Leading Therapeutic Innovation in Retinal Diseases

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

OPTHEA

Disclaimer

This presentation includes general background information about the activities of Opthea Limited (ABN 32 006 340 567) ('Opthea' or 'Company') and its affiliates and subsidiaries (together, the 'Opthea Group'). The information contained in this presentation is in summary form and does not purport to be complete.

This presentation contains forward-looking statements within the meaning of the U.S. federal securities laws that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements as predictions of future events. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law. Please refer to information, including risk factors, set forth in Opthea's filings with the U.S. Securities and Exchange Commission for key factors that could cause actual results to differ materially from those projected in the forward-looking statements contained herein.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

The information contained in this presentation does not constitute investment or financial product advice (nor taxation or legal advice) and is not intended to be used as the basis for making an investment decision. It does not take into account the investment objectives, financial situation, taxation position or needs of any particular investor, which should be considered when deciding if an investment is appropriate. You must consider your own investment objectives, financial situation and needs and conduct your own independent investigations and enquiries, including obtaining taxation, legal, financial or other professional advice in relation to the information contained in this presentation as appropriate to your jurisdiction. This presentation should not be relied upon by the Recipient in considering the merits of any particular transaction.

This presentation may contain trade marks and trade names of third parties, which are the property of their respective owners. Third party trademarks and trade names used in this presentation belong to the relevant owners and use is not intended to represent sponsorship, approval or association by or with any of the Opthea Group.

OPT-302 has the potential to revolutionize the treatment of wet AMD and improve and preserve vision for millions of patients

We are developing OPT-302, a first-in-class VEGF-C/D ‘trap’, to be used in combination with standard of care anti-VEGF-A therapies

- First and **only** retina asset with strong clinical evidence of **better visual outcomes** over anti-VEGF-A therapy for wet AMD, with well tolerated safety profile
- Currently available treatment options and those in development focus only on reducing burden of care, **OPT-302 is designed to transform patient outcomes by improving vision**
- OPT-302 expected to be **rapidly adopted** by patients, physicians and payers globally due to:
  - High unmet need
  - Established wet AMD market and clinical practice
  - Favorable physician and health system economics
- FDA granted **Fast-Track** designation based on superior Phase 2b results
- Pivotal Phase 3 trials ongoing, on-track for topline data 2H 2023 and **commercial launch 2024**
- OPT-302 represents a **multi-billion dollar** commercial opportunity
- **Long-term value** opportunity substantial:
  - Composition of Matter and Methods of Use Patents through 2034
  - Further opportunity for Patent Term Extension (PTE), Data and Market Exclusivity periods beyond 2034
  - Expansion in to DME, RVO and PCV represent blockbuster upside opportunity

OPTHEA

Opthea's Experienced Leadership Team

Management Team

Megan Baldwin, PhD
CEO & Managing Director (1)

- Joined Opthea in 2008 and has been Chief Executive Officer and Managing Director since February 2014
- **Selected Experience:** Over 20 years of experience focusing on angiogenesis and therapeutic strategies for cancer and ophthalmic indications; prior to Opthea, was employed at Genentech (now Roche) in the US in market planning and research roles. Holds a PhD in Medicine, having conducted doctoral studies on the biology of VEGF-C and VEGF-D.

Karen Adams
VP Finance & Company Secretary

- VP Finance & Company Secretary since April 2021
- **Selected Experience:** Directed financial operations at several ASX-Nasdaq listed companies. Formerly CFO of Victor Smorgon group and Director Finance Nexvet Biopharma and Financial Controller of Biota Pharmaceuticals, both companies having listed on the Nasdaq and subsequently been acquired.

Mike Gerometta, PhD
Head of CMC Development

- Head of Chemistry, Manufacturing and Controls Development since December 2008
- **Selected Experience:** Has over 30 years of experience in the Australian biotech industry, working with numerous contract manufacturing organizations overseas and locally in all facets of translational CMC from concept through to Phase 2 studies

Clare Price
Director of Clinical Development

- Director of Clinical Development since July 2016
- **Selected Experience:** Previously Director of Clinical Development at Commercial Eyes Pty Ltd., and Clinical Programme Director at Starpharma Holdings Ltd. Formerly held roles at SmithKline Beecham and GlaxoSmithKline with project management and clinical operations responsibilities.

Non-Executive Board Members

Jeremy Levin, DPhil, MB BChir
Chairman

- Appointed Chairman in October 2020
- **Selected Experience:** Has extensive experience in the global biopharma industry. Currently CEO, Chairman and Founder of Ovid Therapeutics. Formerly President & CEO of Teva Pharmaceutical Industries Ltd, and Senior Vice President of Strategy, Alliances & Transactions at Bristol Myers Squibb. Joined BMS from Novartis where he was Global Head of Strategic Alliances. Has served on the board of directors of various public and private companies, including Biocon Ltd, and is currently on the Board of Lundbeck.

Julia Haller, MD
Director

- Appointed in June 2021
- **Selected Experience:** Internationally recognized ophthalmologist and vitreoretinal surgeon. Ophthalmologist-in-Chief and Endowed Chair at Wills Eye Hospital in Philadelphia. Professor and Chair of the Department of Ophthalmology at the Sidney Kimmel Medical College at Thomas Jefferson University, and a director Bristol Myers Squibb. Previously a director of Celgen Corporation and Professor of Ophthalmology, Johns Hopkins University School of Medicine, The Wilmer Eye Institute. Dr Haller received a BA from Princeton, graduating magna cum laude, and completed her medical training at Harvard Medical School.

Michael Sistenich, MSc
Director, Chair Remuneration Committee

- Appointed in November 2015
- **Selected Experience:** Healthcare specialist in international investment management and investment banking. Previously led the Bell Potter team which advised the Company through a financing in 2014 and served as Director of international Equities and Head of Global Healthcare Investments at DWS, Deutsche Bank Frankfurt. Currently Chairman of Enlitic Inc. Long-standing capital market connections and experience in the global healthcare investment community.

Daniel Spiegelman, BA, MBA
Director, Chair Audit & Risk Committee

- Appointed in September 2020
- **Selected Experience:** Former Exec Vice President, CFO and member of the Board of Directors of Biomarin Pharmaceutical Inc. Has provided strategic financial management and insight to life sciences companies, and previously held roles at Genentech, including Treasurer, and CFO of CV Therapeutics. Currently serves as a director of several companies, including Myriad Genetics, Jiya Acquisitions Corp. and Spruce Bioscience.

Judith Robertson, BA, MBA
Director

- Appointed in June 2021
- **Selected Experience:** Commercial executive with track record of leading commercial organisations and launching multiple ophthalmic products. Previously Chief Commercial Officer of Aerie Pharmaceuticals, Vice President Immunology and Ophthalmology Global Commercial Strategy Leader at Johnson & Johnson and Opthalmology Global Business Franchise Head at Novartis (formerly Alcon). Has also held roles in sales and marketing at Novartis, Bristol Myers Squibb and Searle USA.

Lawrence Gozlan, BSc (Hons)
Director, Chair Nomination Committee

- Appointed in July 2020
- **Selected Experience:** Biotechnology investor and advisor. Life Sciences Investment Manager at Jagen Pty Ltd, an international private investment organization. Chief Investtment Officer and Founder of Scientia Capital providing investment advice for high net-worth individuals, family offices and institutional investors. Previously responsible for the largest biotechnology investment portfolio in Australia as the institutional biotechnology analyst at the Queensland Investment Corporation, QIC

OPTHEA

(1) Serves on the Board of Directors

Pipeline

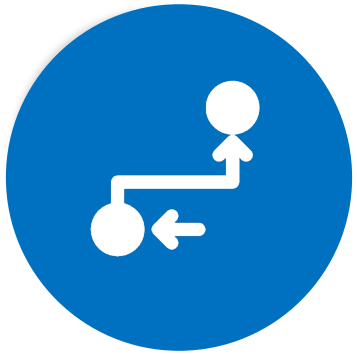
Product	Clinical Trials & Combination Agent(s)	Research/ Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Anticipated Milestone	Commercial Rights
Wet Age-Related Macular Degeneration (Wet AMD) *(Est. patients US and EU: 3.5 million)*								
OPT-302 Target:VEGF-C/D	**Completed Phase 2b:** Ranibizumab **Two Phase 3 trials:** Ranibizumab (ShORe), Aflibercept (COAST)						**March 2021:** Initiated two concurrent Phase 3 trials **2H 2023:** Phase 3 top-line data	OPTHEA *(Worldwide)*
Diabetic Macular Edema (DME) *(Est. patients Worldwide: 2 million)*								
OPT-302 Target:VEGF-C/D	**Phase 1b/2a:** Aflibercept						Company may choose to initiate study in DME	OPTHEA *(Worldwide)*
Co-Formulation (OPT-302 + VEGF-A Inhibitor) (Wet AMD) *(Est. patients US and EU: 3.5 million)*								
Co-Formulated OPT-302 + VEGF-A Inhibitor Target:VEGF-C/D & VEGF-A	**TBD**						**2022:** File IND (FDA)	OPTHEA *(Worldwide)*

OPTHEA

THE PROBLEM

The majority of wet AMD patients experience an incomplete response to VEGF-A inhibitors

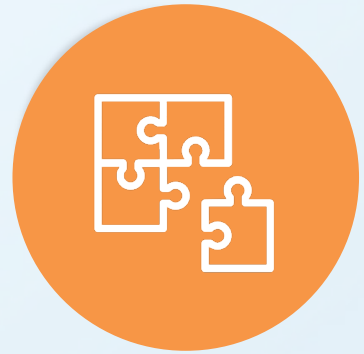
- 45% do not achieve meaningful vision gain, >60% have persistent fluid and 25% suffer further vision loss despite anti-VEGF-A treatment
- The majority fail to achieve 20/40 vision and most patients cannot resume routine daily activities such as driving or reading



THE CAUSE

Wet AMD is a multi-factorial disease and driven by more than just VEGF-A

- VEGF-C and VEGF-D activate validated wet AMD disease pathways, driving angiogenesis and vascular permeability
- VEGF-C and VEGF-D are elevated when VEGF-A is inhibited, which may contribute to suboptimal clinical responses to anti-VEGF-A treatments

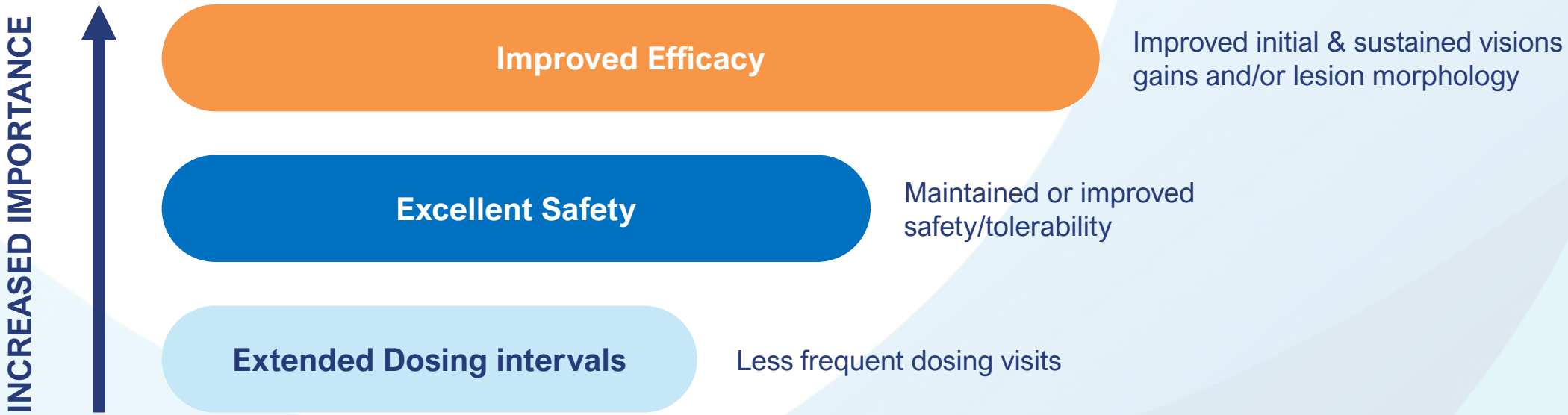


THE SOLUTION

OPT-302 has the potential to be the next **transformative** step in the treatment of wet AMD

- Strategies to improve clinical outcomes focussed on switching anti-VEGF-A, with limited or no further improvement
- OPT-302 is the most advanced asset targeting a novel mechanism of action with demonstrated evidence of improved visual outcomes

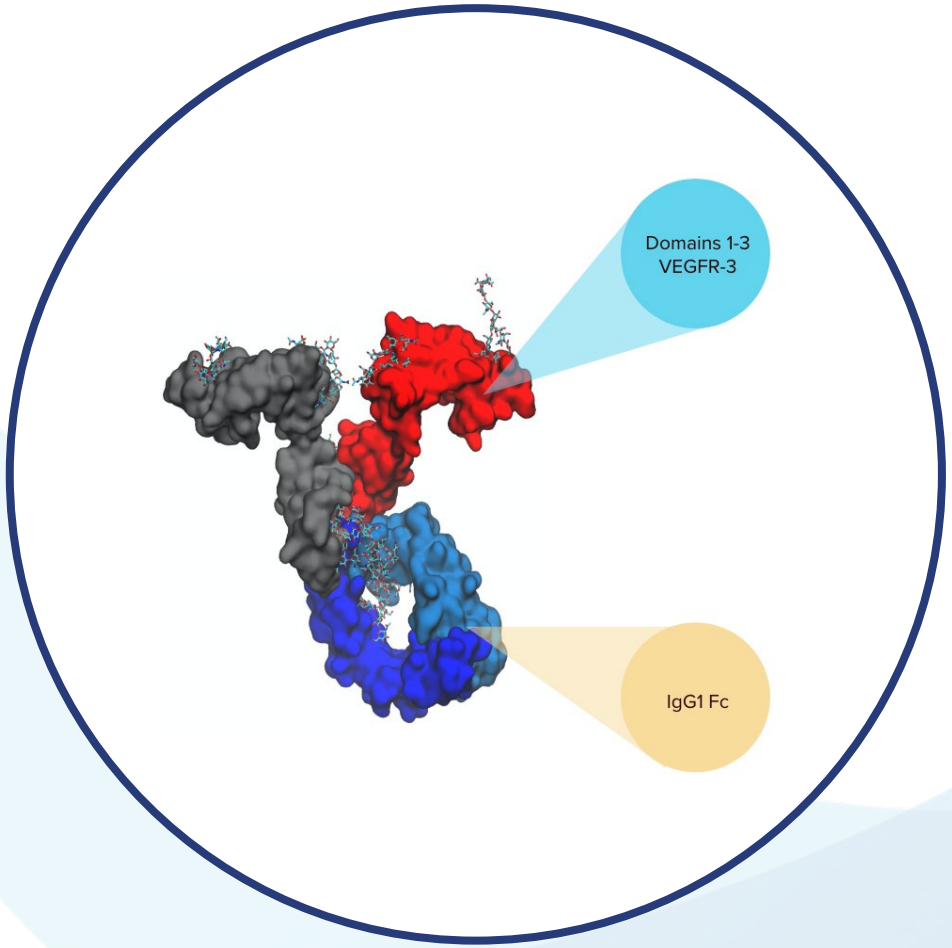
Improved EFFICACY is the #1 Unmet Medical Need in Wet AMD



OPTHEA

Boulanger-Scemama E, Querques G, About F, Puche, et al. Ranibizumab for exudative age-related macular degeneration: A five year study of adherence to follow-up in a real life setting. J Fr Ophtalmol. 2015 Sep;38(7):620–7.
Boyle J, Vukicevic M, Koklanis K, et al. Experiences of patients undergoing repeated intravitreal anti-vascular endothelial growth factor injections for neovascular age-related macular degeneration. Psychol Health Med. 2018 Feb;23(2):127–40.
Mueller S, Agostini H, Ehlken C, Bauer-Steinhusen U, Hasanbasic Z, Wilke T. Patient preferences in the treatment of neovascular age-related macular degeneration: A discrete choice experiment. Ophthalmology. 2016 Apr;123(4):876–83.
ClearView Commercial Assessment.

OPT-302 : A “Trap” Inhibitor of VEGF-C and VEGF-D

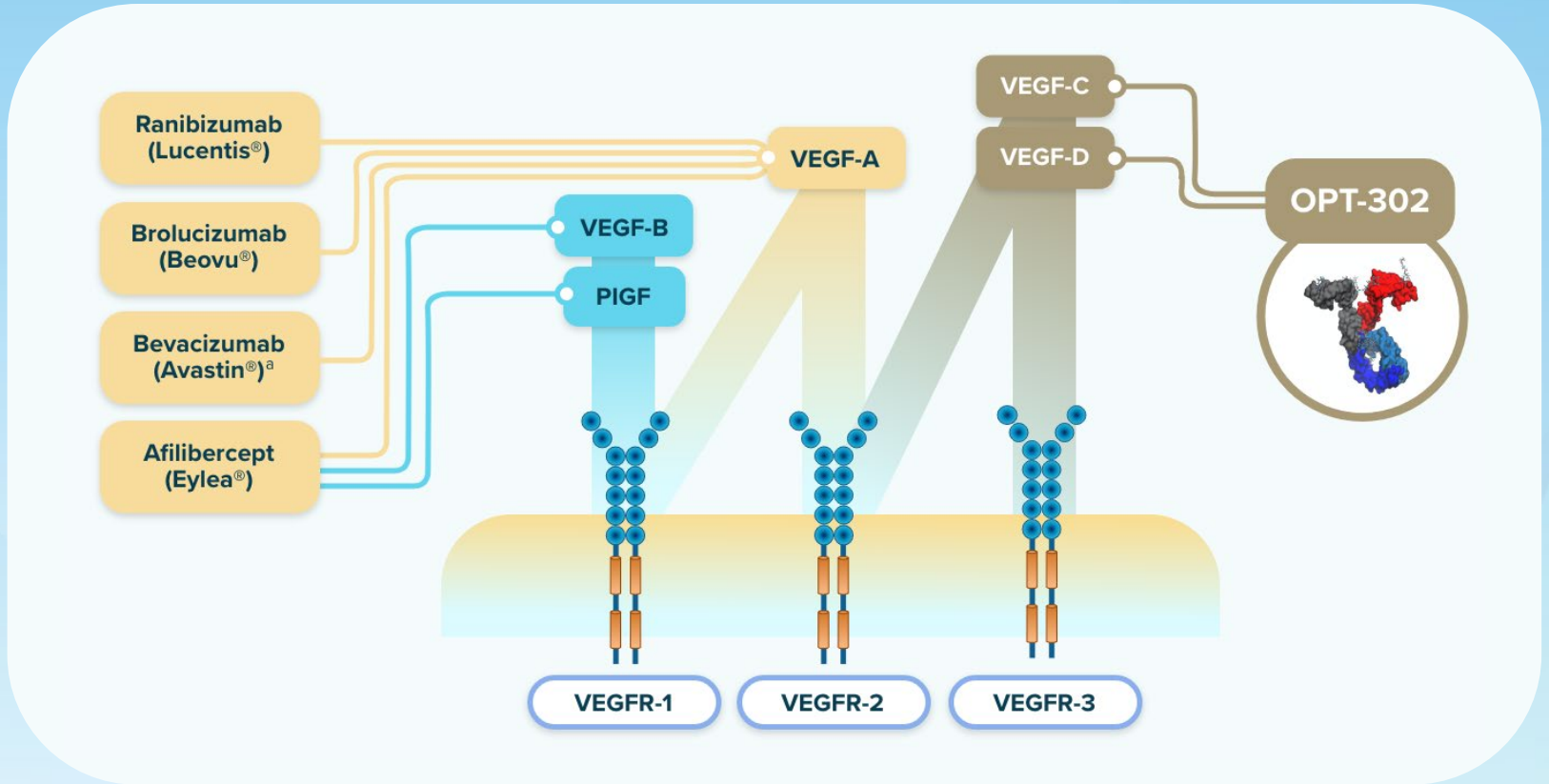


- A ‘trap' comprising the extracellular domains 1-3 of VEGFR-3 and the Fc fragment of IgG1
- Potent inhibitor of VEGF-C and VEGF-D
- 140 kDa
- Comparable ocular biodistribution and similar ocular PK to Eylea

OPT-302 has characteristics to ‘match’ extended dosing regimens and well tolerated safety profiles of SoC therapies

OPT-302 Combination Therapy Achieves Broad Blockade of the Validated Pathway in wet AMD

Used in combination with any VEGF-A inhibitor, OPT-302 **completely blocks** VEGFR-2 and VEGFR-3 signaling, inhibiting the most important pathways driving angiogenesis and vascular leakage



VEGF-A inhibition elevates VEGF-C and VEGF-D which can contribute to sub-optimal clinical efficacy of anti-VEGF-A treatments

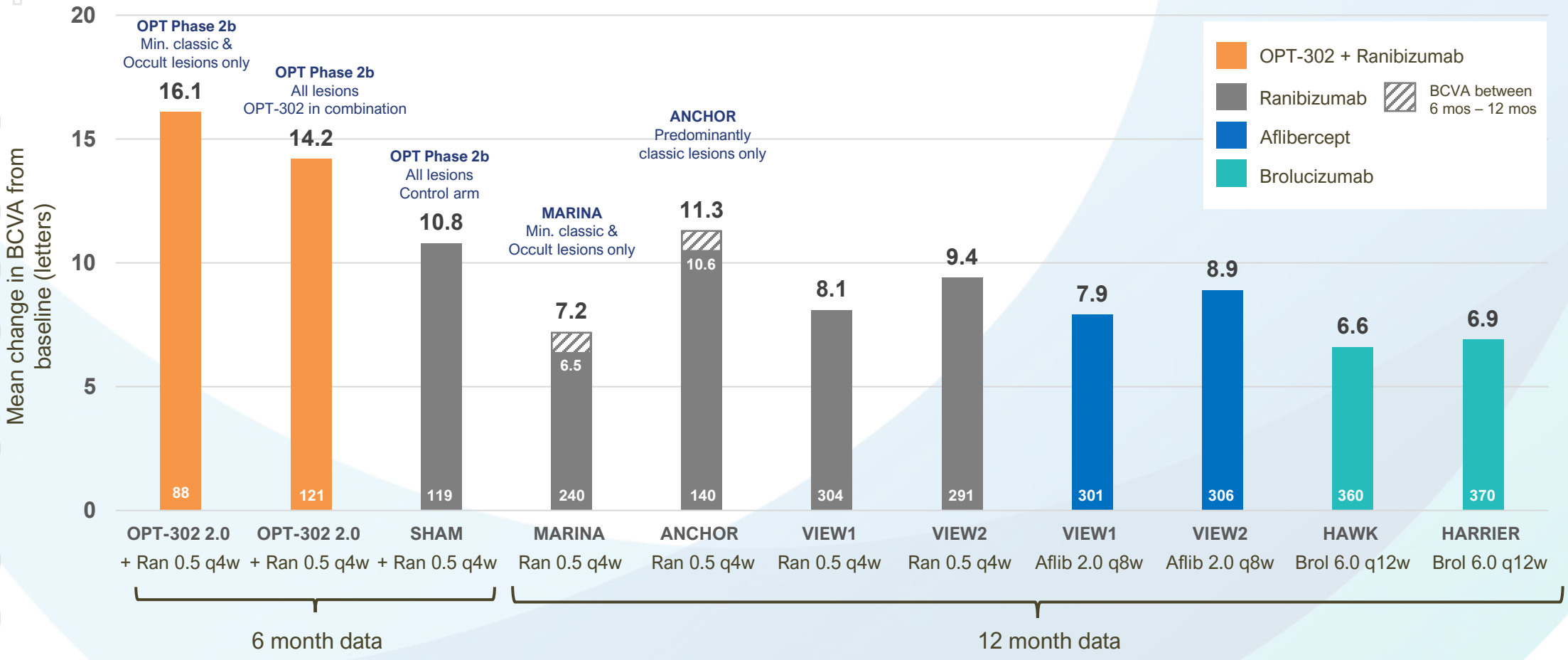
OPTHEA

[a] *Bevacizumab is used 'off-label' for the treatment of nAMD*

Comparison with Other Trials

Mean visual acuity higher vs previous VEGF-A inhibitor trials

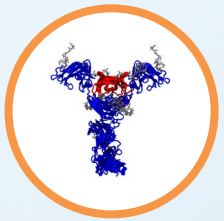
Efficacy at 6 months is typically maintained or greater at 12 months in Phase 3 trials with VEGF-A inhibitors



All trials shown, excluding Opthea's Phase 2b data, are Phase 3 registrational studies. 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; OPT-302 2.0, 2.0mg OPT-302; P2B, Phase 2b study 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

OPT-302 is the Next Transformational Step in Treatment for Retinal Diseases

There have been no new targeted therapies with novel mechanisms approved for wet AMD since the approval of the first VEGF-A inhibitor >15 years ago



New Mechanism of Action:

OPT-302 targets VEGF-C/D

Most advanced product in clinical development with demonstrated potential to **IMPROVE** patient visual outcomes

EYLEA® (aflibercept) Injection For Intravitreal Injection

Targets VEGF-A, VEGF-B, & PlGF

LUCENTIS® RANIBIZUMAB INJECTION

Off-label use AVASTIN® bevacizumab

Target all isoforms of VEGF-A

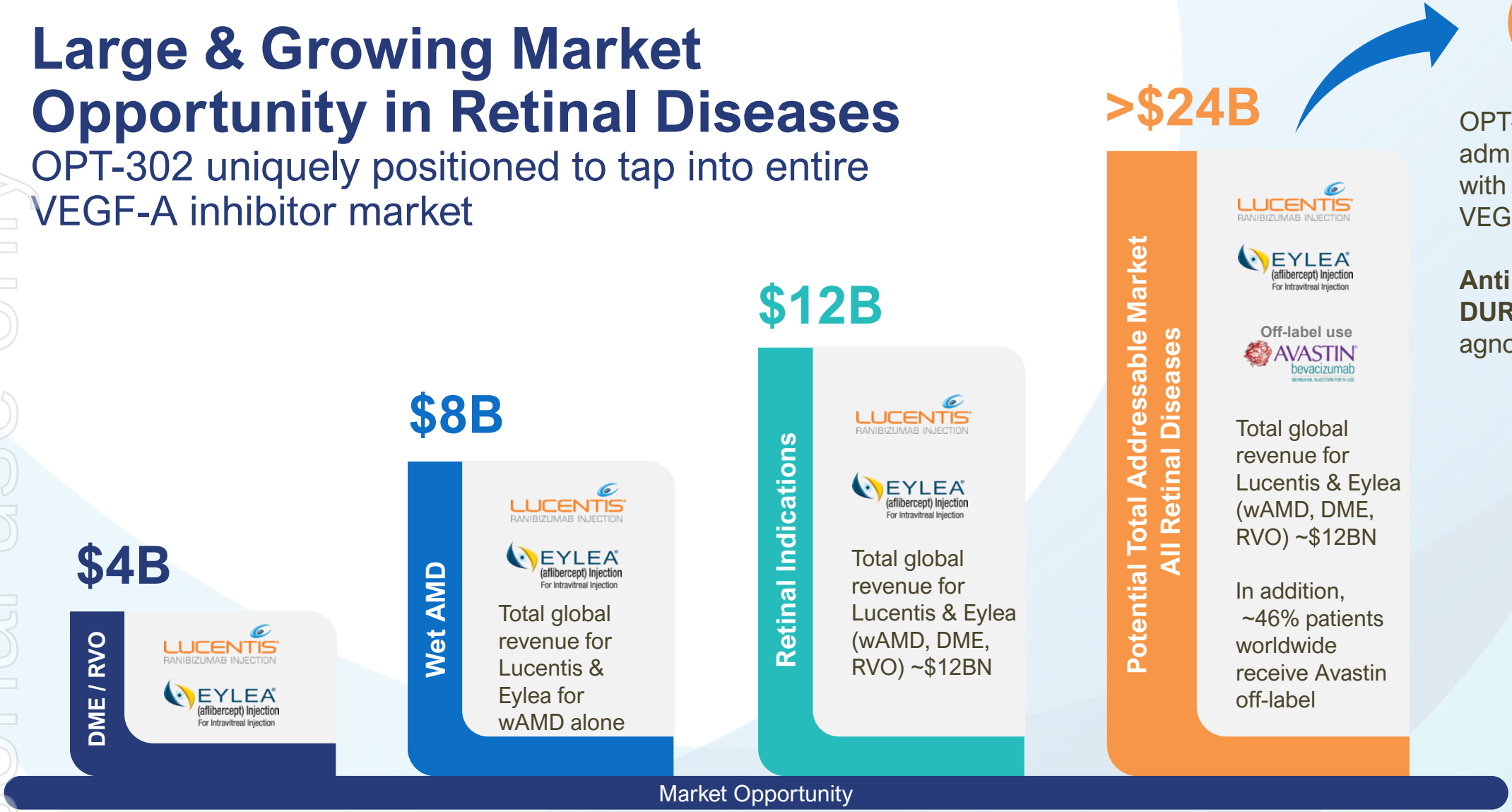
MACUGEN® PEGAPTANIB SODIUM INJECTION

Isoform-specific VEGF-A_{165} inhibition

OPTHEA

Large & Growing Market Opportunity in Retinal Diseases

OPT-302 uniquely positioned to tap into entire VEGF-A inhibitor market



OPT-302 to be administered with any anti-VEGF-A therapy:

Anti-VEGF-A & **DURABILITY** agnostic

OPTHEA

Strong OPT-302 Commercial Value Drivers

1 Large growing patient population
High unmet need
Large market opportunity

- 3.5 M wet AMD patients (US & EU)
- >45% of anti-VEGF A treated patients do not achieve meaningful vision gain
- $12B global market opportunity

2 Highly differentiated asset

- First and only VEGF-C/D 'trap'
- Only current therapy to have demonstrated superior visual outcomes over anti-VEGF–A therapy

3 Favorable competitive landscape

- No other asset with potential to **disrupt treatment paradigm on basis of EFFICACY** for wet AMD in near or long-term pipeline
- Biosimilars will accelerate OPT-302 uptake

4 Expedited regulatory pathway

- **Fast Track designation granted** for OPT-302 combination therapy for nAMD
- Offers earlier and expedited review opportunities

5 Commercially scalable

- 1500 centralized retina specialists in USA enables lean commercial organization
- 80 -100 sales reps anticipated (<150 total FTEs across commercial organization)

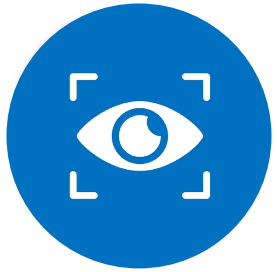
6 Financially attractive – short & long term

- Multi-billion dollar peak sales opportunity in USA and EU for wet AMD
- Additional multi-billion dollar peak sales opportunity in DME, RVO, and PCV
- Composition of Matter and Methods of Use Patents till 2034
- Further opportunity for Patent Term Extension (PTE), Data and Market Exclusivity periods beyond 2034

Strong OPT-302 Stakeholder Value Drivers

PATIENTS

- Superior gains in visual acuity over standard of care treatments meaningfully improve quality of life, independence and ability to continue routine daily activities such as driving and reading
- Negligible additional treatment burden
  - OPT-302 administered at the same anti-VEGF-A injection visit



RETINA SPECIALISTS

- Potential to maximise visual acuity and improve long-term outcomes for patients
- Seamlessly integrates into current anti-VEGF-A clinical practice
  - OPT-302 injected within minutes following anti-VEGF-A injection
  - Utilizes same diagnostics: OCT and Fluorescein Angiography
  - OPT-302 is agnostic to anti-VEGF–A treatment type and duration
- Advantageous clinic practice financials:
  - No increased staff, visits or diagnostics
  - Potential to increase revenue with OPT–302 injections and volume-based discounts

PAYERS

- Payers want better efficacy outcomes from retinal therapy
  - VEGF–A therapy represents a significant budget burden to all payers
  - Profound cost inefficiency considering limitations of anti-VEGF-A efficacy (>45% of anti-VEGF-A paid treatments are limited in efficacy)
- Payers unlikely to pay for longer durability or convenience; will reimburse for patient efficacy and value to the healthcare system
- Better clinical outcomes represent better health economics
- Biosimilars will increase health cost effectiveness for anti-VEGF–A and OPT–302 sequential IVT injections

Clinical Data:

Phase 1/2a trial in treatment naïve and prior treated wet AMD patients (n=51)

Phase 2b randomized, controlled, double-masked & statistically powered wet AMD trial (n=366)

Phase 1b/2a trial in prior-treated DME patients

OPT-302 Combination Therapy – Clinical Program

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

Now Recruiting

ShORe
Phase 3
wet AMD
(n=990)

Comparator

Ranibizumab
once every month

Standard Dosing	Extended Dosing
OPT-302 *once every month*	OPT-302 *once every 2 months after 3 monthly doses*
Monthly Dosing	Every Two Months Dosing

Treatment naïve Patients

COAST
Phase 3
wet AMD
(n=990)

Comparator

Aflibercept
once every 2 months after 3 monthly doses

Standard Dosing	Extended Dosing
OPT-302 *once every month*	OPT-302 *once every 2 months after 3 monthly doses*
Monthly Dosing	Every Two Months Dosing

Treatment naïve Patients

OPTHEA

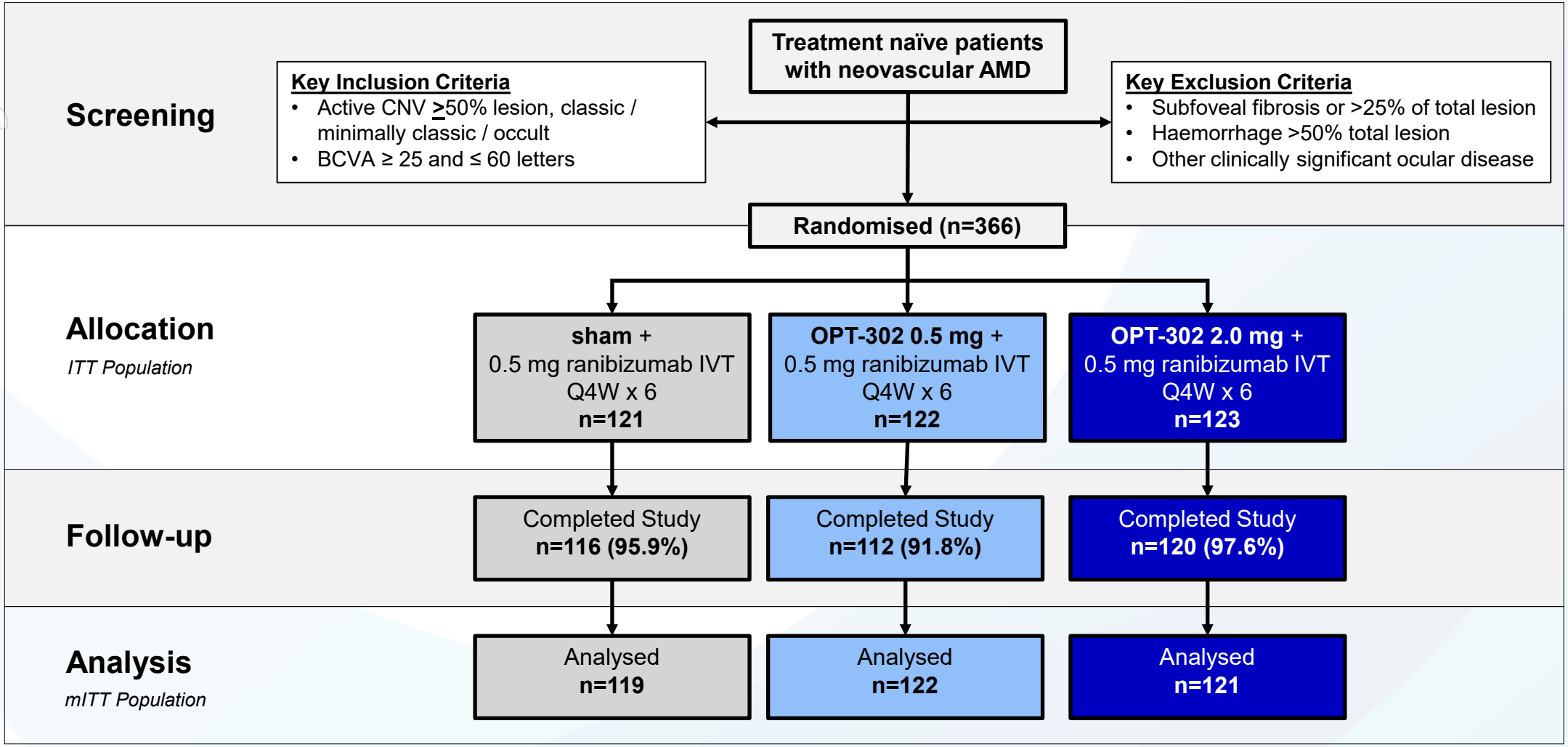
ShORe and COAST Phase 3 pivotal trials incorporate key learnings from our Phase 2b clinical trial in wet AMD patients which demonstrated superior vision outcomes following OPT-302 combination therapy, supporting a high level of confidence in our OPT-302 development program.

Phase 2b

A multicenter, randomized, double-masked, sham controlled study of intravitreal OPT-302 in combination with ranibizumab, in participants with neovascular (wet) AMD

Conducted at 109 sites across 10 countries: US, EU, Israel
OPT-302-1002; NCT ClinicalTrials.gov Identifier: NCT03345082

Study 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

OPTHEA

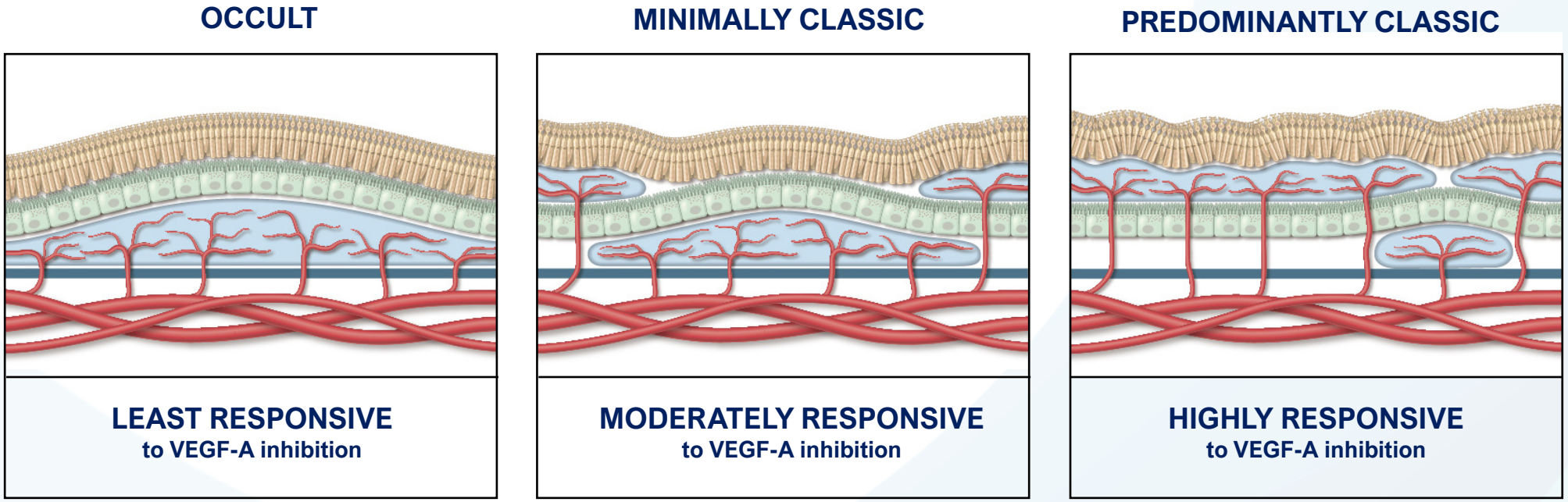
Study Demographics and Baseline Characteristics

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) - 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

Neovascular (wet) AMD Lesion Types

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



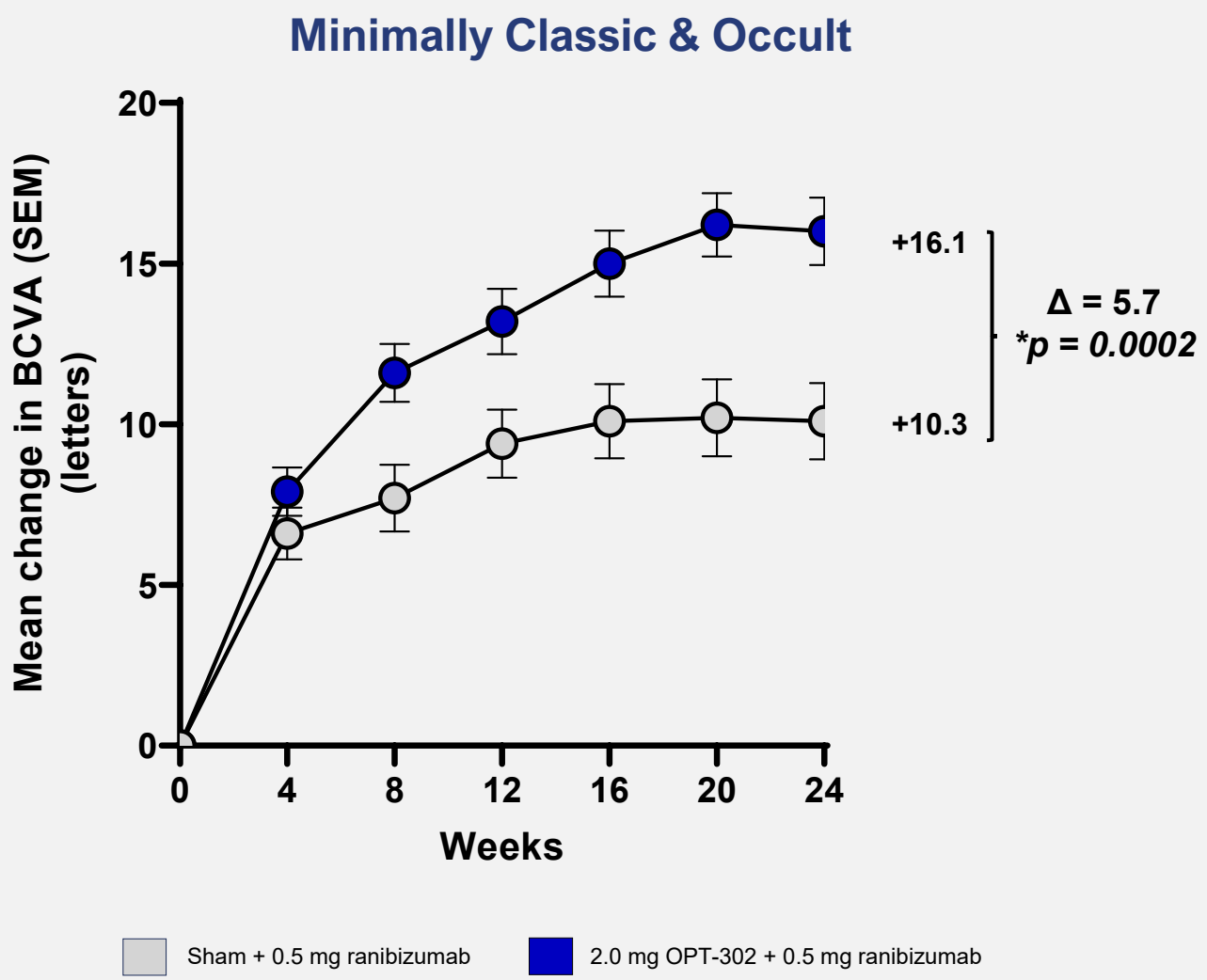
A majority of wet AMD patients, 65-80% of the real-world population, have occult and minimally classic lesions

Best Responders:

Minimally Classic & Occult lesions
(RAP Absent)

Achieved greatest vision benefit

Represents primary analysis population in OPT-302 phase 3 program



OPTHEA

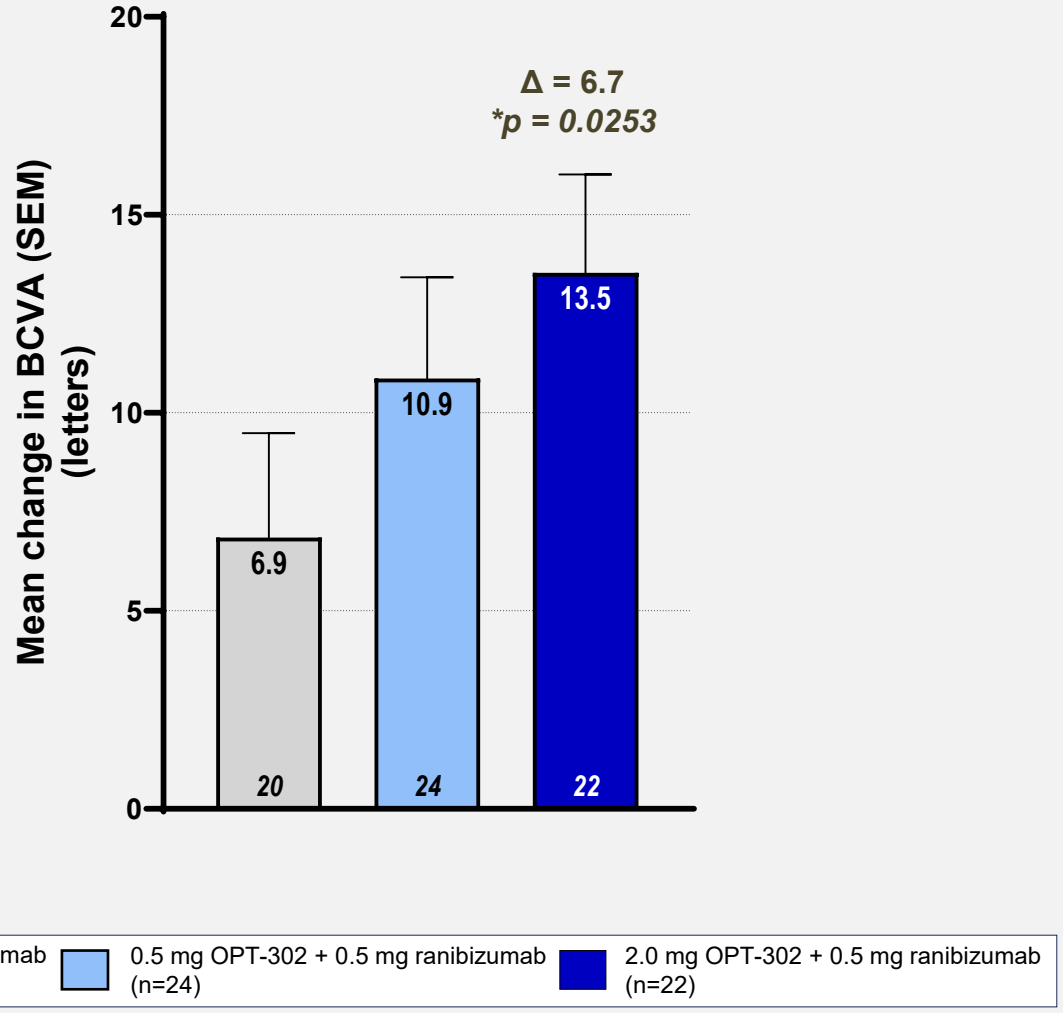
* Unadjusted p-value

Polypoidal Choroidal Vasculopathy (PCV)

PCV is a difficult-to-treat wet AMD subtype, with large unmet need

OPT-302 combination therapy has demonstrated potential to improve vision outcomes for patients with PCV

- **PCV is highly prevalent in Asian populations (up to ~60%)**
- **Described as the most prevalent form of wet AMD worldwide**



OPTHEA

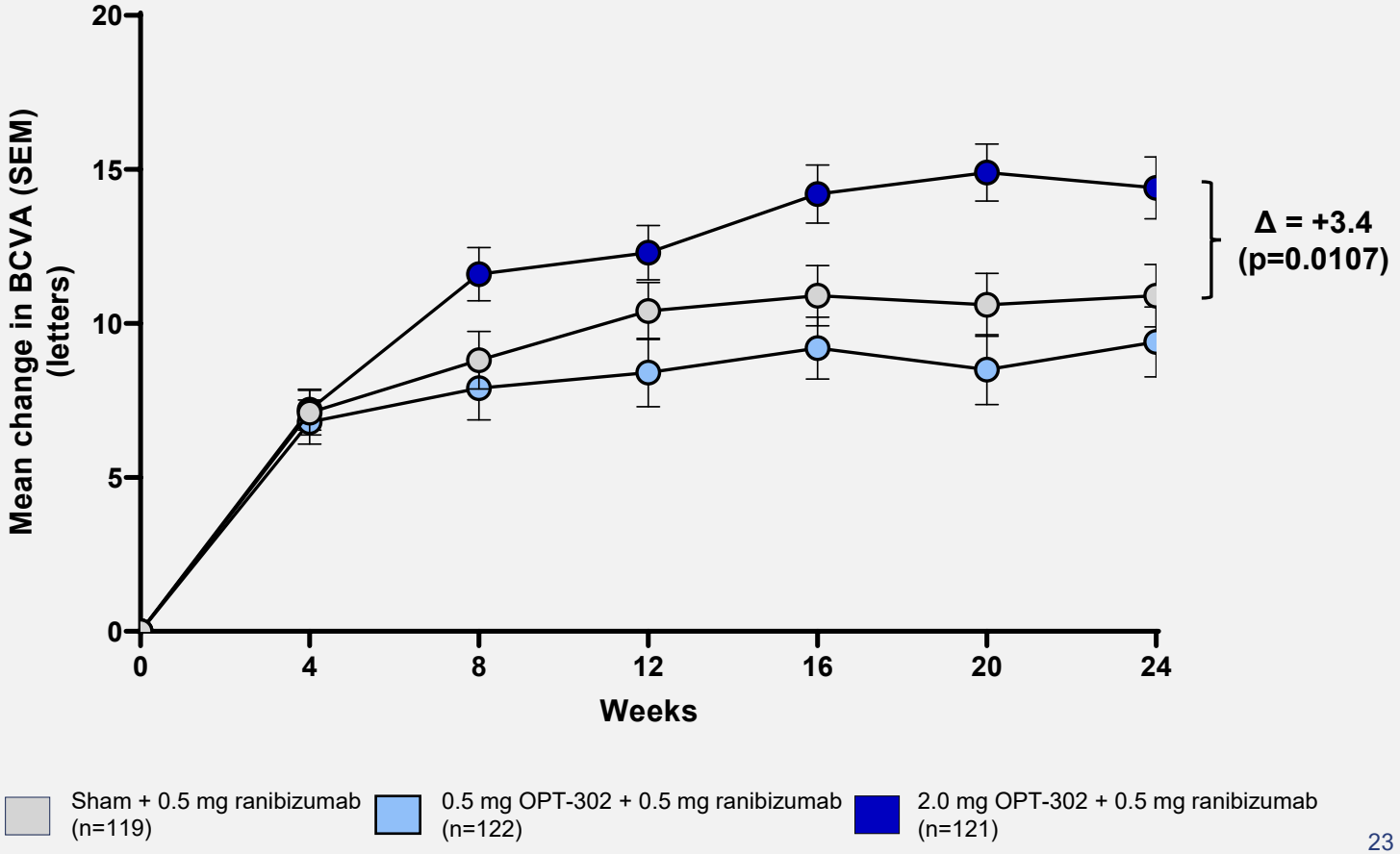
* Unadjusted p-value

OPT-302 (2.0 mg) Combination Therapy:

Superiority in Visual Acuity over Ranibizumab

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

Secondary Endpoints Supportive of Visual Acuity Improvement

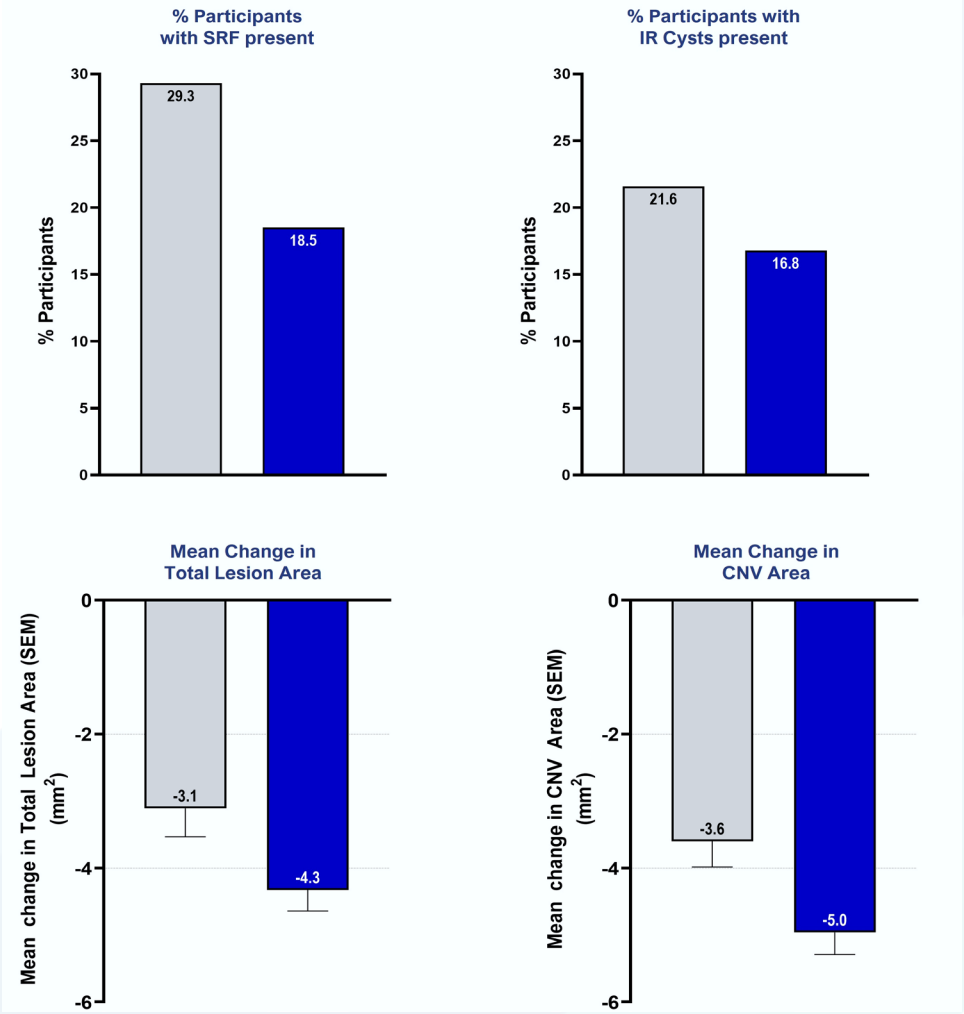
Vision:

- ✓ More patients gained ≥ 15, ≥10 and ≥5 letters of vision
- ✓ Fewer patients lost vision

Retinal anatomical improvements:

Greater reductions in:

- ✓ Retinal thickness
- ✓ Subretinal fluid
- ✓ Intraretinal fluid
- ✓ Lesion size
- ✓ Neovascular area



Safety

OPT-302 well-tolerated with very low incidence of ocular inflammation, comparable to SoC therapy

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 (TEAEs)	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 – Severe[2]	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 inflammation[4] – Study Eye	2[5,6] (1.7%)	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[7] (0.8%)	0 (0.0%)	0 (0.0%)
Any APTC event	0 (0.0%)	1[8] (0.8%)	0 (0.0%)
Deaths	2[9] (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] *Transient anterior chamber cell (trace 1-4 cells)*

[6] *Not reported as a TEAE*

[7] *Squamous cell carcinoma of the lung diagnosed shortly after Baseline visit*

[8] *Non-fatal myocardial infarction*

[9] *Pneumonia (n=1), infective endocarditis (n=1)*

Conclusions

OPT-302 Phase 2b wet AMD Trial

Primary endpoint achieved

Phase 2b trial met primary endpoint

- ✓ OPT-302 (2.0 mg) combination therapy demonstrated superiority in visual acuity over ranibizumab + sham
- ✓ Additional **+5.7 letter gain** observed in high responder subgroup (minimally classic & occult lesions, RAP absent, >70% study population), **represents Phase 3 primary analysis population**
- ✓ Additional +6.7 letter gain (p=0.025)* in PCV lesions, a difficult-to-treat wet AMD subtype, predominant in Asian populations, with large unmet need
- ✓ Additional +3.4 letter gain (p=0.0107) in total patient population
- ✓ High performing ranibizumab control arm

Secondary outcomes were supportive of the primary endpoint

Greater vision gains observed in minimally classic/occult lesions

Favorable tolerability profile similar to ranibizumab alone

- ✓ Promising treatment option for wet AMD suitable for Phase 3

OPTHEA

Phase 3 Pivotal Trials

Two concurrent, randomized, controlled, 3-arm Phase 3 studies investigating OPT-302 administered every four-weeks and every-eight weeks in combination with standard of care anti-VEGF-A therapy:

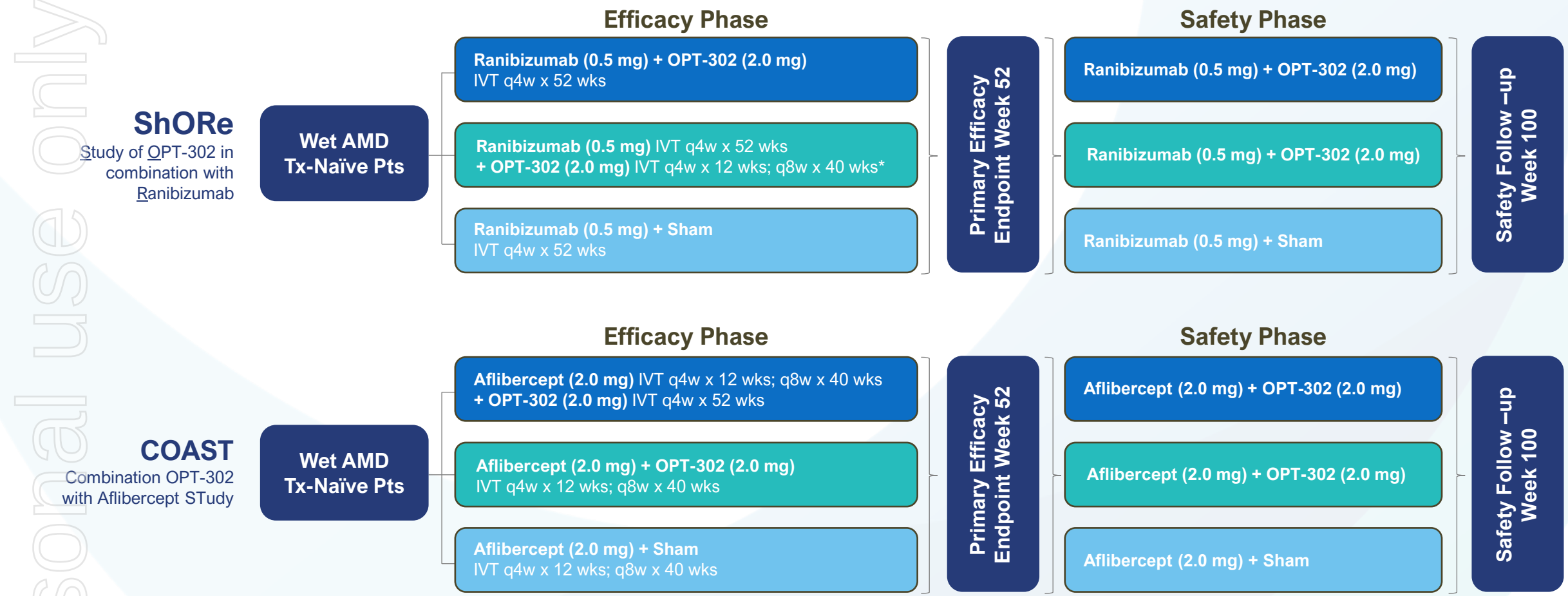
ShORe: Study of OPT-302 in combination with Ranibizumab (Study OPT-302-1004)

COAST: Combination OPT-302 with Aflibercept STudy (Study OPT-302-1005)

OPT-302 Phase 3 Pivotal Program

Topline primary data analysis 2H CY 2023

Opthea intends to submit Biologics License and Marketing Authorization Applications 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 study
- **Primary Objective:** Mean change from Baseline in BCVA at Wk 52

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

Opthea's Phase 3 Program is Optimised for Success

We know the patients which respond best

- Patients with minimally classic & occult lesions are the majority (~80%) of the wet AMD population

Primary Analysis will be first conducted in the Minimally Classic/Occult population

- Maximises opportunity to demonstrate most compelling vision benefit
- In Phase 2b, +5.7 letters superior benefit of OPT-302 combination therapy compared to Lucentis® alone

Our Phase 3 trials are designed to maximise the commercial opportunity

- Efficacy assessed in minimally classic/occult, followed by 'all-comer' total patient population
- OPT-302 investigated in combination with two standard of care treatments respectively

OPT-302 positioned for use in combination with any VEGF-A inhibitor

Investigates OPT-302 standard and extended dosing regimens:

- Analysis of efficacy on q4w and q8w dosing regimens provides insight into OPT-302 durability

Meetings to discuss Phase 3 design and analysis plan completed with US (FDA) and European (EMA) regulatory agencies

OPT-302: The potential to revolutionize the treatment of wet AMD and improve and preserve vision

1 Market Background

- Large treated (80%) wet AMD market (2.7M patients[#]) in a US$12B dollar anti-VEGF-A category
- Standard of Care is anti–VEGF-A injections once per month or every two months by intravitreal delivery

2 High Unmet Need

- Highest unmet need in wet AMD is EFFICACY, **to improve visual outcomes**
- >45% do not achieve meaningful vision gain, >60% have persistent fluid and 25% suffer further vision loss despite anti-VEGF-A treatment
- Current innovation is focused on durability rather than improving visual outcomes

3 OPT-302: first in class VEGF-C/D 'trap'

- When combined with anti-VEGF–A, OPT-302 broadly shuts down the VEGF/VEGFR pathways driving angiogenesis and vascular leakage
- **Only** current therapy demonstrating **superior visual outcomes** over anti-VEGF–A, with comparable safety
- Phase 2b results demonstrate visual acuity gains over standard of care:
  - Additional +5.7 letter gain (p=0.0002)* in minimally classic and occult lesion patients (80% of patient population)
  - Additional +6.7 letter gain (p=0.025)* in PCV lesions, a difficult-to-treat wet AMD subtype, predominant in Asian populations, with large unmet need
  - Additional +3.4 letter gain (p=0.0107) in total patient population
  - **FDA Fast Track** status granted based on Phase 2b results
- Two global pivotal Phase 3 trials, ShORe & COAST, currently recruiting, topline data second half calendar year 2023

4 Launch

- USA launch 2024; EU, Japan, and ROW to follow
- Compelling patient, physician and payer value propositions will propel acceptance, adoption and uptake
- Only VEGF-C/D 'trap', no viable threat in competitive pipelines

5 Financials

- Multi-billion dollar commercial opportunity in USA and in EU for wet AMD alone
- Additional indications DME, RVO, polypoidal (PCV) wet AMD represent blockbuster upside opportunity
- Strong Composition of Matter and Methods of Use patents till 2034
- Further opportunity for Patent Term Extension (PTE), Data and Market Exclusivity periods beyond 2034

OPTHEA

*[#] USA & EU; * Unadjusted p-value*

Megan Baldwin, PhD
CEO & Managing Director
Opthea Limited
Level 4, 650 Chapel Street
South Yarra 3141
Victoria Australia
P: +61 9826 0399 M: +61 447 788 674 E: megan.baldwin@opthea.com