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Equity Raising Presentation

Institutional Placement

2 December 2019

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Placement Overview

Placement Details

Issuer	<ul style="list-style-type: none"> Opthea Limited (“Opthea”)
Ticker / Exchange	<ul style="list-style-type: none"> OPT / ASX
Placement size	<ul style="list-style-type: none"> Opthea has undertaken a non-underwritten private placement to a certain small number of professional and sophisticated investors in Australia and the United Kingdom and has received commitments which will raise approximately A\$50 million Approximately 19 million fully paid ordinary shares (“New Shares”) are to be issued under the Placement at the Placement Price (defined below) representing approximately 7.5% of current issued capital New Shares to be issued under Opthea’s placement capacity per ASX Listing Rule 7.1
Placement price	New Shares issued under the Placement will be issued at a subscription price of A\$2.65 per New Share
Use of proceeds	<ul style="list-style-type: none"> Proceeds from the Placement will be used to: <ul style="list-style-type: none"> fund further clinical development of OPT-302 as a therapy for wet Age-related Macular Degeneration (“wet AMD” or “wAMD”) through commencement of two concurrent Phase 3 pivotal registrational trials in approximately 660 wet AMD patients each; and manufacture sufficient quantities of clinical grade OPT-302 for Phase 3 clinical development. Proceeds from the Placement, together with the Company’s existing cash and cash equivalents, will enable the Company to fund its operations into the first half of calendar 2021
Ranking of New Shares	<ul style="list-style-type: none"> New Shares issued under the Placement will rank equally with existing fully paid ordinary shares of Opthea on issue

Sources and Uses of Funds

Sources and uses of Placement funds

Sources of funds	A\$m
Placement	50 ⁽¹⁾
Total	50

Uses of Funds	A\$m
Phase 3 clinical trial costs	26
Other Phase 3 related costs (including OPT-302 manufacturing)	20
Other general corporate purposes	4
Total	50

Funding commitments from capital raise

- Proceeds from the Placement will be used to:
 - fund further clinical development of OPT-302 as a therapy for wet AMD through commencement of two concurrent Phase 3 pivotal registrational trials in approximately 660 wet AMD patients each; and
 - manufacture sufficient quantities of clinical grade OPT-302 for phase 3 clinical development
- Proceeds from the Placement, together with the Company's existing cash and cash equivalents, will enable the Company to fund its operations into the first half of calendar 2021
- Other costs to be funded from existing cash and R&D tax incentives include:
 - close-out activities of Phase 2b clinical trial of OPT-302 in wet AMD
 - completion of Opthea's Phase 2a clinical trial of OPT-302 in patients with DME
 - R&D support, employee and operating costs

General note: Figures should be considered indicative estimates only and reflect Opthea's current expectations in respect of the design and scope of the proposed Phase 3 clinical program. All figures are therefore subject to change. Proceeds of the Placement will not be sufficient to fully fund all anticipated costs of the Phase 3 clinical trials.

Note (1): Opthea may, in its discretion, increase the amounts raised by the Placement.

Timetable

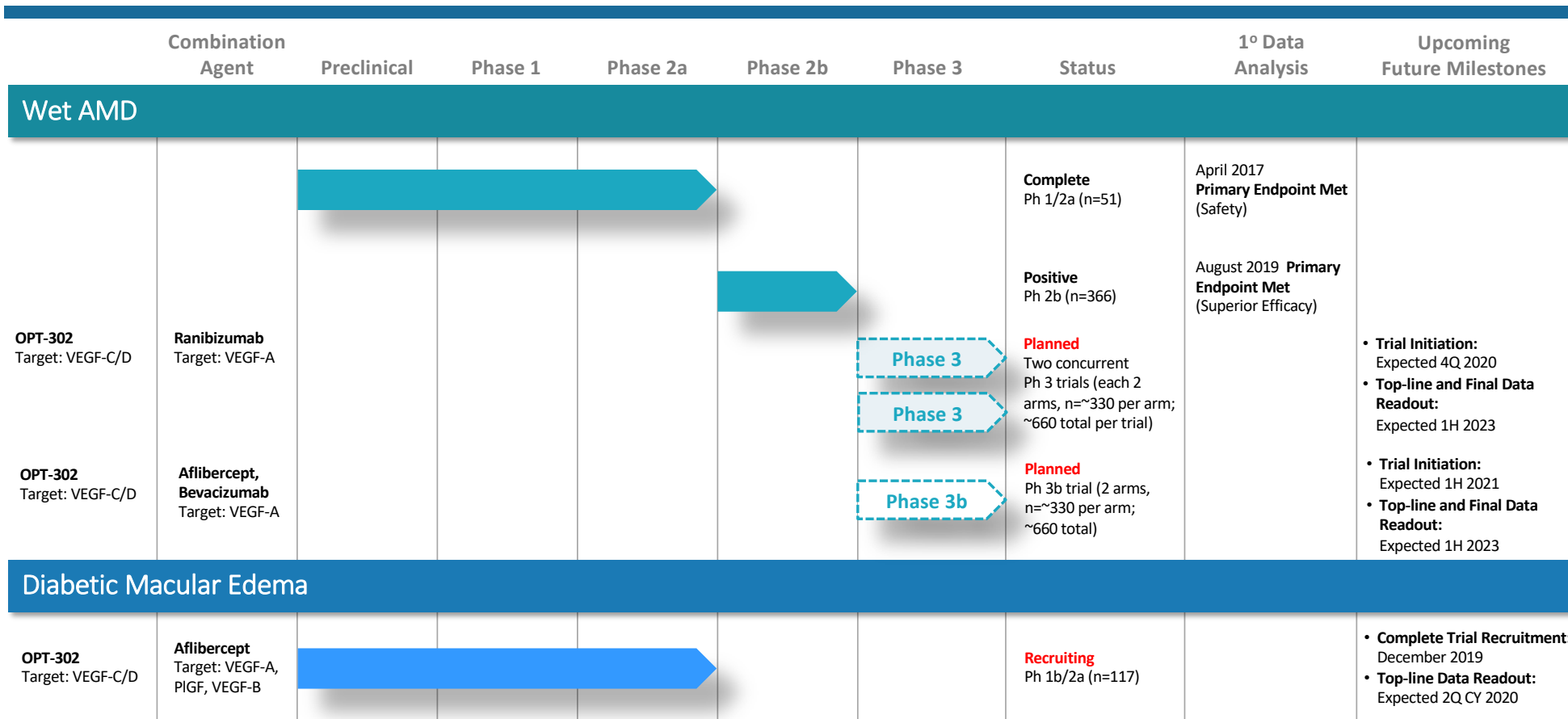
Event	Date
Participating investors execute Placement Agreements	Sunday , 1 December 2019
Announcement of the Placement	Monday, 2 December 2019
Settlement of Placement	Thursday, 5 December 2019
Allotment and trading of New Shares under the Placement	Friday, 6 December 2019

Company Overview

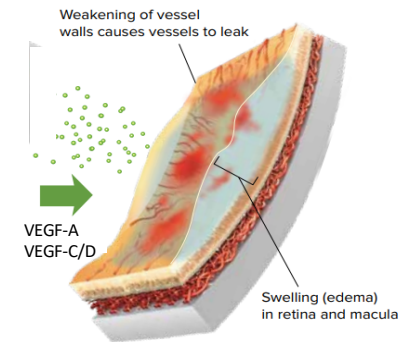
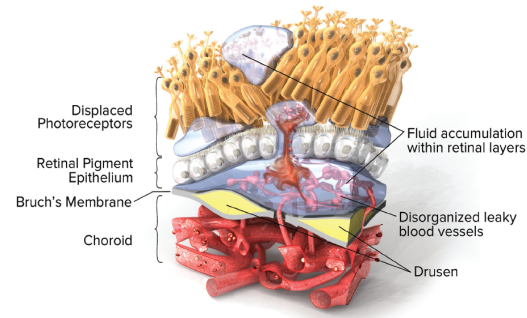
Business Snapshot

<p>Opthea Limited</p>	<ul style="list-style-type: none"> Public company listed on ASX (ASX:OPT) developing OPT-302 for wet AMD and Diabetic Macular Edema (“DME”) Market capitalisation prior to capital raise of A\$683m at 29 November 2019 and cash on hand of A\$30m at 30 October 2019
<p>OPT-302 has a novel mechanism of action</p>	<ul style="list-style-type: none"> OPT-302 (sVEGFR-3) is the first ‘Trap’ inhibitor of VEGF-C and VEGF-D designed specifically for the eye In combination with anti-VEGF-A therapies, shown to completely shut-down VEGFR-2 and VEGFR-3 activity Targets mechanisms of resistance and sub-optimal clinical response to existing therapies
<p>Strong and growing commercial potential</p>	<ul style="list-style-type: none"> Current and growing market opportunity estimated at US\$10B+ worldwide* OPT-302 being developed for use in combination with any of the existing anti-VEGF-A agents, biosimilars or novel therapies in development for wet AMD as well as in DME A novel approach seeking to provide additional visual acuity benefit over standard of care Potential future extension to Retinal Vein Occlusion (“RVO”) and other retinal pathologies
<p>Primary endpoint met in Phase 2b study of OPT-302 in wet AMD</p>	<ul style="list-style-type: none"> OPT-302 combination therapy demonstrated superiority in visual acuity over ranibizumab (Lucentis®) alone at 24 weeks in an international, randomised, controlled, double-masked trial of 366 patients Secondary endpoint results also supportive of primary outcome Exploratory and pre-specified sub-group analyses suggest greater activity of OPT-302 in lesion-types considered more difficult to treat with anti-VEGF-A therapy and highest unmet need Completed Phase 1/2a trial in 51 wet AMD patients
<p>Phase 2a trial of OPT-302 in DME; Data anticipated in 2Q 2020</p>	<ul style="list-style-type: none"> Nearing completion of patient recruitment in Phase 2a trial of OPT-302 in combination with aflibercept (Eylea®) for the treatment of persistent centre-involving DME Completed Phase 1b dose-escalation trial in 9 persistent DME patients Dose-responsive improvements in visual acuity, reductions in retinal fluid and swelling
<p>Well tolerated safety profile of OPT-302</p>	<ul style="list-style-type: none"> Well tolerated safety profile of OPT-302 administered IVT in combination with ranibizumab and aflibercept Extensive global clinical dosing experience with repeated IVT administration in ~400 patients across three international clinical studies in two disease indications

OPT-302 Clinical Program



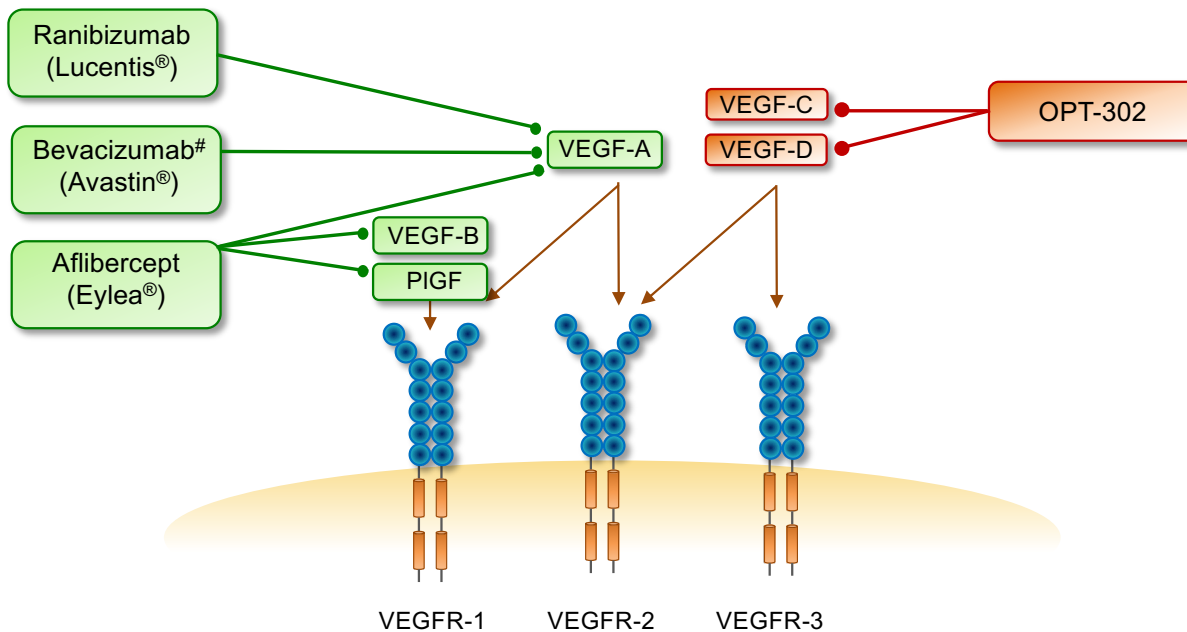
Wet AMD and DME are Leading Causes of Vision Loss in the Elderly and Diabetic Populations Respectively



	Wet AMD	DME
Driver:	Ageing	Sustained hyperglycaemia
Prevalence:	<ul style="list-style-type: none"> Increasing prevalence due to ageing population ~3M people worldwide, including ~1.8M in the US 	<ul style="list-style-type: none"> Increasing due to diabetes epidemic DME with visual impairment affects ~1-3% diabetes patients ~1.3M – 2M people worldwide, many undiagnosed
Primary macular site of pathology:	<ul style="list-style-type: none"> Choroid 	<ul style="list-style-type: none"> Intra-retinal layers
Pathogenesis:	<ul style="list-style-type: none"> Changes in ageing eye Upregulation VEGF-A, -C, -D and other cytokines Choroidal Neovascularization (CNV) Sub-retinal, intra-retinal fluid accumulation 	<ul style="list-style-type: none"> Sustained hyperglycemia Upregulation VEGF-A, -C, -D and inflammatory mediators Inflammation Hyperpermeability and retinal swelling

Existing Therapies Primarily Target VEGF-A

OPT-302 inhibits VEGF-C/D



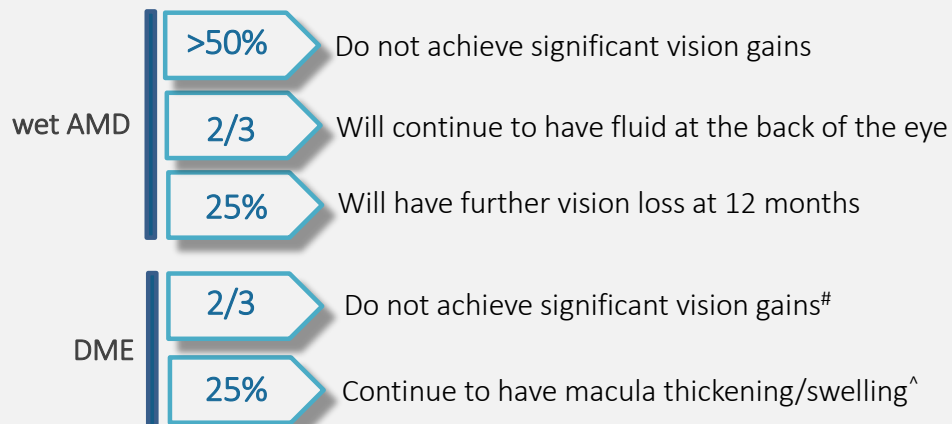
OPT-302: Rationale

- Long-term therapy with selective VEGF-A inhibitors is associated with sub-optimal responses
 - Sub-optimal improvements in visual acuity
 - Persistent retinal fluid
- Resistance to VEGF-A monotherapy may be related to other VEGF family members
- VEGF-C/D signal for angiogenesis and vascular permeability independently of VEGF-A; and
- VEGF-C/D are elevated when VEGF-A is inhibited
- OPT-302 combination therapy achieves a more complete suppression of the VEGF/VEGFR pathway
- OPT-302 targets incomplete response to VEGF-A inhibition

Used in combination with a VEGF-A inhibitor, completely blocks VEGFR-2 and VEGFR-3 signalling

A Currently Unmet Medical Need for wet AMD and DME

Despite receiving a VEGF-A inhibitor (ranibizumab, aflibercept or bevacizumab)*:



Opportunity: New Products that Improve Efficacy and Durability

Large and Growing Market Opportunity

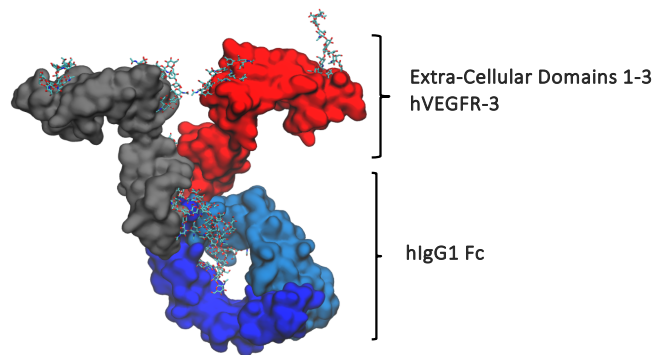
- Wet AMD and DME are the leading causes of blindness in the elderly and diabetic populations respectively
- Prevalence is increasing
- Market opportunity is growing
- Approved VEGF-A inhibitors (ranibizumab and aflibercept) generated revenues >US\$10b in 2018
- Approximately 50% of wet AMD and DME patients worldwide receive bevacizumab as an off-label, less-costly treatment option

Opthea's strategy is to develop OPT-302 as a combination therapy to be administered with any of the approved a-VEGF-A therapies or new VEGF-A inhibitors in development

OPT-302: A 'trap' inhibitor of VEGF-C and VEGF-D

OPT-302: A soluble form of VEGFR-3

- Comprises the extracellular domains 1-3 of VEGFR-3 and the Fc fragment of human IgG1
- Potent inhibitor of VEGF-C (~5 pM) and VEGF-D (~0.5 nM)
- A 'trap' that blocks VEGF-C and VEGF-D binding to the receptors VEGFR-2 and VEGFR-3
- Targets a validated pathway involved in wet AMD progression
- Targets a mechanism of escape from existing therapies that is differentiated to VEGF-A therapies



Strategy

- To develop OPT-302 for use in combination with inhibitors of VEGF-A to address the unmet medical need in wet AMD as well as in DME
- To demonstrate superior gains in visual acuity in patients administered OPT-302 in combination with a VEGF-A inhibitor
- Clinical trials based on administering OPT-302 as a sequential intravitreal injection every 4 weeks (q4w), with the potential to also:
 - investigate OPT-302 efficacy and durability in patients receiving less frequent doses (e.g. q8w, q12w), and
 - co-formulate with other agents
- The wet AMD and DME landscapes include only a limited number of novel combination therapies that may address the sub-optimal clinical responses that many patients experience on anti-VEGF-A therapies

OPT-302 has comparable ocular biodistribution and PK profile to aflibercept, with low systemic exposure

OPT-302 Intellectual Property

Summary covering sVEGFR-3 for Eye Disease

COMPOSITION OF MATTER		TERM
Covering OPT-302 molecule <ul style="list-style-type: none"> • Granted patents in the USA, Japan, Russia, Australia, South Africa and Singapore • Patents accepted for grant in Europe, Malaysia and Mexico • Applications pending in a further 10 jurisdictions including China, Brazil and India 		2034*
Covering sVEGFR-3 molecules (incl. OPT-302) <ul style="list-style-type: none"> • Granted patents in Europe, Japan, Canada, and Australia • Granted patent in the USA 		2022 2026
<ul style="list-style-type: none"> • Separate US patent granted covering generic use of sVEGFR-3 capable of binding VEGF-C to inhibit blood vessels in mammal having disease characterised by expression of VEGFR-3 in blood vessels 		2023
PATENT TERM EXTENSION / DATA EXCLUSIVITY		
*Patent Term Extension (PTE)	Up to 5 years additional patent term is available under patent term extension rules in most jurisdictions including the USA, Europe and Japan	
Data Exclusivity (DE) and Market Exclusivity (ME)	Once approved, OPT-302 expects to be entitled to DE, and potentially also ME, in many jurisdictions:	
	USA	12 years DE for biologics
	Europe	10 years made up of 8 years DE + 2 years ME
	Japan	Up to 8 years <i>de facto</i> DE
	Canada	Up to 8 years incl. up to 6 years DE + 2 years ME

OPT-302:

Phase 2b wet AMD

A dose-ranging study of intravitreal OPT-302 in combination with ranibizumab, compared with ranibizumab alone, in participants with wet AMD

*(OPT-302-1002; NCT ClinicalTrials.gov Identifier: NCT03345082
113 sites across 10 countries including the US, EU and Israel)*

Study Outcomes - OPT-302 Phase 2b wet AMD Trial

Phase 2b trial met primary endpoint

- OPT-302 (2.0mg) combination therapy demonstrated superiority in visual acuity over ranibizumab + sham
- Vision gain of +3.4 letters
- Statistically significant ($p=0.0107$)
- Ranibizumab control arm performed exceptionally well

Secondary outcomes were supportive of the primary endpoint

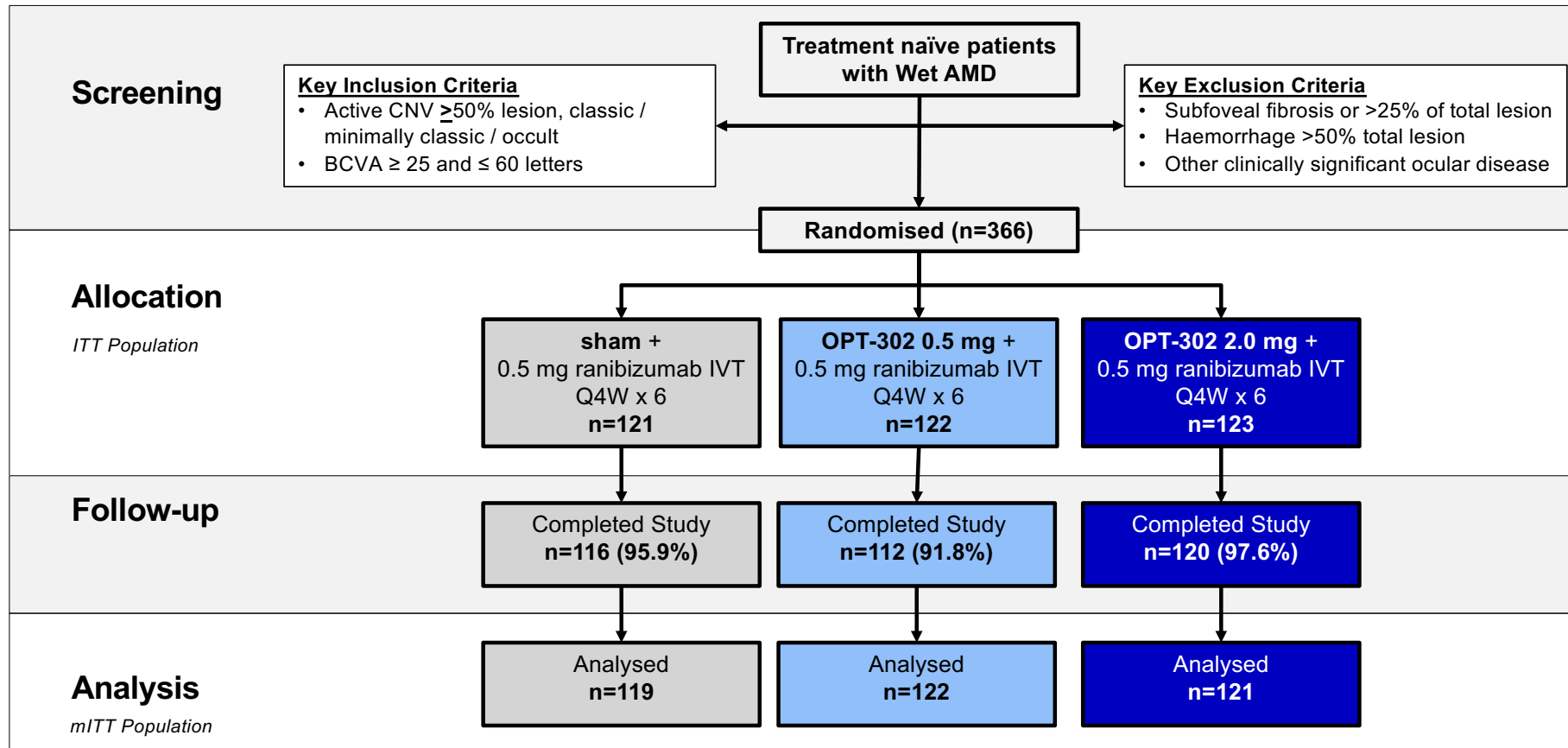
- **Vision**
 - More patients gained ≥ 15 letters of vision
 - Fewer patients lost ≥ 15 letters of vision
- **Retinal anatomical improvements**
 - Reductions in central subfield thickness (CST), sub-retinal and intra-retinal fluid
 - Greater decreases in total lesion area and choroidal neovascularisation (CNV) Area

Exploratory and pre-specified subgroup analyses

- Suggest greater activity of OPT-302 in lesion-types considered more difficult to treat with anti-VEGF-A therapy and highest unmet need
- Promising evidence of activity in polypoidal AMD (PCV) and minimally classic/occult lesions that are less responsive to VEGF-A inhibitors

Favorable safety profile

Study Overview



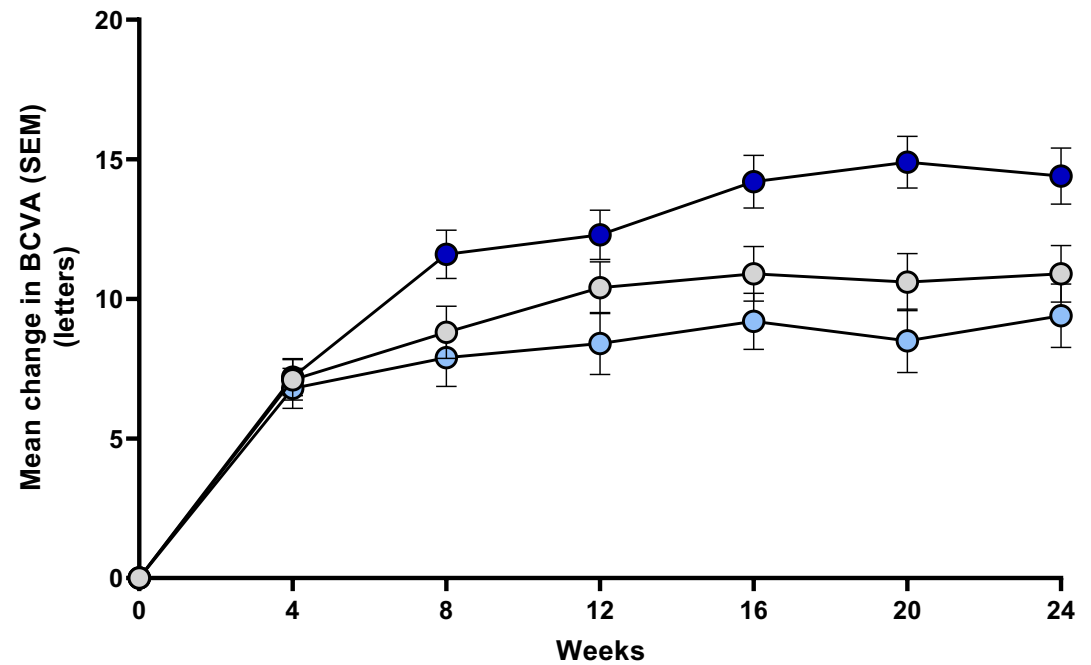
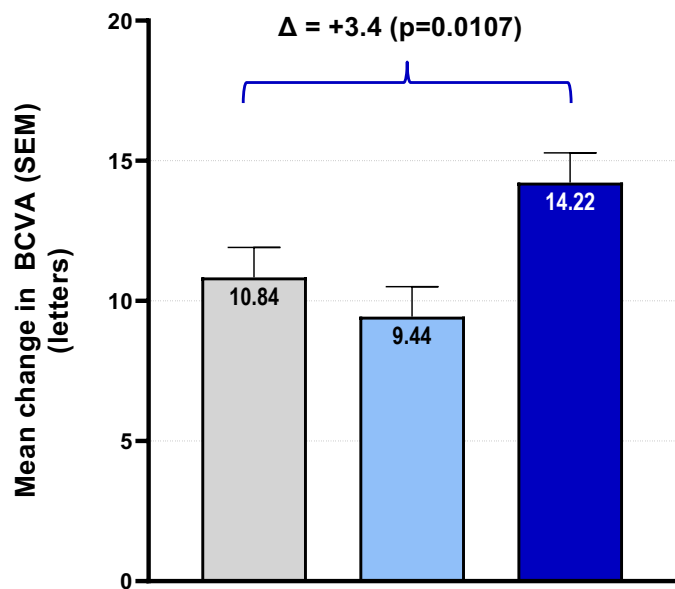
Study Demographics and Baseline Characteristics

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 - 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%)	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) - um ±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%

Primary Analysis – Mean Change in BCVA Baseline to Week 24

Primary endpoint achieved

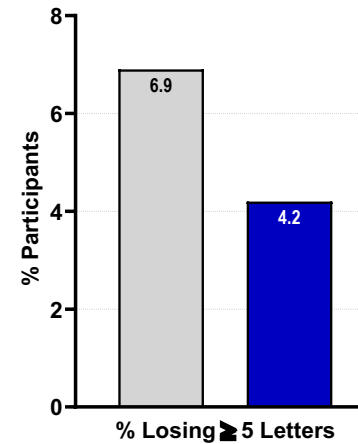
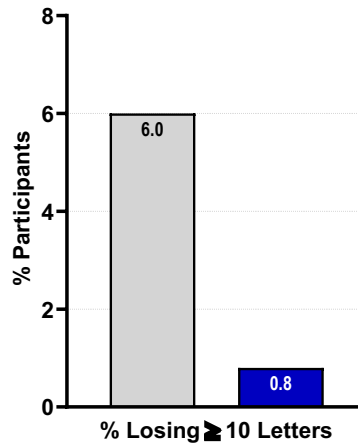
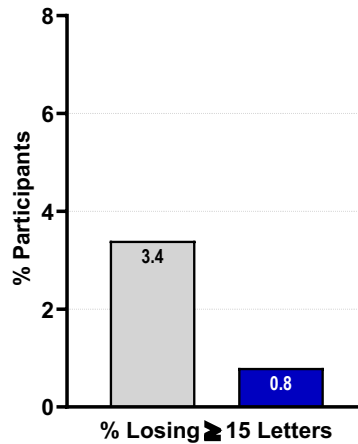
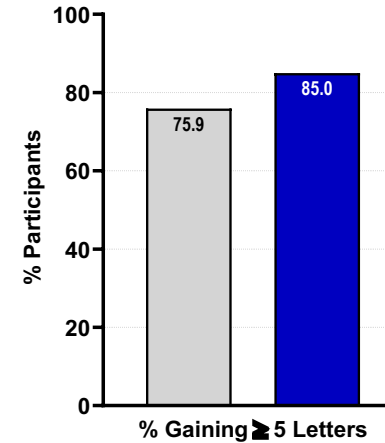
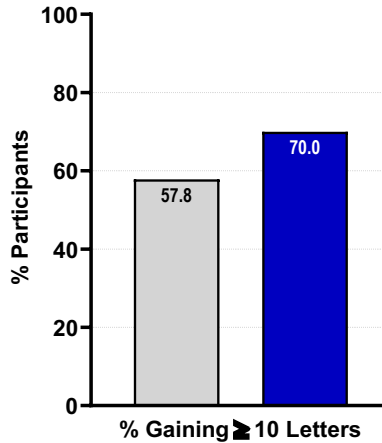
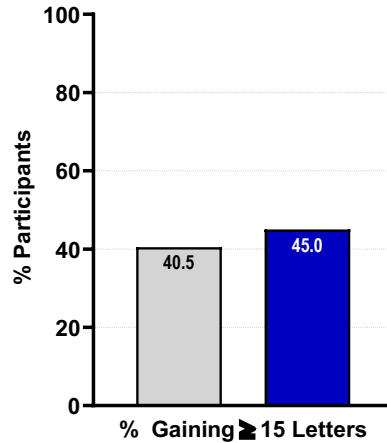
OPT-302 (2.0 mg) Combination Therapy Demonstrated Superiority in Visual Acuity over Ranibizumab



Legend: Sham + 0.5 mg ranibizumab (n=119) | 0.5 mg OPT-302 + 0.5 mg ranibizumab (n=122) | 2.0 mg OPT-302 + 0.5 mg ranibizumab (n=121)

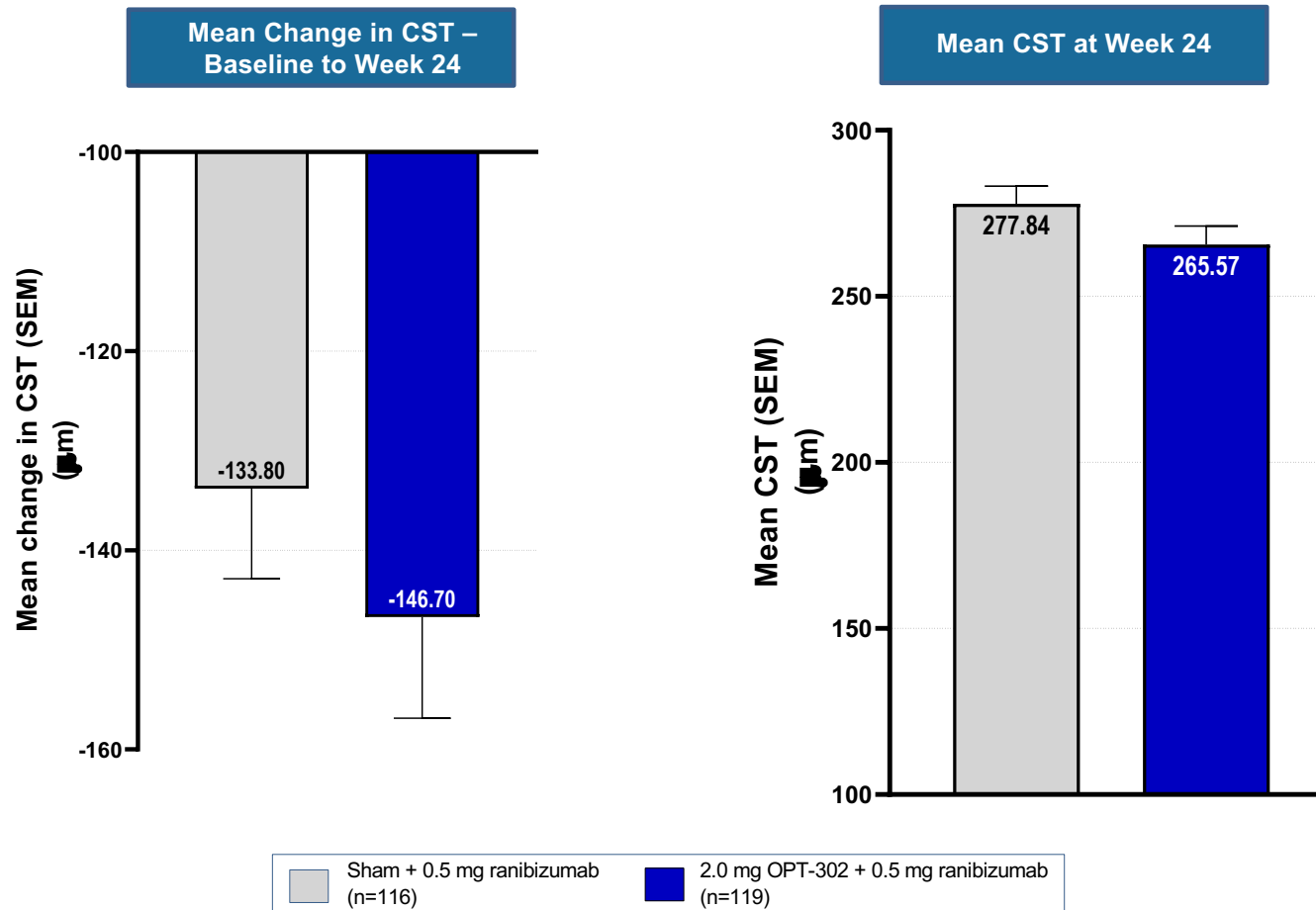
Vision Gain and Vision Loss - Baseline to Week 24

More patients gain, and fewer patients lose, ≥ 15 , ≥ 10 and ≥ 5 letters of vision in OPT-302 combination group



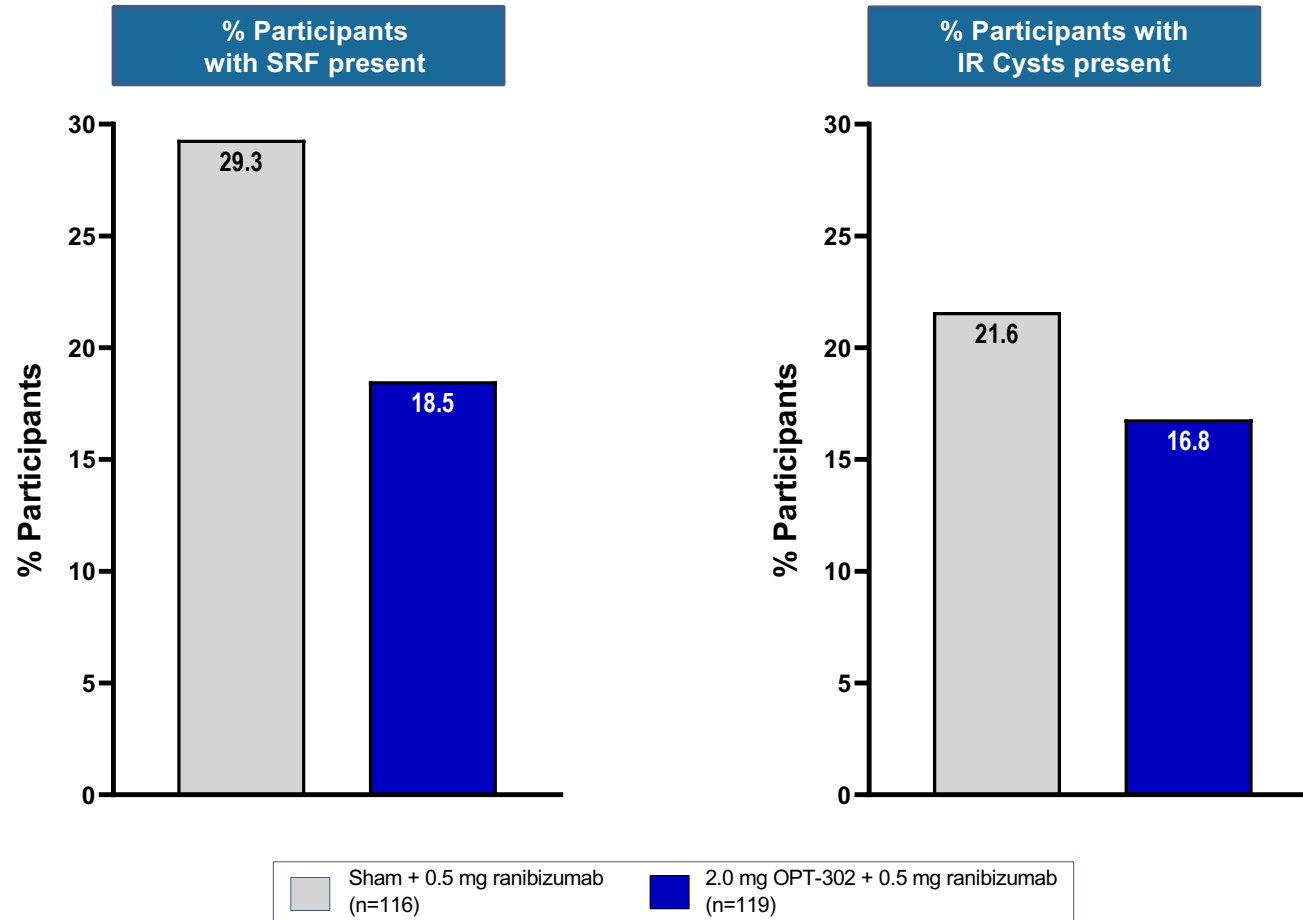
Central Subfield Thickness

Reduction in CST in OPT-302 combination group compared to sham + ranibizumab



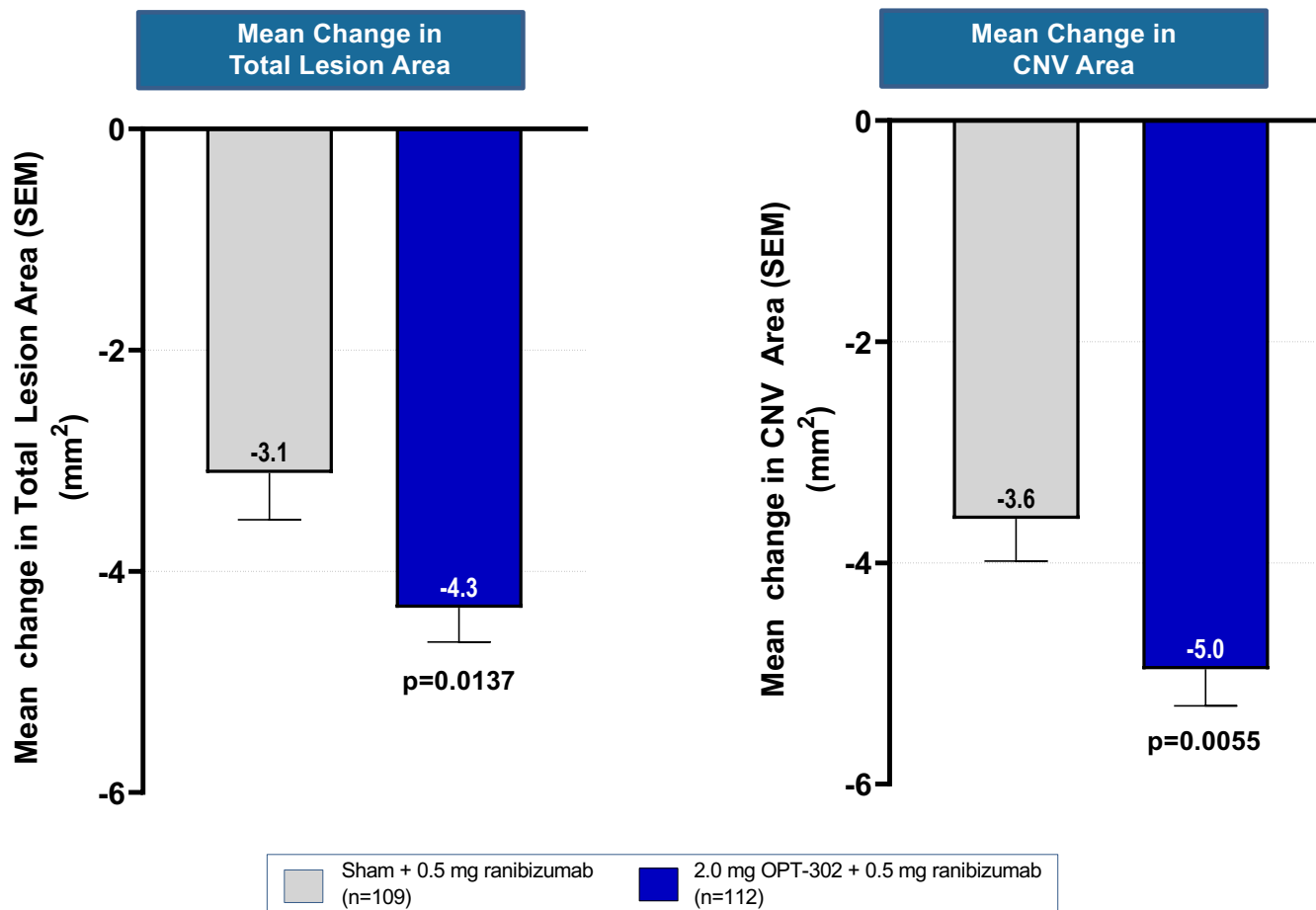
Sub-retinal Fluid and Intra-retinal Cysts at Week 24

Fewer participants with retinal fluid present in OPT-302 combination group compared to sham + ranibizumab



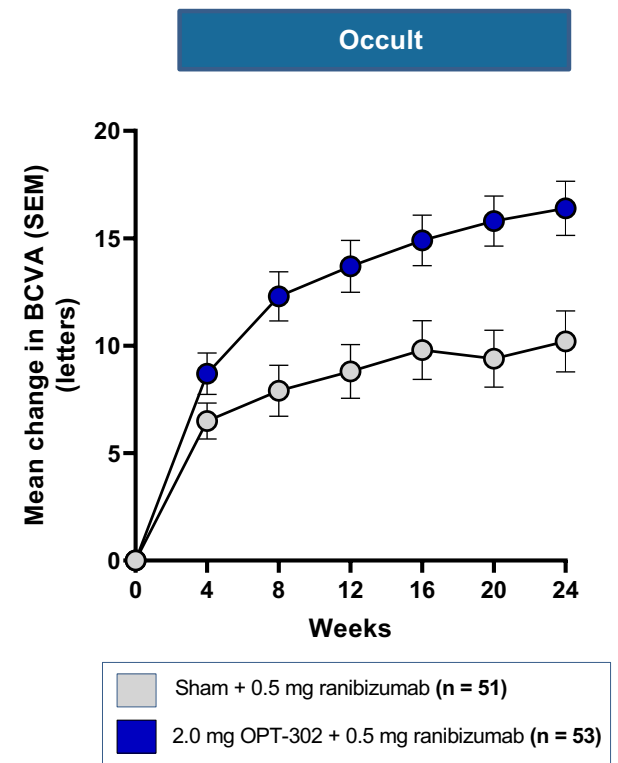
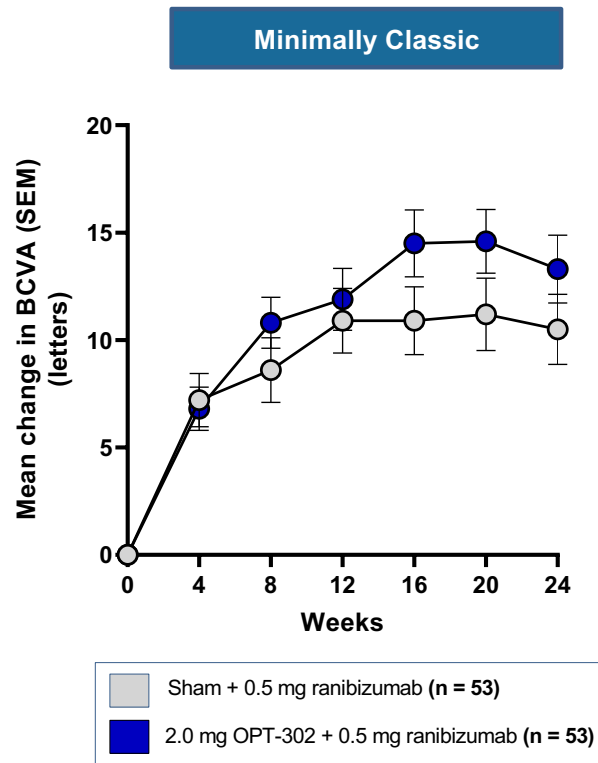
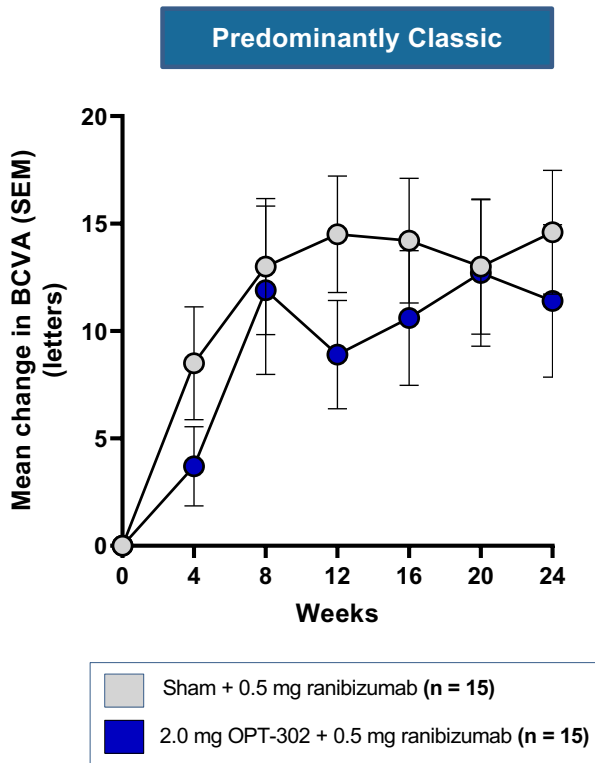
Total Lesion Area and CNV Area – Baseline to Week 24

Greater reduction in Total Lesion and CNV Area in OPT-302 combination group compared to sham + ranibizumab



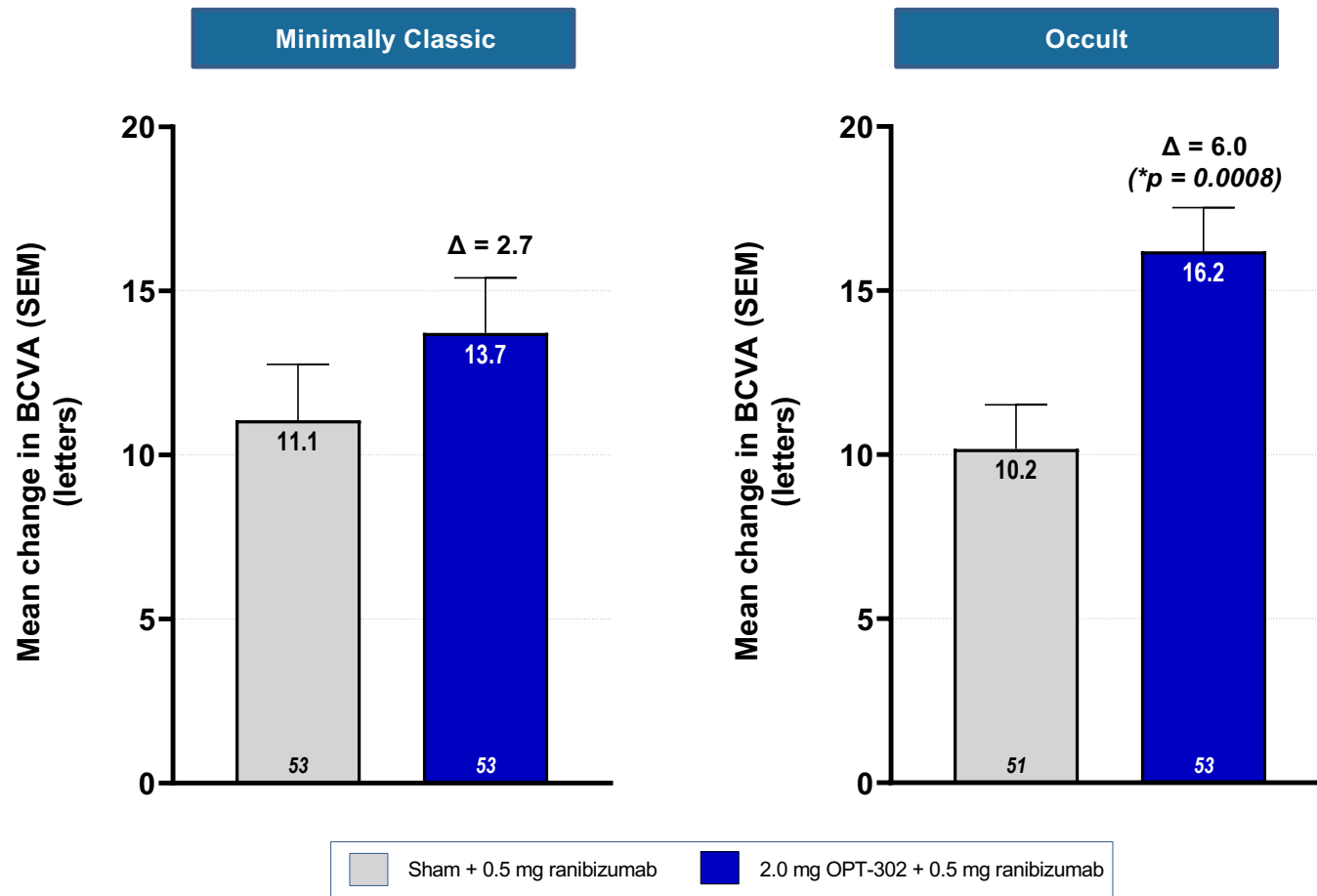
Mean Change in BCVA Over Time by Lesion Type

Small number of predominantly classic patients



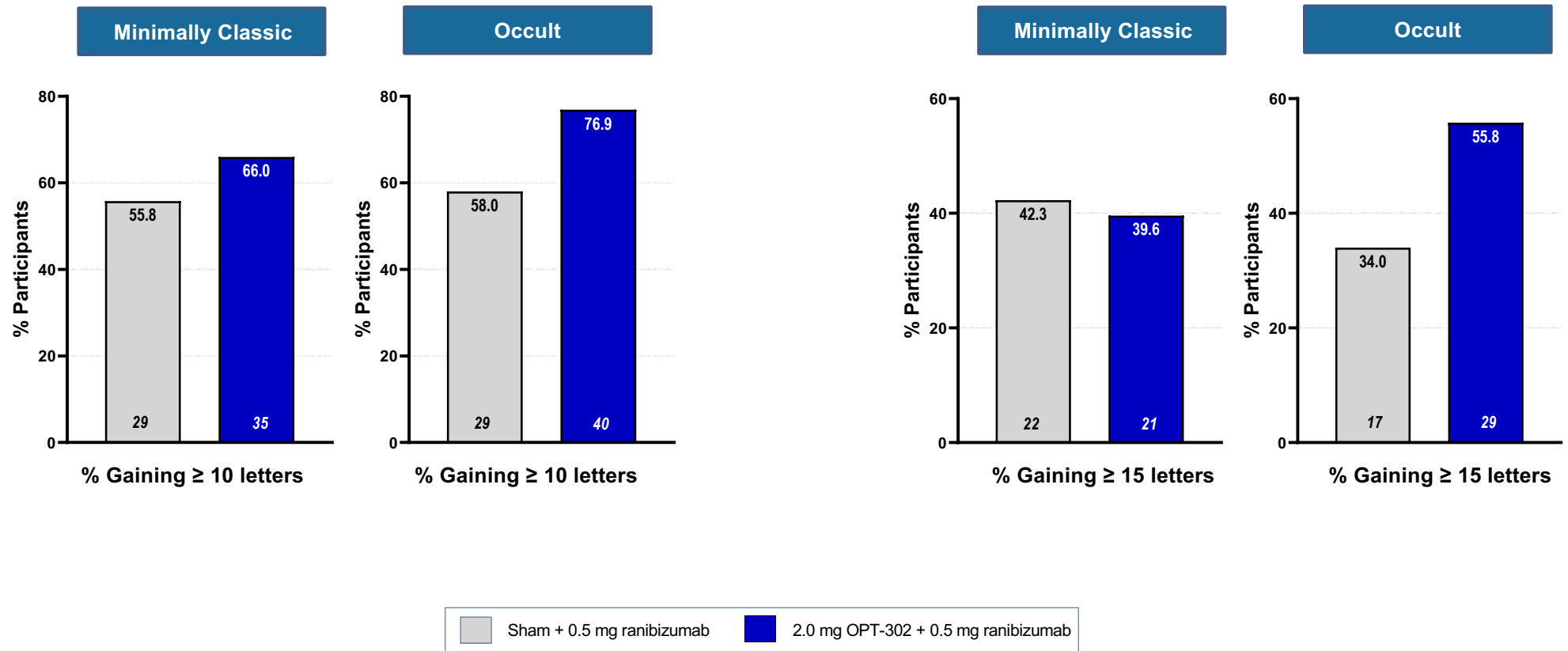
Mean Change in BCVA at Week 24 by Lesion Type

Greater vision gains at Week 24 in OPT-302 2.0 mg group in minimally classic and occult lesions



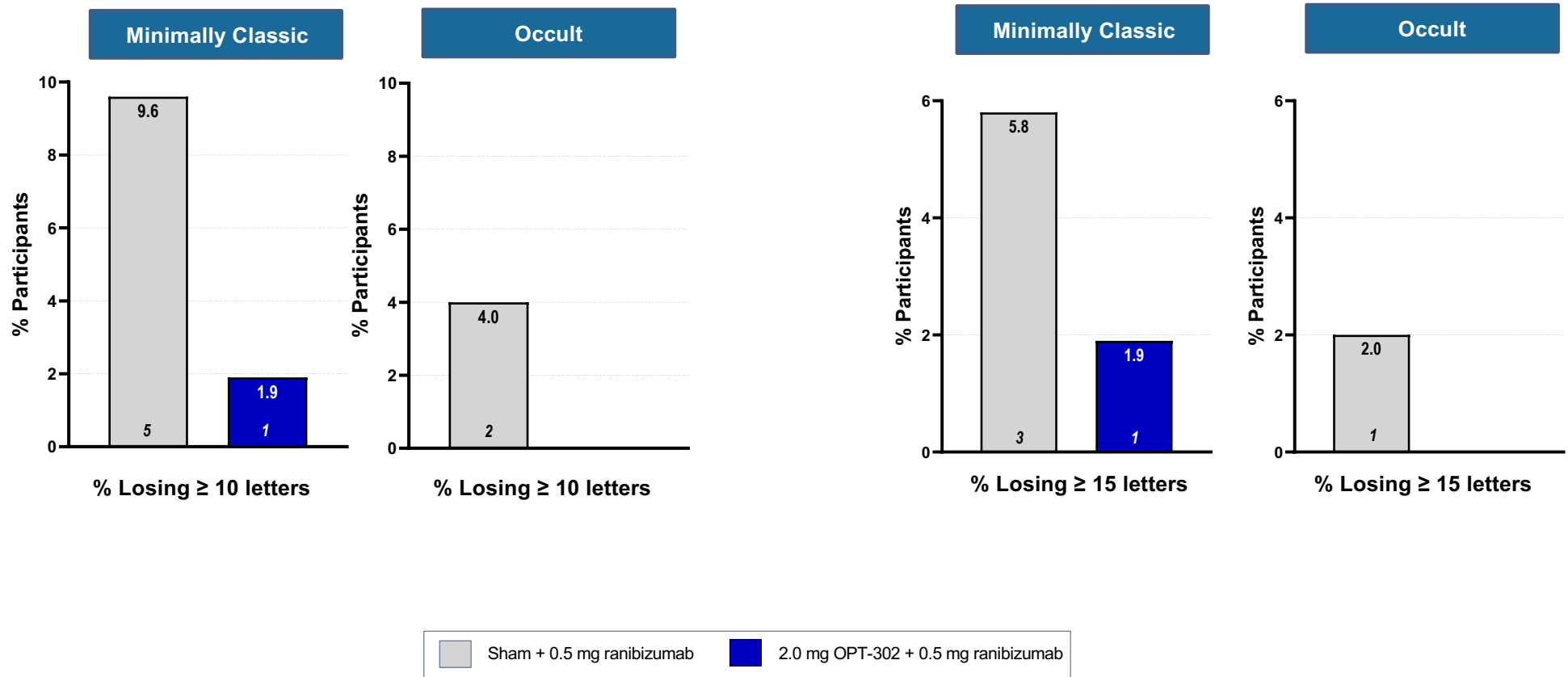
2-Line and 3-Line Vision Gain at Week 24 by Lesion Type

>20% increase in 3-line gainers in participants with occult lesions treated with OPT-302 combination therapy



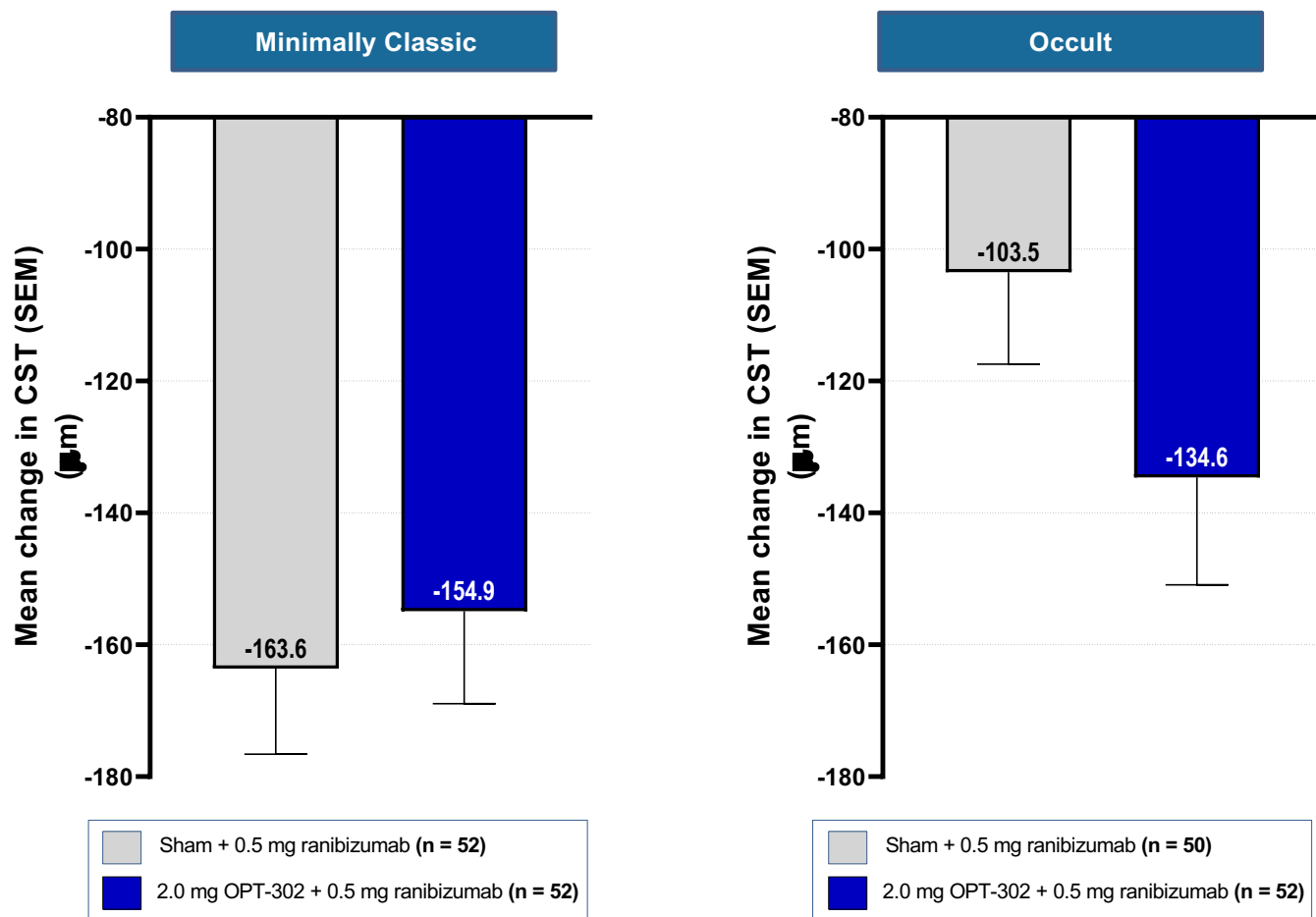
2-Line and 3-Line Vision Loss at Week 24 by Lesion Type

Fewer patients with minimally classic and occult lesions lose ≥ 10 and ≥ 15 letters following OPT-302 combination therapy



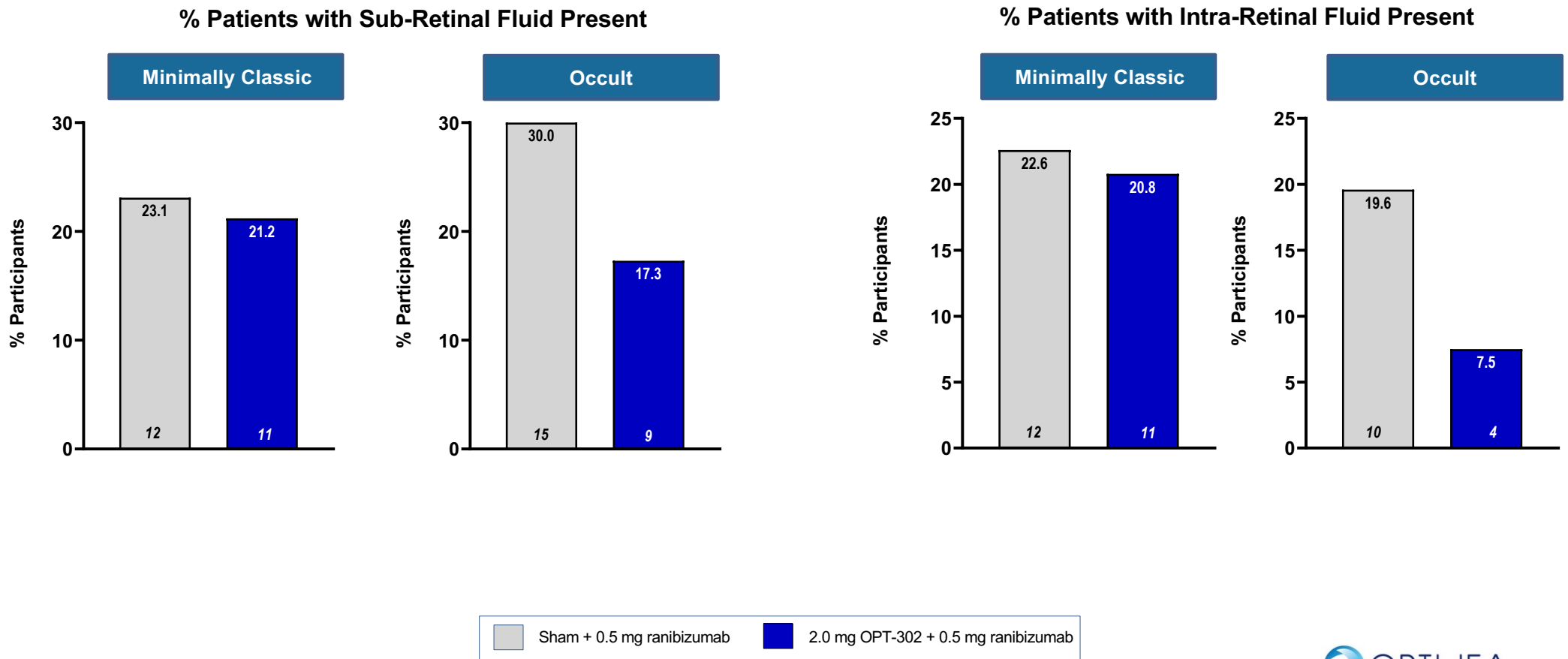
Central Subfield Thickness by Lesion Type

Reduction in CST in participants with occult lesions treated with OPT-302 combination compared to sham + ranibizumab



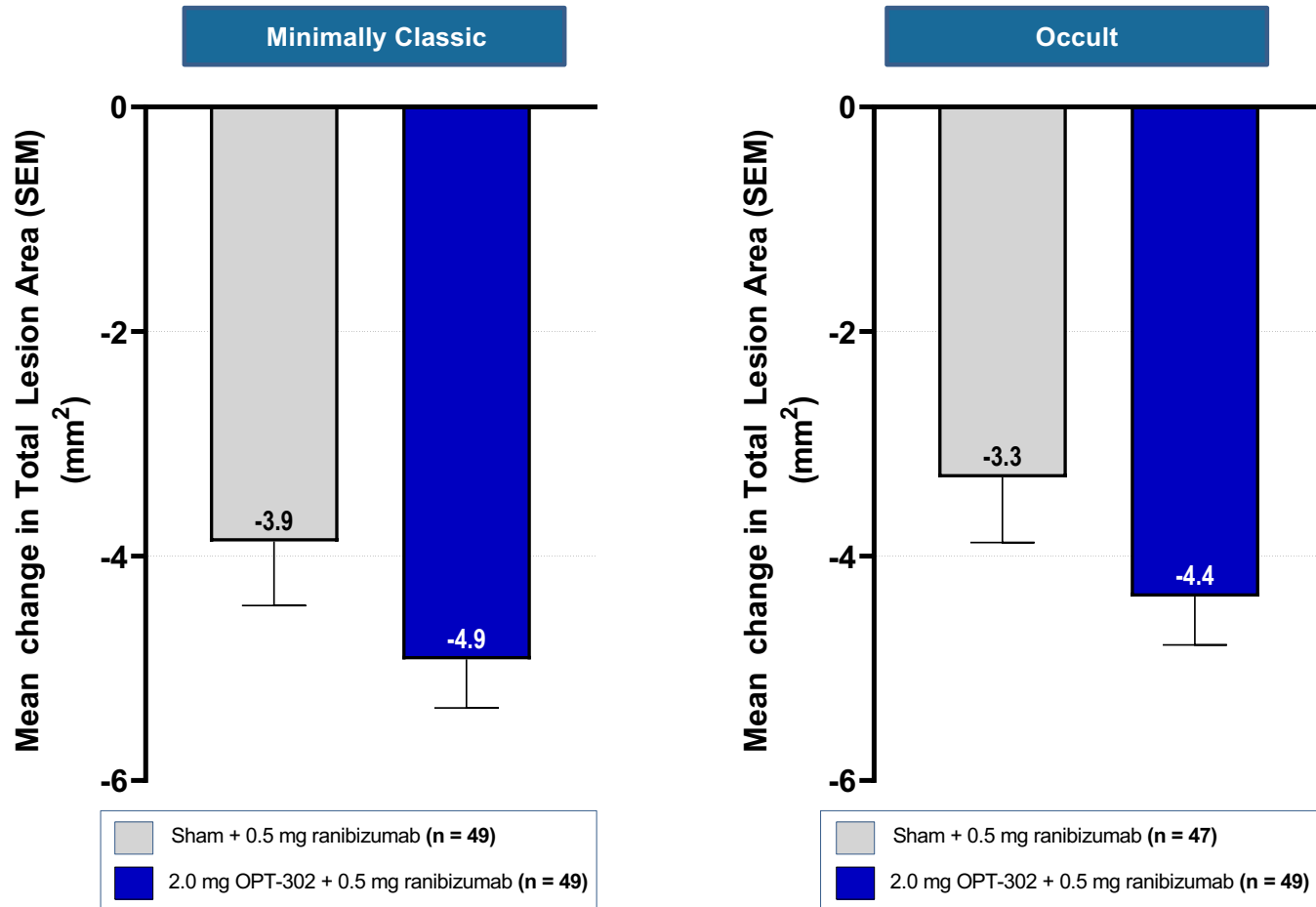
Sub-Retinal Fluid and Intra-Retinal at Week 24 by Lesion Type

Fewer participants with minimally classic and occult lesions have retinal fluid at week 24 following OPT-302 combination therapy



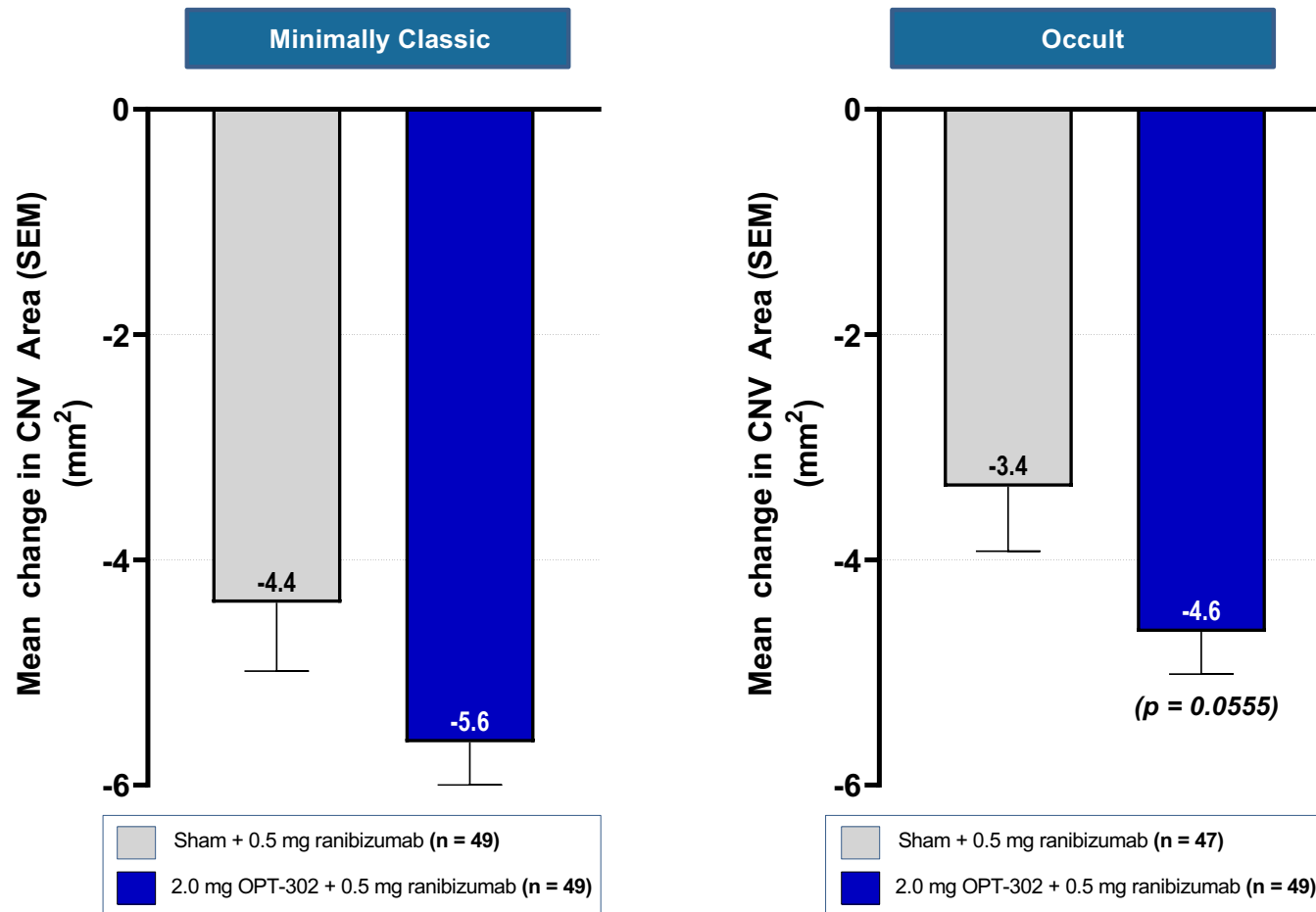
Total Lesion Area at Week 24 in Minimally Classic and Occult Lesions

Greater reductions in Total Lesion Area following OPT-302 combination therapy



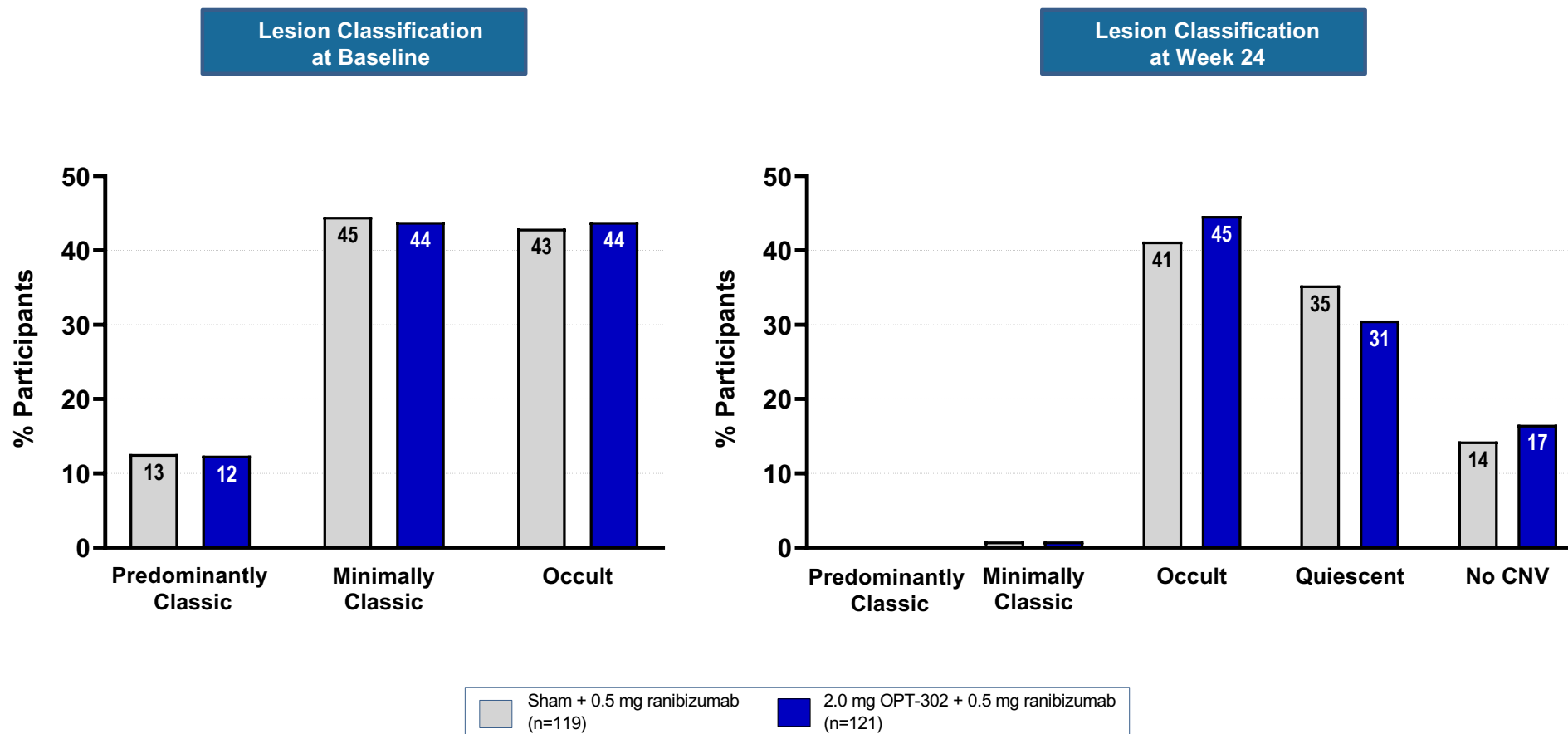
CNV Area at Week 24 in Minimally Classic and Occult Lesions

Greater reductions in CNV Area following OPT-302 combination therapy



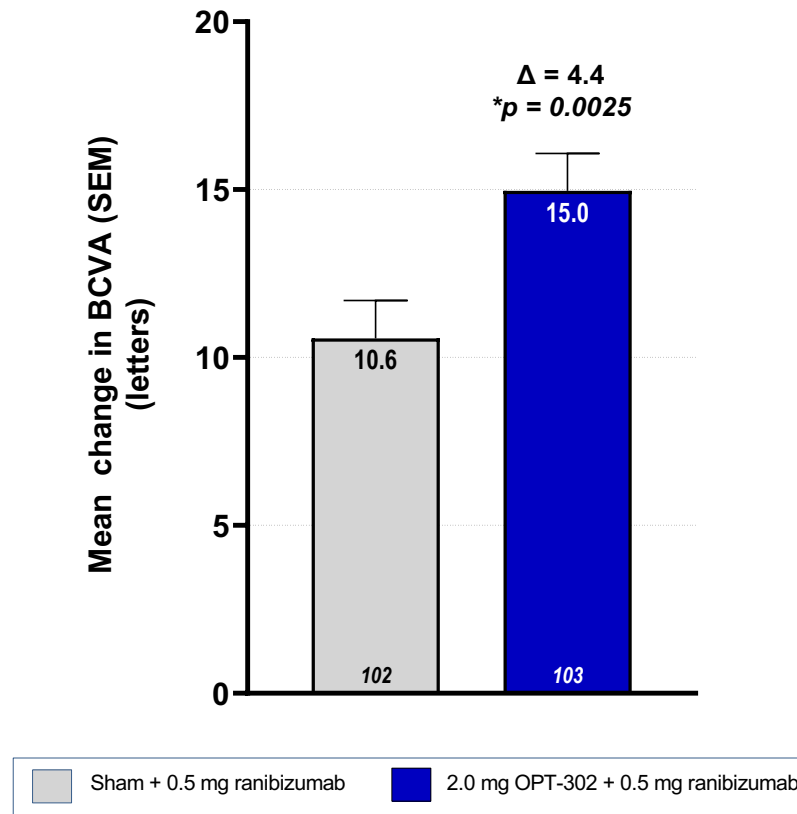
Lesion classification at Baseline and at Week 24

Lesions shift to an occult, quiescent biology or no CNV following treatment



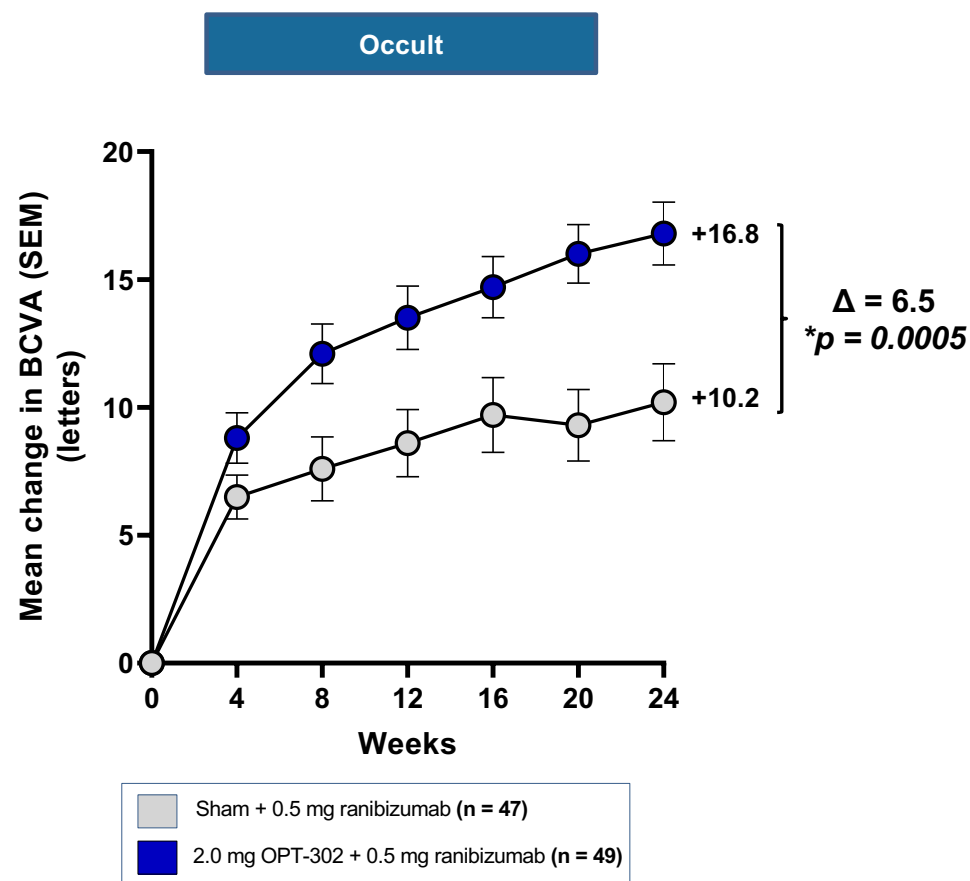
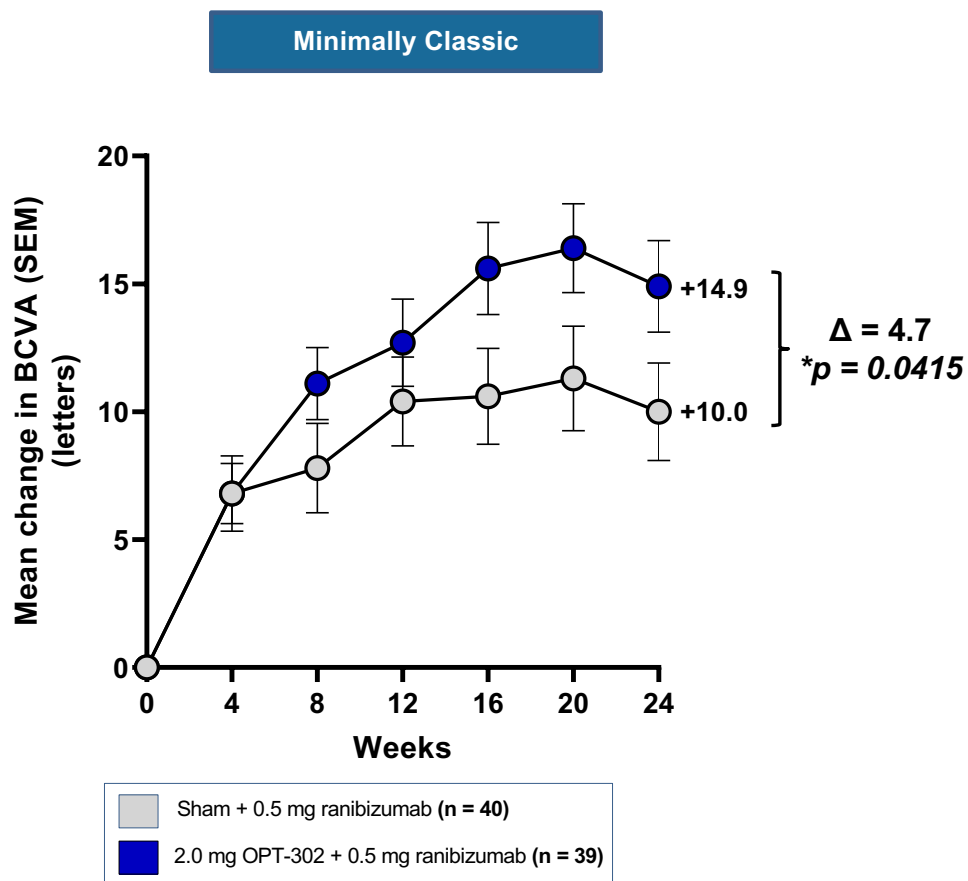
Retinal Angiomatous Proliferation (RAP) Lesions

Mean change in BCVA to Week 24 in participants without RAP at baseline

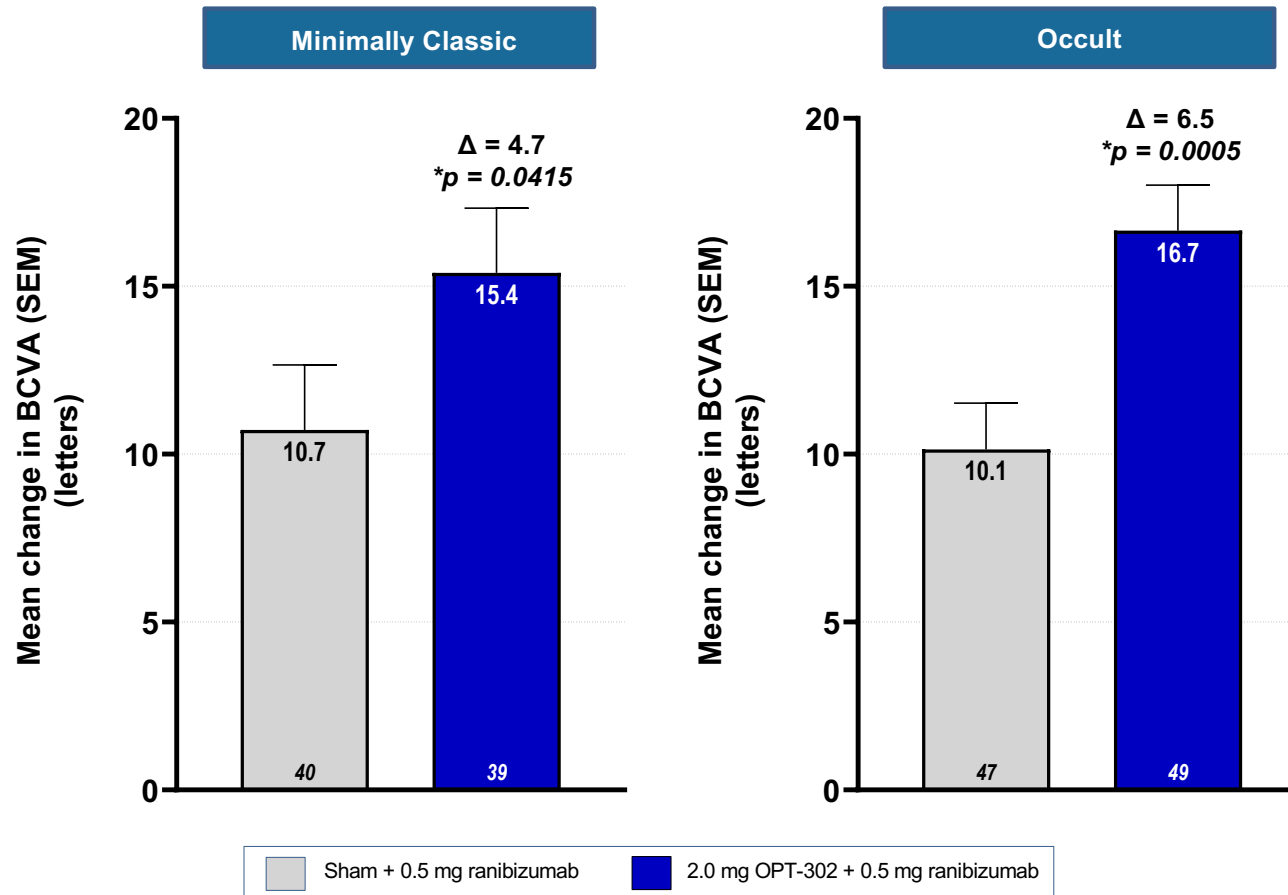


Mean Change in BCVA Over Time by Lesion Type, RAP Absent

In RAP absent participants, +4.7 letter gain in minimally classic and +6.5 letter gain in occult participants treated with OPT-302 combination therapy compared to sham + ranibizumab



Mean Change in BCVA at Week 24 by Lesion Type, RAP Absent



Safety – Adverse Events (AEs)

N Participants (%)	Sham + ranibizumab N=121	0.5 mg OPT-302 + ranibizumab N=120	2.0 mg OPT-302 + ranibizumab N=124
Treatment emergent AEs	84 (69.4%)	87 (72.5%)	93 (75.0%)
Ocular AEs - Study Eye – related to study product(s)¹	17 (14.0%)	17 (14.2%)	19 (15.3%)
Ocular AEs - Study Eye – Severe²	1 (0.8%)	2 (1.7%)	1 (0.8%)
Serious AEs	10 (8.3%)	16 (13.3%)	7 (5.6%)
Ocular SAEs in Study Eye	0 (0.0%)	2 ³ (1.7%)	0 (0.0%)
Intraocular inflammation⁴ – Study Eye	0 (0.0%)	2 ³ (1.7%)	1 ⁵ (0.8%)
Participants with AEs leading to study IP discontinuation only	2 (1.7%)	3 (2.5%)	0 (0.0%)
Participants with AEs leading to study discontinuation	1 ⁶ (0.8%)	0 (0.0%)	0 (0.0%)
Any APTC event	0 (0.0%)	1 ⁷ (0.8%)	0 (0.0%)
Deaths	2 ⁸ (1.7%)	0 (0.0%)	0 (0.0%)

Safety population analysed according to medication received

¹ Assessed by investigator to be “possibly related”, “probably related” or “definitely related” to administration of study drug(s)

² Assessed by Investigator to be National Institutes of Health (NIH) Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or above, or, if CTCAE grade is unavailable, an AE assessed as “causing an inability to perform normal daily activities”

³ SAE of endophthalmitis, with AEs of hypopyon and anterior chamber cell (n=1), SAE of vitritis (n=1)

⁴ AEs considered to be indicative of intraocular inflammation, defined prior to database lock as: Endophthalmitis, iritis, vitritis, iridocyclitis, uveitis, hypopyon, viral iritis, or anterior chamber inflammation

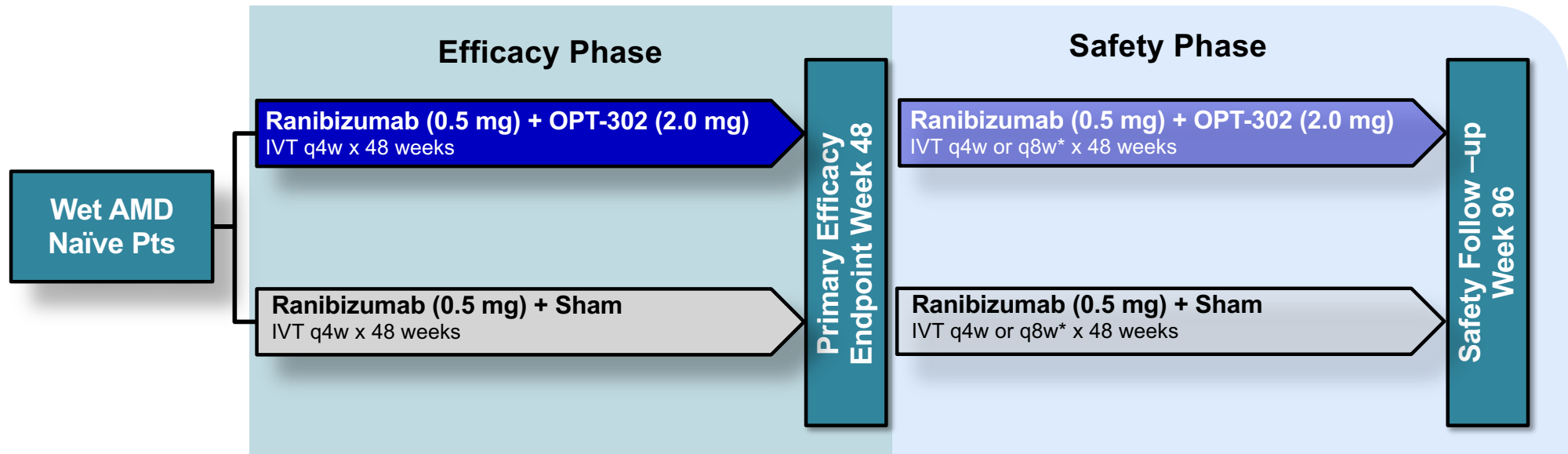
⁵ Anterior chamber cell (trace 1-4 cells)

⁶ Squamous cell carcinoma of the lung diagnosed shortly after Baseline visit

⁷ Non-fatal myocardial infarction

⁸ Pneumonia (n=1), infective endocarditis (n=1)

Planned: OPT-302 Pivotal Phase 3 Program



- **Two studies of similar design:** Multi-centre, double-masked, randomised (1:1), sham controlled
- **Regulatory quality:** 90% power, 5% type I error rate
- **Sample size:** approximately 330 patients per arm, 660 per study (1,320 patients across the two studies)
- **Primary Objective:** Mean change from Baseline in BCVA (visual acuity) (ETDRS) at Week 48
- **Trial Initiation:** 4Q 2020
- **Top-line Data Readout:** 1H 2023
- **Full Data Readout:** 1H 2023

Ongoing Clinical Trials

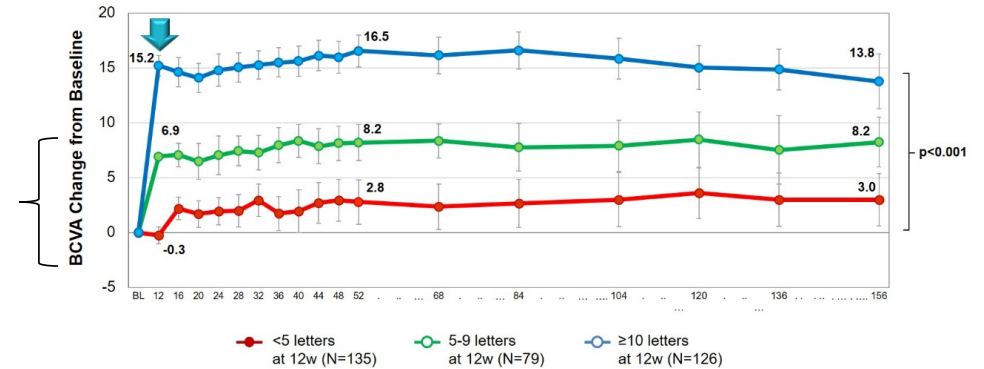
Phase 1b/2a DME

Phase 1b/2a study of OPT-302 in combination with aflibercept for persistent central-involved diabetic macular edema

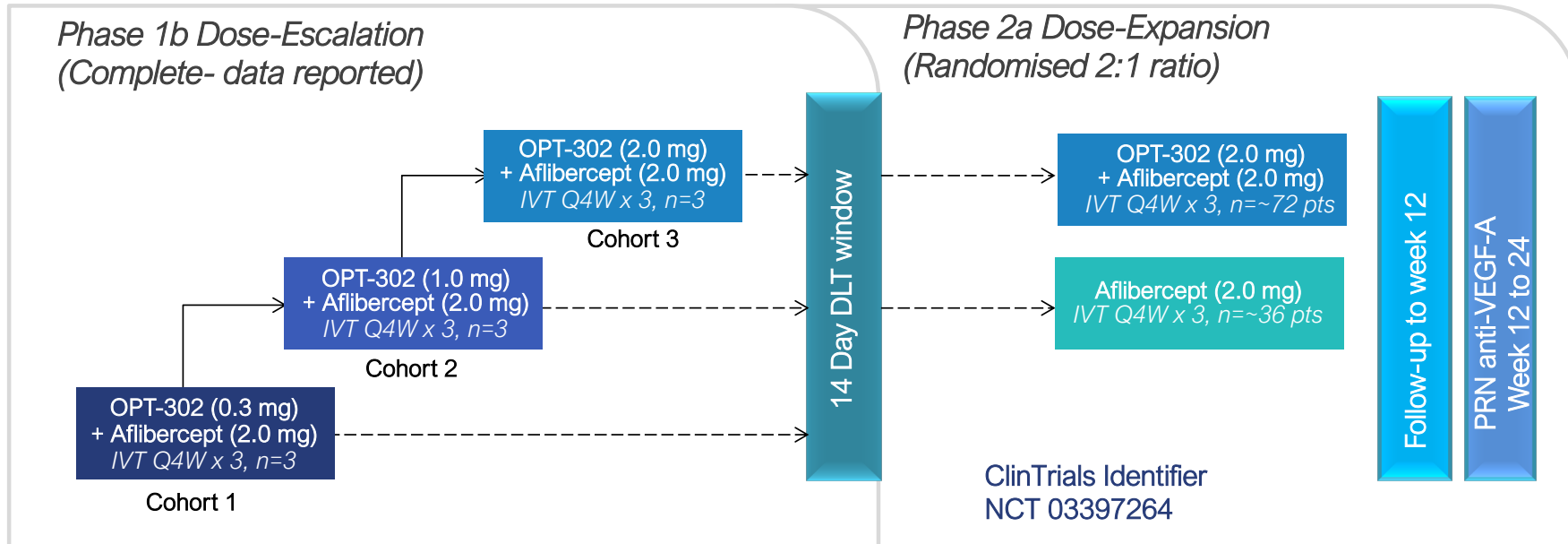
The Majority of DME Patients Sub-Optimally Respond to Current Therapies

- DRCR Protocol I evaluated response to anti-VEGF-A from baseline to 156 weeks
- Lucentis and sham injections every 4 weeks to week 12, then as needed
- At week 12:
 - 40% patients gained < 5 letters (mean -0.3) by week 12
 - > 60% patients gained < 10 letters of improvement in mean BCVA after 3 injections

Response Category (Mean Change BCVA BL to Wk 12)	Mean Change BCVA at Wk 12 in Response Category	# and % Eyes in Response Category at Wk 12
< 5 Letters	- 0.3 Letters	39.7% (135/340 eyes)
5 – 9 Letters	6.9 Letters	23.2% (79/340 eyes)
≥ 10 Letters	15.2 Letters	37% (126/340)



Phase 1b/2a Dose Escalation study of OPT-302 + Aflibercept in DME



Key Inclusion Criteria

- Age ≥ 18 years; centre-involving DME
- CST ≥ 335 μm*
- BCVA 73 – 24 ETDRS letters (20/40 – 20/320 Snellen)
- Prior exposure to anti-VEGF-A therapy with sub-optimal therapeutic response
 - ≥ 3 intravitreal injections
 - Last injection ≤ 6 wks prior to study day 1
 - Prior bevacizumab only allowed if switched to IVT aflibercept or ranibizumab prior to study

*CST as measured by Spectralis (Heidelberg) at screening, ≥ 320 μm for Cirrus.

Key Exclusion Criteria

- HbA1c ≥ 12%
- Uncontrolled hypertension ≥ 180 mmHg systolic or ≥ 110 mmHg diastolic
- Eyes needing PRP within 3 months of screening
- Concurrent / prior use of intravitreal injections of steroids within 4 months of study start
- Concurrent / prior use of dexamethasone or fluocinolone implant in study eye



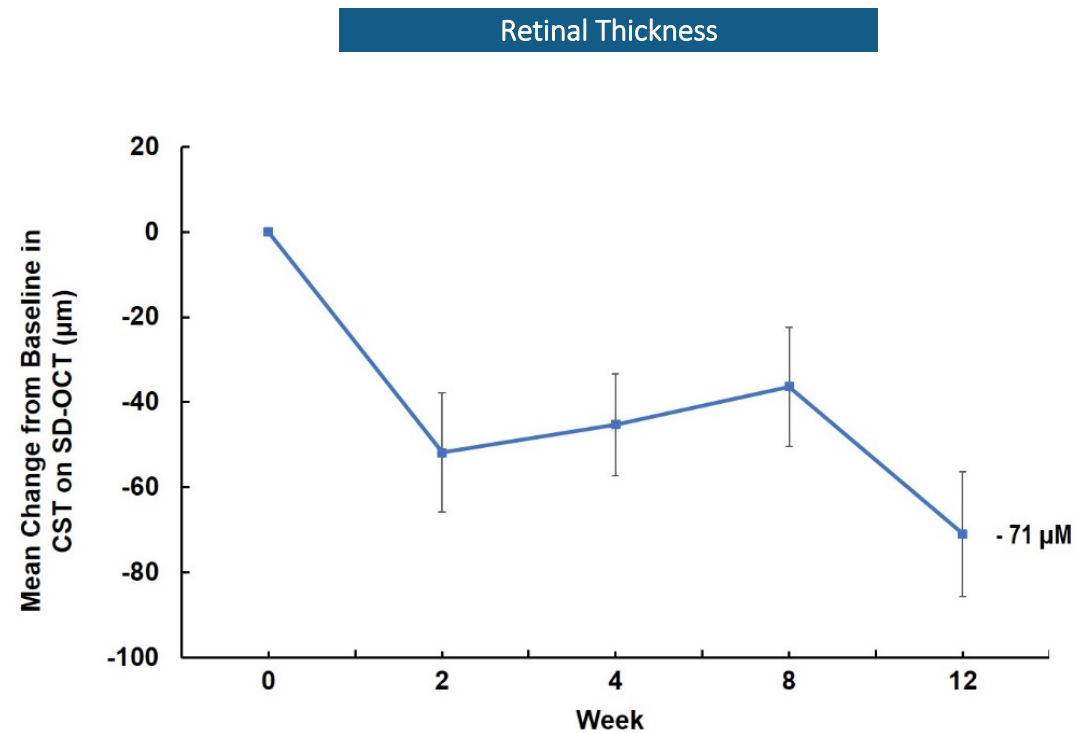
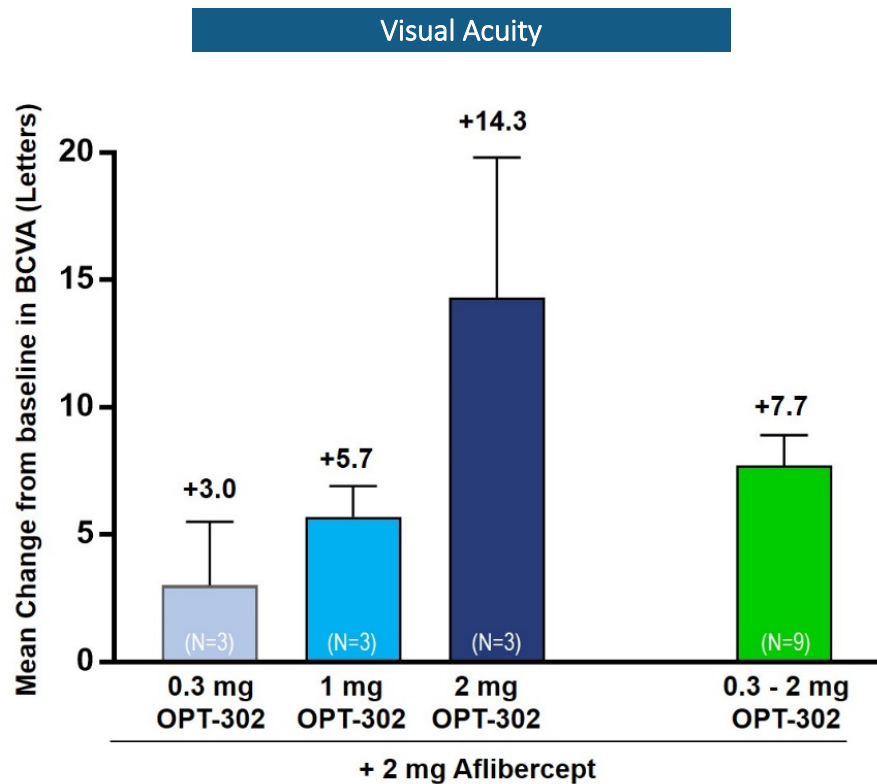
OPT-302 + aflibercept in DME: Phase 1b Safety Results

Selected Adverse Events: Ocular or Systemic	OPT-302 (0.3 mg) + Aflibercept (2.0 mg) (N=3)	OPT-302 (1 mg) + Aflibercept (2.0 mg) (N=3)	OPT-302 (2 mg) + Aflibercept (2.0 mg) (N=3)	Total Number of Subjects (N= 9)
Intraocular inflammation	0	0	0	0
Endophthalmitis	0	0	0	0
Retinal detachment	0	0	0	0
Vitreous hemorrhage	0	0	0	0
Hypertension	1*	0	0	1*
APTC events# (Non-Fatal Stroke, Myocardial Infarction, Vascular/Cardiac Death)				
Combined APTC Events	0	0	0	0
IOP, mmHg: Baseline, week 12; (change from baseline)	13.0; 15.7 (2.7)	17.3; 15.3 (-2.0)	16.7; 17.0 (0.3)	15.7; 16.0 (0.3)

- OPT-302 (0.3, 1 or 2 mg) + aflibercept (2 mg) administered by IVT injection (Baseline, Week 4, Week 8)
- OPT-302 intravitreal doses up to 2 mg in combination with aflibercept (2 mg)
 - No dose limiting toxicities (Maximum Tolerated Dose not reached)
 - No study drug related adverse events
- Ocular AEs in the study eye primarily related to IVT injection procedure (Mild/moderate, resolved)
- No clinically significant changes in IOP, ECG's, or vitals.
- OPT-302 was generally safe and well tolerated + aflibercept

OPT-302 has a favorable safety profile when administered with aflibercept (DME) expanding upon similar results when given as monotherapy or in combination with ranibizumab (wet AMD)

OPT-302 + aflibercept in DME: Gains in Visual Acuity at Week 12



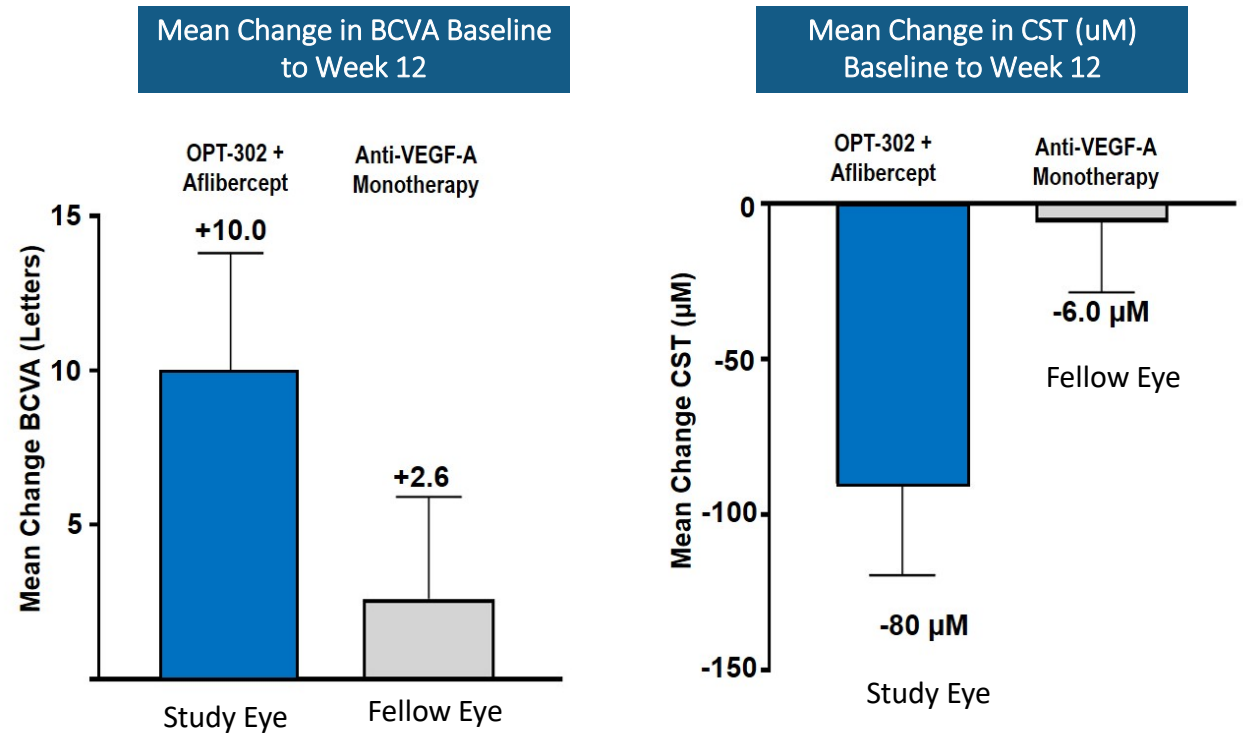
Dose Response Relationship and Reductions in Retinal Swelling in Phase 1b



Patients with Bilateral DME

Gains in Visual Acuity and Reductions in Retinal Thickness in OPT-302 + Aflibercept Treated Eyes

- 5/9 patients enrolled in the Phase 1b trial had bilateral DME (DME in both eyes)
- Study eyes:
 - Received 3 doses OPT-302 + aflibercept q4w
- Fellow eyes:
 - Received standard-of-care anti-VEGF-A therapy*



*Patients with bilateral disease and persistent DME in the fellow eye receiving anti-VEGF-A (ranibizumab or aflibercept) monotherapy
 Prior anti-VEGF-A therapy in Fellow Eyes BL to Wk 12: 3x Aflibercept, 3x Ranibizumab, 1x Ranibizumab, 4x Ranibizumab, 3x Aflibercept

Study Eye:
 0.3 – 2mg OPT-302 + 2 mg Aflibercept

Fellow Eye:
 Anti-VEGF-A Monotherapy*



Appendix – Key risks

Key Risks

This section outlines some of the key risks associated with an investment in Opthea, together with the risks relating to participation in the Placement. Opthea's business is subject to a number of risk factors both specific to its business and of a general nature which may impact on its future performance and forecasts.

This is not an exhaustive list of the relevant risks and the risks set out below are not presented in order of importance. The risks set out below and other risks not specifically referred to may in the future materially adversely affect the value of Opthea shares and their performance. Accordingly, no assurance or guarantee of future performance or profitability is given by Opthea in respect of Opthea shares.

Before subscribing for Opthea shares, prospective investors should carefully consider and evaluate Opthea and its business and whether Opthea shares are suitable to acquire having regard to their own investment objectives and financial circumstances and taking into consideration the material risk factors, as set out below. The risk factors set out below are not exhaustive, and many of them are outside the control of Opthea and its directors.

In deciding whether to participate in the Placement, you should read this presentation in its entirety and carefully consider the risks outlined in this section. Prospective investors should also consider publicly available information on Opthea, examine the full content of this presentation and consult their financial, tax and other professional advisers before making an investment decision.

Business Risks

Research and development activities	Opthea's future success is dependent on the performance of OPT-302 in clinical trials and whether it proves to be a safe and effective treatment. OPT-302 is an experimental product in clinical development and product commercialisation resulting in potential product sales and revenues is likely to be years away, and there is no guarantee that it will be successful. OPT-302 requires additional research and development, including ongoing clinical evaluation of safety and efficacy in clinical trials and regulatory approval prior to marketing authorisation. Drug development is associated with a high failure rate and until Opthea is able to provide further clinical evidence of OPT-302's ability to improve outcomes in patients with eye disease, the future success of the product developed remains speculative. Research and development risks include uncertainty of the outcome of results, difficulties or delays in development and general uncertainty around the scientific development of novel pharmaceutical products and any of these risks, if they were to materialize, could impact Opthea's progress and could have a material adverse effect on Opthea's future financial performance.
Clinical development	Clinical trials are inherently risky, and may prove unsuccessful or non-efficacious, impracticable or costly, which may impact profitability and commercial potential. Difficulties in enrolling patients in clinical trials may cause delays to clinical trial schedules. Failure, or negative or inconclusive results, can occur at many stages in development, and the results of earlier clinical trials are not necessarily predictive of future results. A critical trial may fail to meet its primary or secondary endpoints and as a result inhibit product development, prevent regulatory requirements being met for marketing approval and restrict successful commercialisation. In addition, data obtained from trials is susceptible to varying interpretations, and regulators may not interpret the data as favourably as Opthea, which may delay, limit or prevent regulatory approval. OPT-302 may fail to demonstrate a safety profile or sufficient evidence of therapeutic efficacy in future clinical studies to support its ongoing clinical development. In addition, the ability to recruit wet AMD patients into future clinical studies, or secure clinical locations in which to conduct those studies, may not occur at a sufficient rate to maintain program timelines.

Key Risks – Business Risks *(cont'd)*

Clinical data	Opthea maintains sensitive clinical data. Opthea may be subject to a cyber security attack or data breaches by employees or external parties with either permitted or unauthorised access. There is therefore a risk that sensitive data may be exposed to the public or be permanently lost. A cyber security attack or data breach may also have implications for Opthea’s obligations under any relevant data protection or privacy legislation. Failure to comply with such legislation or regulations can result in penalties, negative publicity and damage to its brand and reputation.
Information technology	Opthea relies on effective information technology, software, data centres and communication systems. There is a risk that these systems may be adversely affected by disruption, failure, service outages or data corruption that could occur as a result of computer viruses, “bugs” or “worms”, malware, internal or external misuse by websites, cyber-attacks or other disruptions including natural disasters, power outages or other similar events. Opthea may be significantly impacted by disruption to any of these systems or platforms.
Regulatory approval	Opthea operates within a highly regulated industry, relating to the manufacture, distribution and supply of pharmaceutical products. There is no guarantee that Opthea will obtain or maintain the required approvals, licenses and registrations from all relevant regulatory authorities in all jurisdictions in which it operates. Further clinical trials may be delayed and Opthea may incur further costs if the Food and Drug Administration (FDA) and other regulatory agencies observe deficiencies that require resolution or request additional studies be conducted in addition to those that are currently planned. Furthermore Opthea is exposed to the risk of changes to existing, or the introduction of new, government policies, regulations and legislation in all jurisdictions in which it operates. A failure to obtain or maintain any required approvals, licenses and registrations or any change in regulation may adversely affect Opthea’s ability to commercialise and manufacture its treatments.
Commercial risk	Opthea may, from time to time, consider acquisition, licensing, partnership or other corporate opportunities for Opthea’s development programs. There can be no assurance that any such acquisition, licensing, partnership or corporate opportunities can be concluded on terms that are, or are believed by Opthea to be, commercially acceptable. In the case of licensing and partnership opportunities, even if such terms are agreed there is a risk that the performance of distributors and the delivery of contracted outcomes by collaborators will not occur due to a range of unforeseen factors relating to environment, technology and market conditions. Future success will also depend on Opthea’s ability to achieve market acceptance and attract and retain customers, which includes convincing potential consumers and partners of the efficacy of Opthea’s products and Opthea’s ability to manufacture a sufficient quantity and quality of products at a satisfactory price.
Competition	The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change, in Australia, the United States and elsewhere, and there are no guarantees about Opthea’s ability to successfully compete. Opthea’s products may compete with existing alternative treatments that are already available to customers. In addition, a number of companies, both in Australia and internationally, are pursuing the development of products that target wet AMD and DME. Some of these companies may have, or may develop, technologies superior to Opthea’s own technology. Some competitors of Opthea may have substantially greater financial, technical and human resources than Opthea does, as well as broader product offerings and greater market and brand presence. Opthea’s services, expertise or products may be rendered obsolete or uneconomical or decrease in attractiveness or value by advances or entirely different approaches developed by either Opthea or its competitors.

Key Risks – Business Risks *(cont'd)*

Access to capital	The Opthea business model requires ongoing re-investment into clinical trials with no revenues currently contracted. As such, Opthea will continue to rely upon cash, raised through equity or debt, to fund the business as an on-going concern, including in respect of its Phase 3 clinical trials. Any unforeseen events which restrict the ability of Opthea to access capital is likely to affect Opthea's ability to become profitable in future.
Future capital requirements	Opthea's activities will require substantial expenditures. While Opthea expects that the proceeds of the Placement will provide funding for the activities set out in this presentation, proceeds of the Placement will not be sufficient to fully fund all anticipated costs of the Phase 3 clinical trials and meet Opthea's project development and working capital requirements, general and administrative expenditure and studies relating to future potential projects. If Opthea is unable to issue debt or equity to fund the costs of the Phase 3 clinical trials after the substantial exhaustion of the net proceeds of the Offer, there can be no assurances that Opthea will have sufficient capital resources for that purpose, or other purposes, or that it will be able to obtain additional resources on terms acceptable to Opthea or at all. Any additional equity financing may be dilutive to shareholders and any debt financing, if available, may involve restrictive covenants, which may limit Opthea's operations and business strategy. Opthea's failure to raise capital, if and when needed, could delay or suspend Opthea's business strategy and could have a material adverse effect on Opthea's activities. If additional funds are raised by issuing equity, this may result in additional dilution to the Shareholders. The pricing of future security issues will also depend on the results of Opthea's scientific research projects, market factors, demand for securities and the need for capital. If Opthea is unable to secure funding in the short term, there is a risk that Opthea will not be able to continue operating. The Placement is also not underwritten, therefore if the Placement does not proceed or does not raise sufficient funds to meet Opthea's future funding requirements, Opthea would need to find alternative financing to meet its future funding requirements. There is no guarantee that alternative funding could be sourced, either at all or on satisfactory terms and conditions.
Intellectual property	Securing rights in technology and patents is an integral part of securing potential product value in the outcomes of biotechnology research and development. Competition in retaining and sustaining protection of technology and the complex nature of technologies can lead to patent disputes. Opthea's success depends, in part, on its ability to obtain patents, maintain trade secret protection and operate without infringing the proprietary rights of third parties. Because the patent position of biotechnology companies can be highly uncertain and frequently involves complex legal and factual questions, neither the breadth of claims allowed in biotechnology patents nor their enforceability can be predicted. There can be no assurance that any patents which Opthea may own, access or control will afford Opthea commercially significant protection of its technology or its products or have commercial application, or that access to these patents will mean that Opthea will be free to commercialise its drug candidates. The granting of a patent does not guarantee that the rights of others are not infringed or that competitors will not develop technology or products to avoid Opthea's patented technology. Patenting strategies do not cover all countries which may lead to generic competition arising in those markets.
Manufacturing	Scale-up of OPT-302 manufacture to support Phase 3 clinical studies is underway but not complete. As such, there is a risk that scale-up may present technical difficulties. Technical difficulties could include the inability to generate material that meets regulatory specifications for human administration or the product yield from manufacturing batches may be insufficient to conduct the clinical studies as currently planned. Any unforeseen difficulty relating to manufacturing, including disruption to supply, shortages of input materials or changes to arrangements with, or capacity of, any third-party manufacturers, may negatively impact Opthea's ability to generate profit in the future.

Key Risks – Business Risks *(cont'd)*

Joint venture parties, agents, suppliers, distributors and contractors	<p>Opthea is unable to predict the risk of financial failure or default by a participant in any joint venture to which Opthea may become a party or the insolvency or managerial failure by any of the contractors used by Opthea in any of its activities or the insolvency or other managerial failure by any of the other service providers used by Opthea for any activity. Opthea may engage with various third parties to assist with different stages of the research and development process, including agents, suppliers, distributors and contractors, and there is no guarantee that these third parties will comply with their respective contractual obligations. This could adversely impact Opthea's progress and cause delays in or impede research or production, or result in cost increases</p>
Reliance on key personnel	<p>Opthea is reliant on key personnel it employs or engages. Loss of such personnel may have a material adverse impact on the performance of Opthea. In addition, recruiting qualified personnel is critical to Opthea's success. This includes attracting and retaining staff with sufficient skills to develop intellectual property. As Opthea's business grows and progresses to Phase 3 development, it will require additional key staff for clinical development operations as well as additional key financial and administrative personnel. There can be no assurance that Opthea will be successful in attracting and retaining qualified personnel. The loss of key personnel or the inability to attract suitably qualified additional personnel could have a material adverse effect on Opthea's financial performance.</p>
Insurance and uninsured risks	<p>Although Opthea maintains insurance to protect against certain risks in such amounts as it considers to be reasonable, its insurance will not cover all the potential risks associated with its operations and insurance coverage may not continue to be available, commercially acceptable, or may not be adequate to cover any resulting liability. It is not always possible to obtain insurance against all such risks and Opthea may decide not to insure against certain risks because of high premiums or other reasons.</p>
Product safety and efficacy	<p>Serious or unexpected health, safety or efficacy concerns with products may expose Opthea to reputational harm or reduced market acceptance of its products, and may lead to product recalls and/or product liability claims and resulting liability, and increased regulatory reporting. There can be no guarantee that unforeseen adverse events or manufacturing defects will not occur. Opthea may seek to obtain product liability insurance at the appropriate time in order to seek to minimise its liability to such claims, however there can be no assurance that adequate insurance coverage will be available at an acceptable cost. Any health, safety or efficacy concerns are likely to lead to reduced customer demand and impact on the potential future profitability of Opthea.</p>
Litigation	<p>In the ordinary course of conducting its business, Opthea is exposed to potential litigation and other proceedings, including through claims of breach of agreements, intellectual property infringement or in relation to employees (through personal injuries, occupational health and safety or otherwise). If such proceedings were brought against Opthea, it could incur considerable defence costs (even if successful), with the potential for damages and costs awards against Opthea if it were unsuccessful, which could have a significant adverse financial impact on Opthea's business. Changes in laws can heighten litigation risk (for example, antitrust and intellectual property). Circumstances may also arise in which Opthea, having received legal advice, considers that it is reasonable or necessary to initiate litigation or other proceedings, including for example to protect its intellectual property rights. There has been substantial litigation and other proceedings in the pharmaceutical industry, including class actions from purchasers and end users of pharmaceutical products.</p>

Key Risks – Offer and General Risks

Offer and General Risks

Share price fluctuations	The market price of Opthea shares will fluctuate due to various factors, many of which are non-specific to Opthea and beyond the control of Opthea, including recommendations by brokers and analysts, Australian and international general economic conditions, inflation rates, interest rates, changes in government, fiscal, monetary and regulatory policies, global geo-political events and hostilities and acts of terrorism, and investor perceptions. Fluctuations such as these may adversely affect the market price of Opthea shares. Neither Opthea nor the directors warrant the future performance of Opthea or any return on investment in Opthea.
Dilution risk	Shareholders will be diluted by the issue of New Shares under the. In addition, Opthea’s need to raise additional capital in the future in order to meet its operating or financing requirements, including by way of additional borrowings may change over time. Future equity raisings or equity funded acquisitions may dilute the holdings of particular shareholders to the extent that such shareholders do not subscribe for additional equity, or are otherwise not invited to subscribe for additional equity.
Economic risks	Opthea is exposed to economic factors in the ordinary course of business. A number of economic factors / conditions, both Australian and global, affect the performance of financial markets generally, which could affect the price at which Opthea shares trade on ASX. Among other things, adverse changes in macroeconomic conditions, including movements on international and domestic stock markets, interest rates, exchange rates, cost and availability of credit, general consumption and consumer spending, input costs, employment rates and industrial disruptions, inflation and inflationary expectations and overall economic conditions, economic cycles, trade tariffs and restrictions, investor sentiment, political events and levels of economic growth, both domestically and internationally, as well as government taxation, fiscal, monetary, regulatory and other policy changes may affect the demand for, and price of, Opthea shares and adversely impact Opthea’s business, financial position and operating results. Trading prices can be volatile and volatility can be caused by general market risks such as those that have been mentioned. New Shares in Opthea may trade at or below the price at which they commence trading on ASX including as a result of any of the factors that have been mentioned, and factors such as those mentioned may also affect the income, expenses and liquidity of Opthea. Additionally, the stock market can experience price and volume fluctuations that may be unrelated or disproportionate to the operating performance of Opthea.
Taxation	<p>Future changes in Australian taxation law, including changes in interpretation or application of the law by the courts or taxation authorities in Australia, may affect taxation treatment of an investment in Opthea shares, or the holding and disposal of those shares. Further, changes in tax law, or changes in the way tax law is expected to be interpreted, in the various jurisdictions in which Opthea operates, may impact the future tax liabilities of Opthea.</p> <p>Opthea projects that it will receive material cash refunds under the Research and Development Tax Incentive scheme (the “Scheme and R&D Tax Credits”) to offset the costs of its clinical programs and other qualifying expenditure, incurred both in Australia and overseas. The assumptions underlying the Company’s projected Scheme and R&D Tax Credits are based on actual amounts received for the 2019 financial year as a proportion of qualifying expenditure under the scheme. The Commonwealth Government and/or the Australian Taxation Office could change the rules of the regulatory regime with the effect that future amounts paid to Opthea as a proportion of its expenses could be materially lower than assumed in the Company’s projections. Any rule changes made that materially reduce the amount Opthea was able to claim under the scheme would have a material effect on the cash flows of the Company.</p> <p>Opthea believes that it is not a passive foreign investment company (PFIC) for U.S. federal income tax purposes for its current taxable year and it expects that it will likely not be a PFIC in the foreseeable future, although there can be no assurance in this regard and this determination depends on legal and factual considerations that cannot be predicted.</p>

Key Risks – Offer and General Risks *(cont'd)*

Accounting standards	<p>Opthea prepares its general purpose financial statements in accordance with Australian International Financial Reporting Standards (AIFRS) and the Corporations Act 2001 (Cth), which may differ significantly from the accounting standards applied by other companies (such as U.S. GAAP). Australian Accounting Standards are subject to amendment from time to time, and any such changes may impact on Opthea's statement of financial position or statement of financial performance.</p>
Forward-looking statements	<p>There can be no guarantee that the assumptions and contingencies on which the forward-looking statements, opinions and estimates are based will ultimately prove to be valid or accurate. The forward-looking statements, opinions and estimates included in this presentation depend on various factors, including known and unknown risks, many of which are outside the control of Opthea. Actual performance of Opthea may materially differ from expected performance.</p>
Dividends	<p>No assurances can be given in relation to the payment of future dividends. Future determinations as to the payment of dividends by Opthea will be at the discretion of Opthea and will depend upon the availability of profits, the operating results and financial conditions of Opthea, future capital requirements, covenants in relevant financing agreements, general business and financial conditions and other factors considered relevant by Opthea. No assurance can be given in relation to the level of tax deferral of future dividends. Tax deferred capacity will depend upon the amount of capital allowances available and other factors.</p>
Changes in applicable law and regulations	<p>Opthea will be subject to changes in laws, regulations and government policy which may affect its operations and/or financial performance. Such changes may impact income or operational expenditure. Opthea is also subject to changes in taxation regimes and Accounting Standards. There can be no assurance that such changes will not have a material adverse effect on Opthea's business, operational performance or financial results or returns to shareholders. As noted above under "Taxation", adverse changes to tax law may also reduce Opthea's capacity to claim research and incentive grants or rebates, thereby increasing expenses and reducing Opthea's assets.</p>
Cost inflation	<p>Higher than expected inflation rates generally, or specific to the biotechnology and pharmaceuticals industry in particular, could be expected to increase operating and development costs and potentially reduce the value of future project developments. While, in some cases, such cost increases might be offset by increased selling prices, there is no assurance that this would be possible or that Opthea will be in its production and supply phase of its business when this occurs.</p>

Appendix – Foreign Selling Restrictions

Foreign Selling Restrictions

Foreign selling restrictions

This document does not constitute an offer of New Shares of the Company in any jurisdiction in which it would be unlawful. In particular, this document may not be distributed to any person, and the New Shares may not be offered or sold, in any country outside Australia except to the extent permitted below.

New Zealand

This document is not a product disclosure statement or any other form of disclosure document under the Financial Markets Conduct Act 2013 (the "FMC Act"). This document has not been registered, filed with or approved by any New Zealand regulatory authority under the FMC Act. The New Shares are not being offered or sold in New Zealand (or allotted with a view to being offered for sale

in New Zealand) other than to a person who:

- is an investment business within the meaning of clause 37 of Schedule 1 of the FMC Act;
- meets the investment activity criteria specified in clause 38 of Schedule 1 of the FMC Act;
- is large within the meaning of clause 39 of Schedule 1 of the FMC Act;
- is a government agency within the meaning of clause 40 of Schedule 1 of the FMC Act; or
- is an eligible investor within the meaning of clause 41 of Schedule 1 of the FMC Act.

United Kingdom

Neither this document nor any other document relating to the offer has been delivered for approval to the Financial Conduct Authority in the United Kingdom and no prospectus (within the meaning of section 85 of the Financial Services and Markets Act 2000, as amended ("FSMA")) has been published or is intended to be published in respect of the New Shares.

This document is issued on a confidential basis to "qualified investors" (within the meaning of section 86(7) of the FSMA) in the United Kingdom, and the New Shares may not be offered or sold in the United Kingdom by means of this document, any accompanying letter or any other document, except in circumstances which do not require the publication of a prospectus pursuant to section 86(1) of the FSMA. This document should not be distributed, published or reproduced, in whole or in part, nor may its contents be disclosed by recipients to any other person in the United Kingdom.

Any invitation or inducement to engage in investment activity (within the meaning of section 21 of the FSMA) received in connection with the issue or sale of the New Shares has only been communicated or caused to be communicated and will only be communicated or caused to be communicated in the United Kingdom in circumstances in which section 21(1) of the FSMA does not apply to the Company.

In the United Kingdom, this document is being distributed only to, and is directed at, persons (i) who have professional experience in matters relating to investments falling within Article 19(5) (investment professionals) of the Financial Services and Markets Act 2000 (Financial Promotions) Order 2005 ("FPO"), (ii) who fall within the categories of persons referred to in Article 49(2)(a) to (d) (high net worth companies, unincorporated associations, etc.) of the FPO or (iii) to whom it may otherwise be lawfully communicated (together "relevant persons"). The investments to which this document relates are available only to, and any offer or agreement to purchase will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Foreign Selling Restrictions *(cont'd)*

United States

This document may not be distributed or released in the United States. This document does not constitute an offer to sell, or a solicitation of an offer to buy, securities in the United States or in any other jurisdiction in which such an offer would be illegal or impermissible. The New Shares have not been, and will not be, registered under the U.S. Securities Act or the securities laws of any state or other jurisdiction of the United States and may not be offered or sold, directly or indirectly, in the United States unless they have been registered under the U.S. Securities Act (which Opthea has no obligation or intention to do or procure) or are offered and sold in a transaction exempt from, or in a transaction not subject to, the registration requirements of the U.S. Securities Act and other applicable securities laws. Accordingly, the New Shares may only be offered and sold in the Placement outside the United States in “offshore transactions” (as defined in Rule 902(h) under Regulation S of the U.S. Securities Act (“Regulation S”)) in reliance on Regulation S.



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