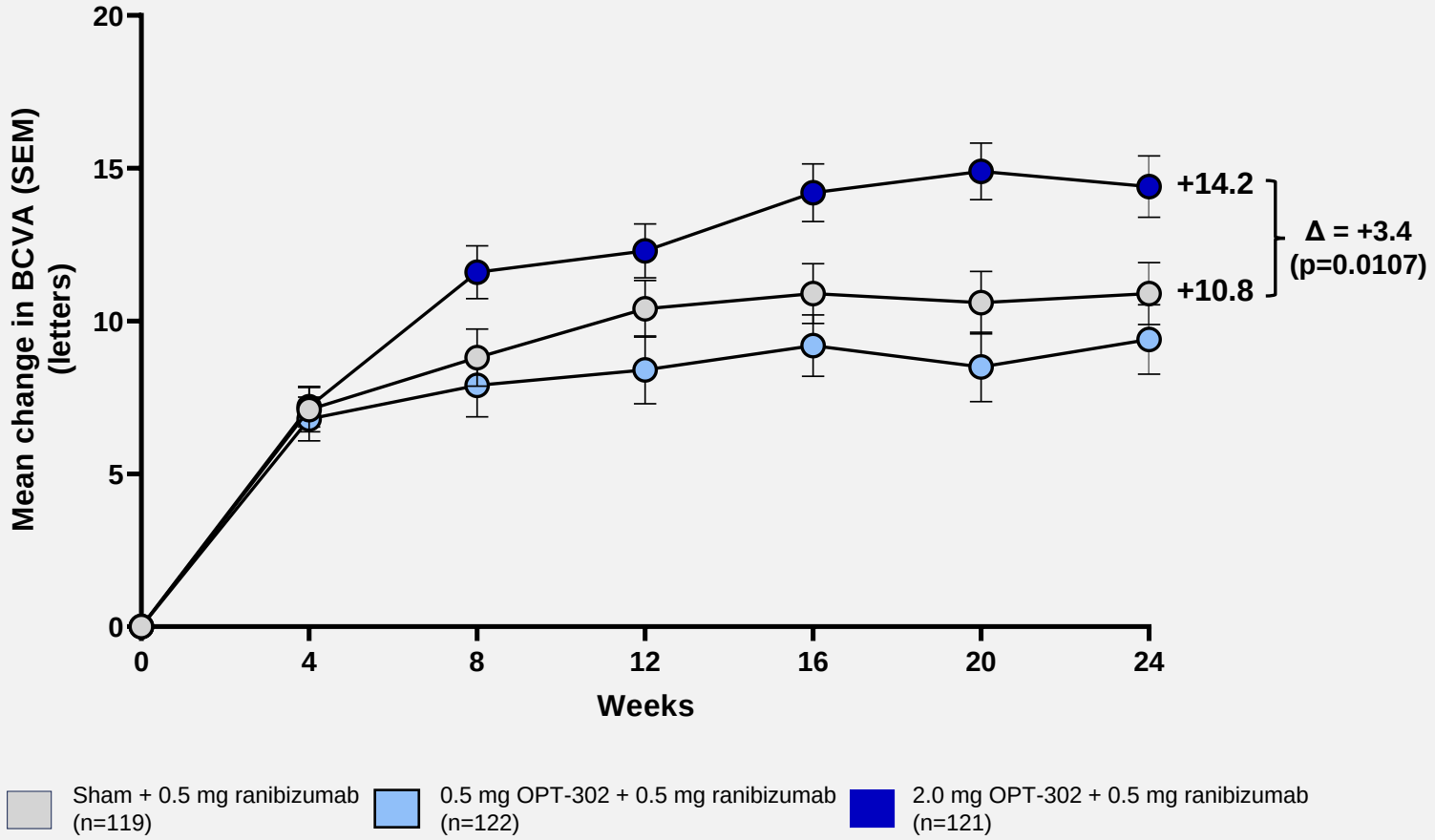
Intent-to-Treat (ITT) population; SD: standard deviation; BCVA: Best Corrected Visual Acuity.
[1]PCV - polypoidal choroidal vasculopathy, detected by SD-OCT, FA and fundus photography.
[2]RAP - retinal angiomatous proliferation, detected by SD-OCT, FA and fundus photography.

Sozinibercept (2 mg) Combination Therapy:

Superiority in Visual Acuity over Ranibizumab

Phase 2b primary endpoint achieved

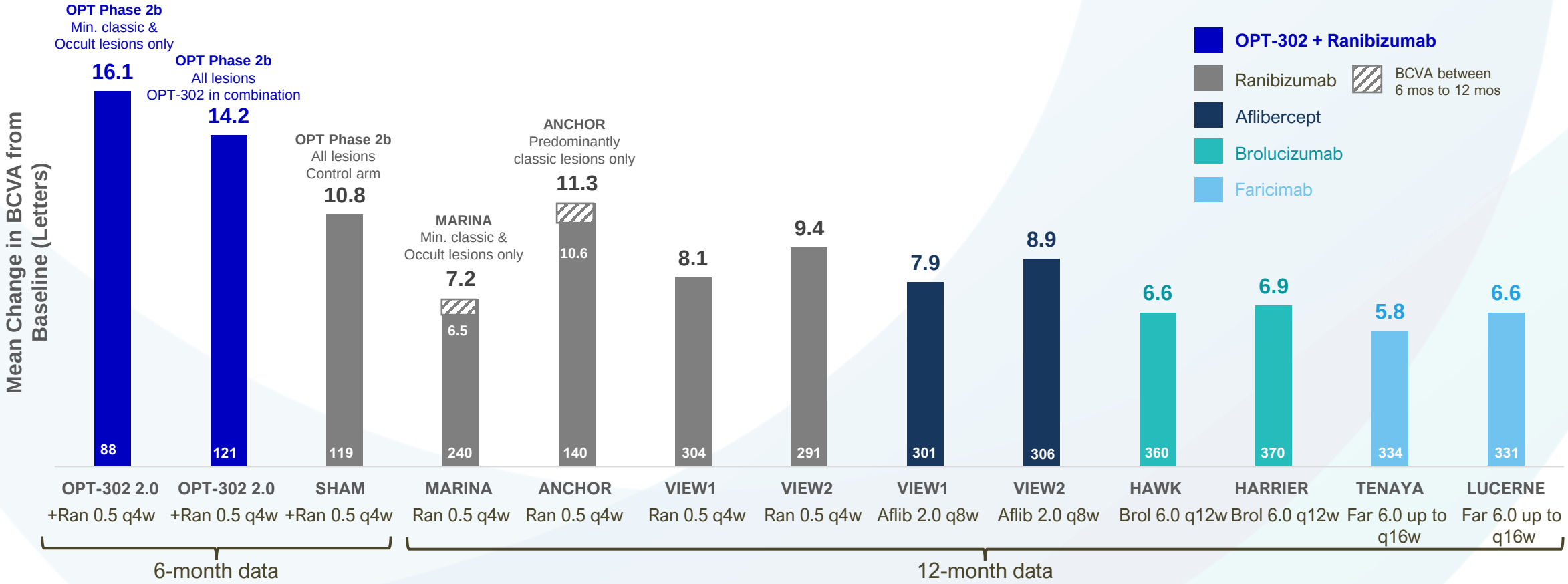
Mean Change in Best Corrected Visual Acuity Baseline to Week 24



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

OPT-302 2 mg in Combination Delivered Better Visual Outcomes Relative to Previous VEGF-A Inhibitor Trials

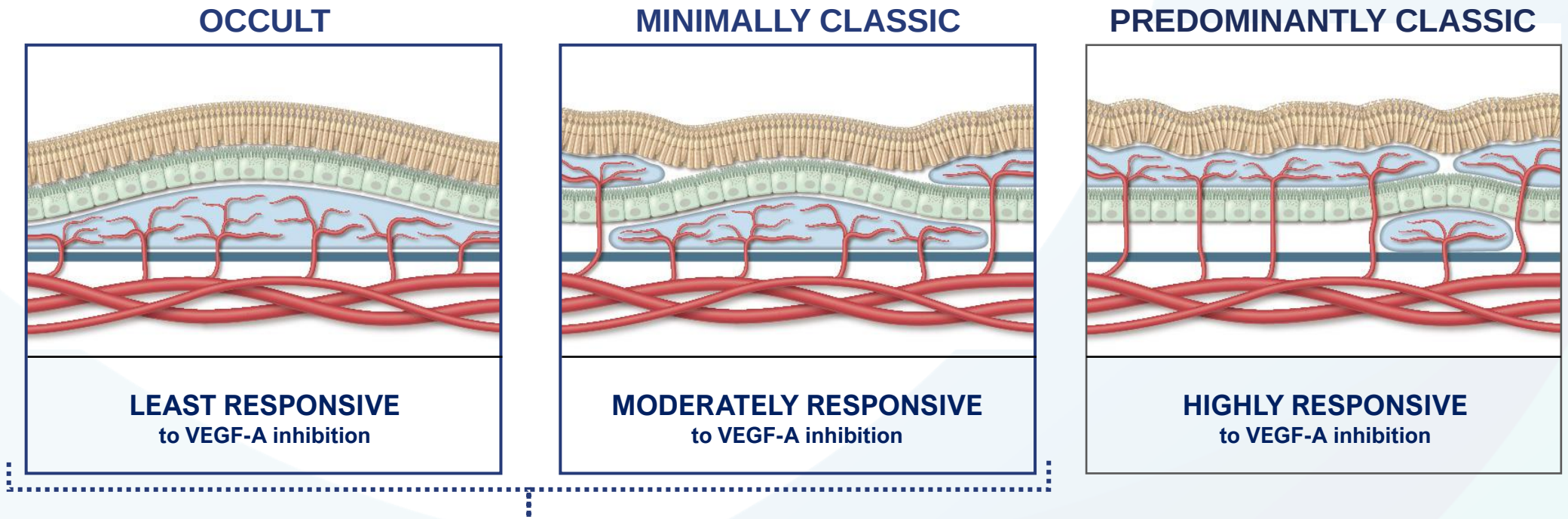
BCVA at 6 months is typically maintained or greater at 12 months in Phase 3 trials with VEGF-A inhibitors



All trials shown, excluding Opthea's Phase 2b data, are Phase 3 registrational studies. Baseline BCVA values in the Phase 3 registrational studies vary. Number of patients randomised to treatment group (n, bottom of bars). Mean change in Best Corrected Visual Acuity (BCVA) from baseline shown in ETDRS letters (top of bars). Aflib 2.0, aflibercept 2.0mg; Brol 6.0, brolucizumab 6.0mg; Far 6.0, faricimab 6.0mg; OPT-302 2.0, 2.0mg OPT-302; P2B, Phase 2b trial OPT-302-1002; Ran 0.5, ranibizumab, 0.5 mg; administered every four weeks; q8w, administered every 8 weeks (following 3 x 4-weekly loading doses); q12w, administered every 12 weeks; up to q16w, administered up to every 16 weeks based on protocol defined disease activity assessments.

Neovascular Wet AMD Lesion Types

Differ in vessel location, leakiness, and responsiveness to VEGF-A inhibitors



65-80% of wet AMD patients have occult and minimally classic lesions

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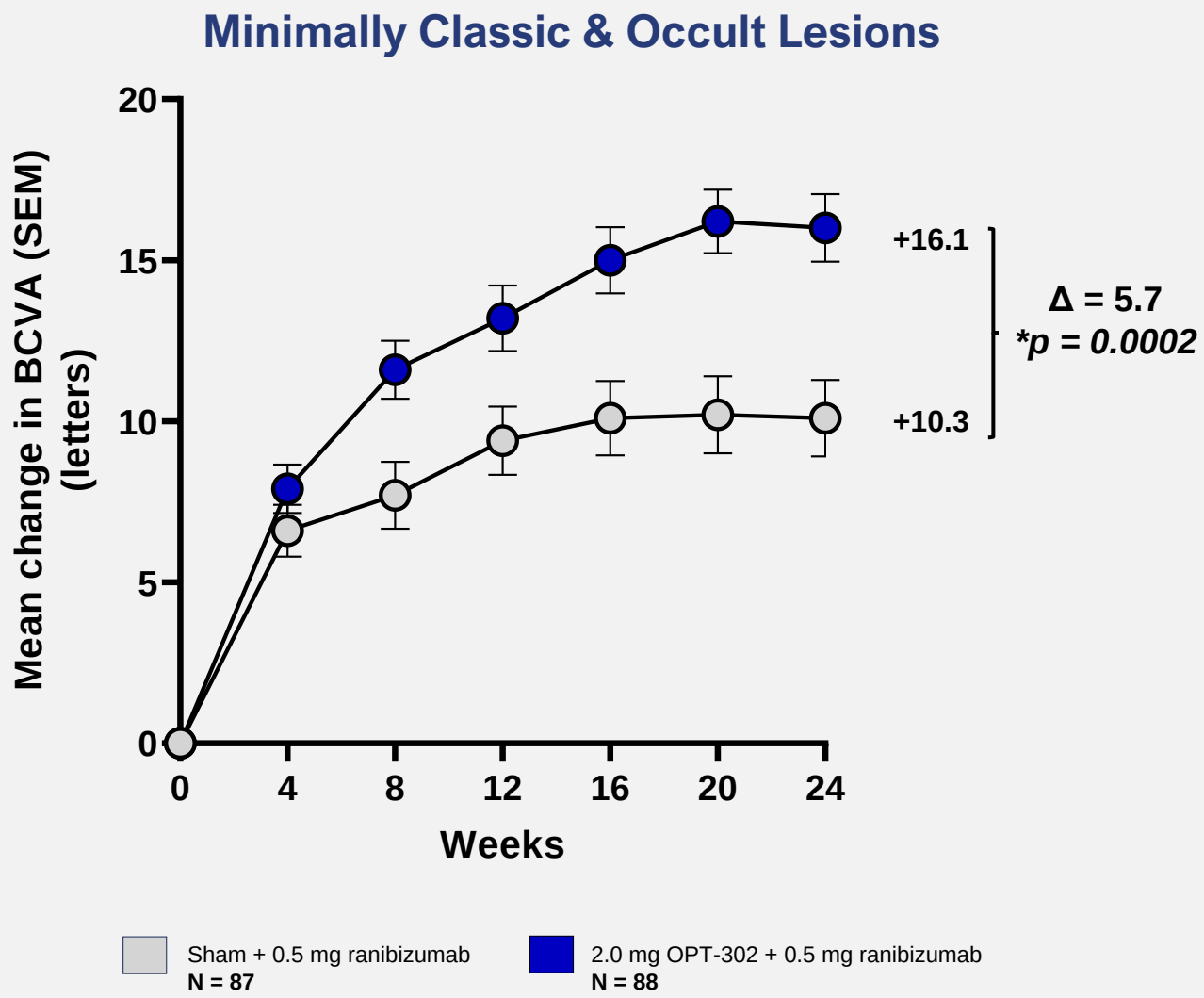
Primary Analysis in Pivotal Trials to Be Performed on Best Responding Sub-Population to Maximize Probability of Success

Patients with minimally classic and occult lesions (RAP absent) achieved greatest vision benefit

Phase 2b demonstrated higher efficacy of +5.7 letter gain in this patient population, based on a pre-determined analysis

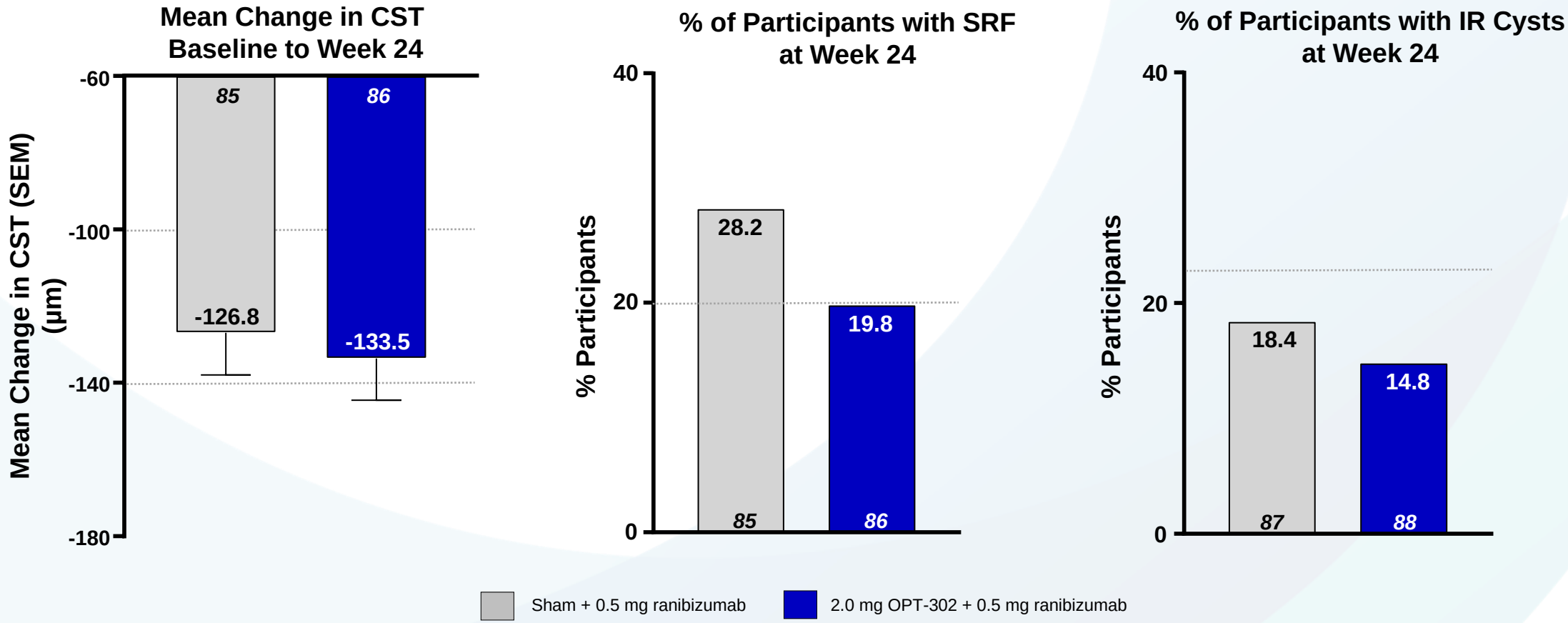
Pivotal program designed to maximize probability of success



** Unadjusted p-value.*

Reduced Retinal Thickness and Better Retinal Drying

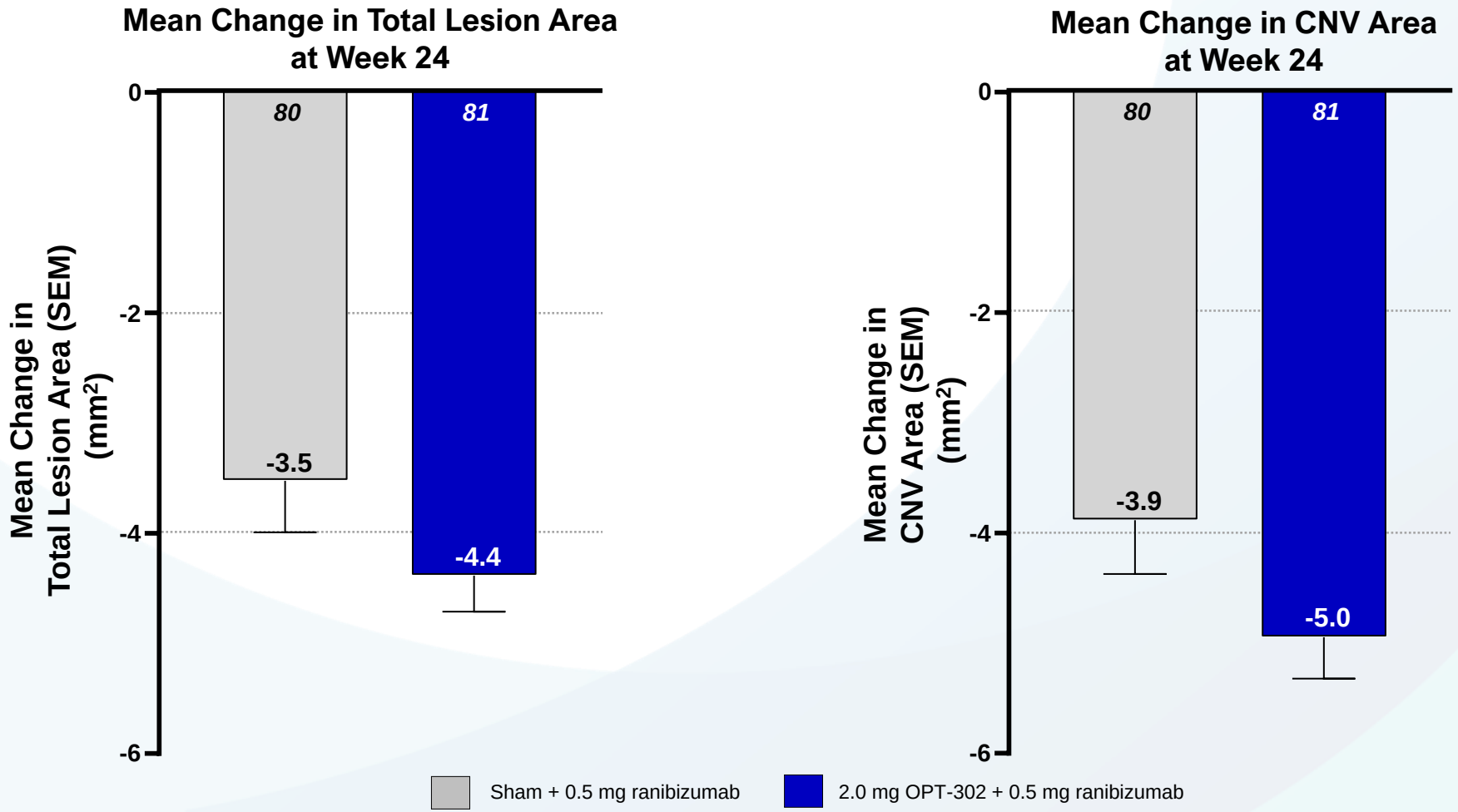
In Combination Therapy in Min. Classic & Occult, RAP Absent Patients



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

Reduced the Total Lesion Area

In Combination at Week 24 in Min. Classic, Occult, and RAP Absent Patients



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

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%)

- 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.

[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)

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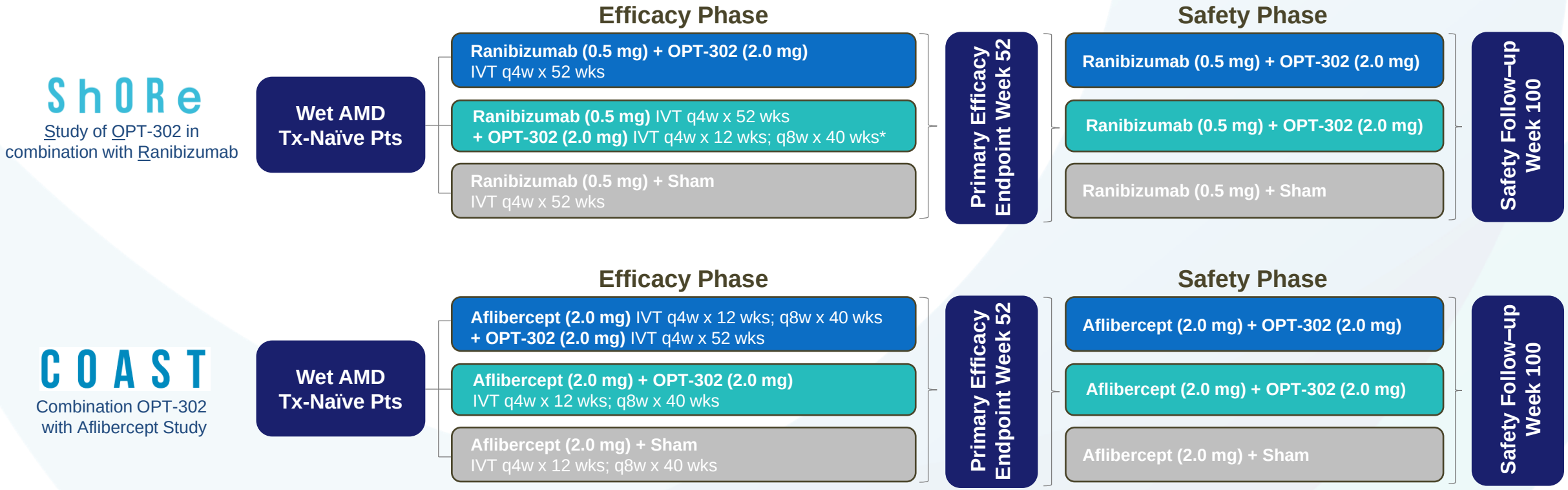
Phase 3 Pivotal Program

Enrollment Completion Anticipated in 1H CY24

Opthea intends to submit Biologics License Application (BLA) and Marketing Authorization Application (MAA) with the FDA and EMA, respectively, following completion of the primary efficacy phase of the trials.



- **Design:** Multi-centre, double-masked, randomised (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 Wk 52

**Sham administered at visits when OPT-302 is not administered.*

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Sozinibercept is a Potential Multibillion Dollar Drug

✓ **Strong Phase 2b Data**
- **Superior vision gains** of OPT-302 combination therapy over standard of care
- Consistent improvement across anatomical endpoints
- Safety profile similar to standard of care in our trials to date

✓ **Pivotal Phase 3 Trials Ongoing; Enrollment Completion Anticipated in 1H CY24**
- Phase 3 clinical trials **~90% enrolled** at the beginning of January 2024; topline data expected in mid-CY2025
- Design informed by Phase 2b data to **maximize probability of success**
- Aligned with FDA to allow **use with any VEGF-A inhibitors**
- FDA Fast Track designation granted

✓ **Multibillion Dollar Commercial Opportunity**
- Existing **> US$8 billion p.a. global market** for wet AMD alone
- DME provides additional opportunity
- Co-formulation with approved therapies possible
- Most advanced product in clinical development to address #1 unmet need for wet AMD patients: **improvement in vision outcomes**

✓ **Differentiated MOA to Improve Efficacy**
- Sozinibercept is a proprietary biologic VEGF-C/D "trap" with **no known late-stage competition**
- The first therapy directly targeting VEGF-C & VEGF-D inhibiting angiogenic signaling through VEGFR-2 and VEGFR-3

Financial Snapshot & Corporate Activities

- Cash and cash equivalents at Fiscal Year End 6/30/2023 of **US$89.2M**
- Completed an Australian rights equity offering and placement in September 2023, raising A$90 million (**~US$58M**)
- Received remaining **US$35M** funding under Development Funding Agreement (DFA), as well as a further **US$50M** option under Amended DFA in December 2023
  - Total funding under DFA: US$170M
  - Provides non-equity funding for the development of OPT-302
  - If sozinibercept is approved in major market, 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
- Expanded U.S. based team with newly appointed CEO and CFO

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