#### UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

#### FORM 6-K

REPORT OF FOREIGN ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 OF THE SECURITIES EXCHANGE ACT OF 1934

For the month of April 2024

Commission File No. 001-39621

### **OPTHEA LIMITED**

(Translation of registrant's name into English)

Level 4

650 Chapel Street South Yarra, Victoria, 3141 Australia (Address of registrant's principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F. Form 20-F  $\boxtimes$  Form 40-F  $\square$ 

Exhibit	Description
99.1	Press Release - Opthea Corporate Presentation - April 2024

#### **SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereto duly authorized.

#### **OPTHEA LIMITED** (Registrant)

By: /s/ Frederic Guerard

Name: Frederic Guerard

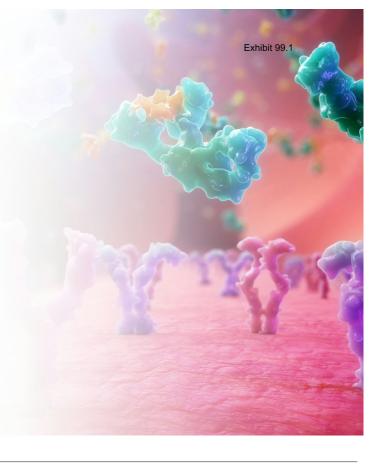
Title: Chief Executive Officer

Date: 04/05/2024



### Transforming Patient Outcomes with Superior Vision Gains

Corporate Presentation | April 2024 NASDAQ (OPT); ASX (OPT.AX)



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"). This presentation is current as of April 3, 2024 (unless otherwise stated herein). The information contained in this presentation is in summary form and does not purport to be complete or to contain all material information about the Opthea Group which a prospective investor or purchaser may require in evaluating a possible investment in Opthea or acquisition of securities in Opthea. The information in this presentation remains subject to change without notice. No member of the Opthea Group or any director, officer, employee, adviser, agent or representative of any member of the Opthea Group (each an Opthea Party and together, the Opthea Parties) has any obligation to update or correct this presentation.

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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 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.

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

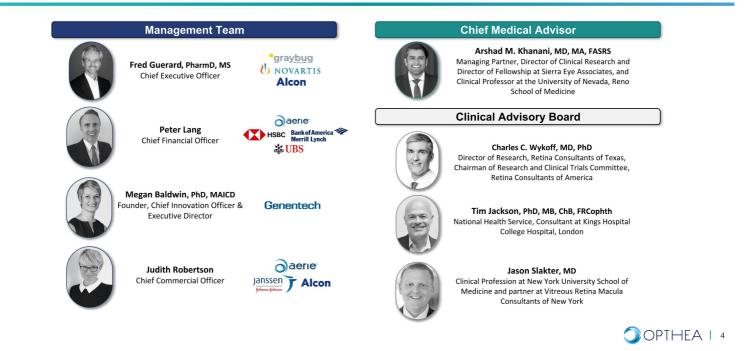
Addressing High Unmet Need	<ul> <li>Wet age-related macular degeneration (wet AMD) is the leading cause of vision loss in the elderly, impacting ~3.5 million patients in the US and Europe, despite wide use of anti-VEGF-A standard of care</li> </ul>
Proprietary Technology	<ul> <li>First-in-class VEGF-C/D TRAP intended for combination with standard of care anti-VEGF-A therapies</li> <li>Composition of Matter and Methods of Use Patents through 2034; opportunities to extend beyond 2034*</li> </ul>
Superior Lead Asset	<ul> <li>Phase 2b demonstrated superiority in combination with SOC therapy, with well tolerated safety profile</li> <li>Sozinibercept has the potential to improve vision for millions of patients with wet AMD</li> </ul>
Two Large Pivotal Trials Ongoing	<ul> <li>COAST enrollment complete as of Feb 2024; ShORe estimated 2Q CY2024 (96% enrolled as of 3 April 2024)</li> <li>Topline data from both trials expected mid-CY 2025</li> </ul>
Substantial Market Opportunity	<ul> <li>Multibillion dollar commercial opportunity in a growing market with an established clinical practice</li> <li>Sozinibercept developed for use in combination with any anti-VEGF-A; not competing with any approved therapy</li> </ul>

MOA – Mechanism of Action; SOC – Standard of care \*Potential for Patent Term Extensions & Data and Market Exclusivity (12 Years for Biologic)



### Experienced Leadership Team

Expertise and Track Record to Make a Positive Impact on the Retinal Community



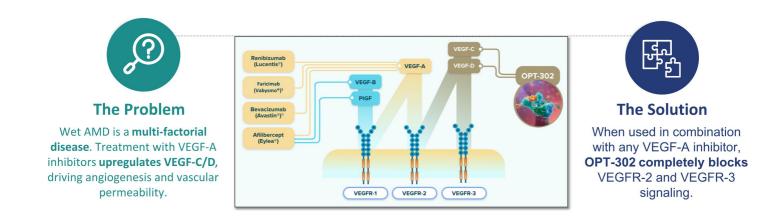
Despite Treatment with Standard of Care Anti-VEGF-A Therapies, the Majority of Patients Achieve Suboptimal Vision Outcomes



\*Based on randomised, controlled clinical trial data; >45% fail to achieve ≥ 2 lines improvement in Best Corrected Visual Acuity (BCVA); Persisting fluid: SD-OCT CST ≥ 300 µM or Time-Domain OCT CST ≥ 250 µM <sup>1</sup> Mettu PS, et al. Prog Retin Eye Res. 2021



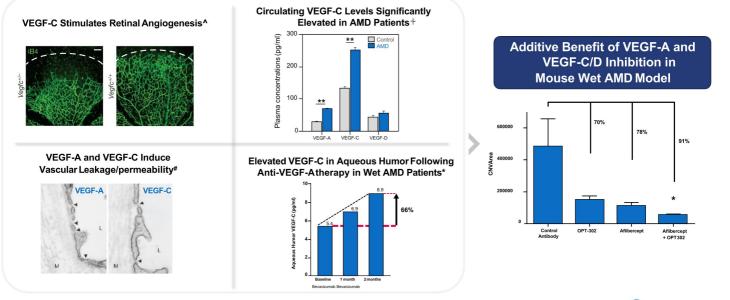
Sozinibercept, a Proprietary VEGF-C/D "Trap" Inhibitor, Has the Potential to Address the Limitations of Anti-VEGF-A Therapies



<sup>1</sup> Faricimab also has inhibitory effect on Ang-2. <sup>a</sup> Bevacizumab is used 'off-label' for the treatment of neovascular (wet) AMD



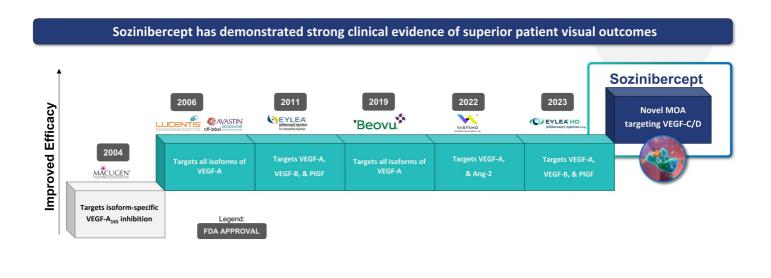
# Published Evidence Supports Broader VEGF Pathway Inhibition with Sozinibercept



<sup>A</sup>Tammela et al., Nature Cell Biology, 2011; # Zhou et al. BMC Ophthalmology (2020) 20:15; # Cao et al., Circ Res., 2004; + Lashkari et al, 2013 ARVO Annual Meeting, 4999-A0128; \*Cabral et al., 2018 Ophthalmology Retina (2018).

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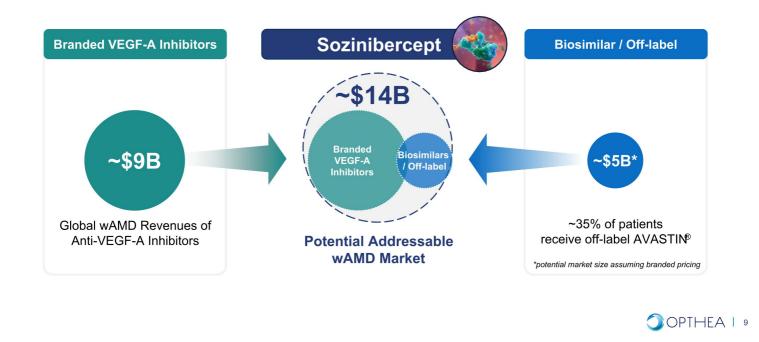
## Sozinibercept Has the Potential to Be the First Therapy in More Than 15 Years to Improve Visual Outcomes in Patients with Wet AMD



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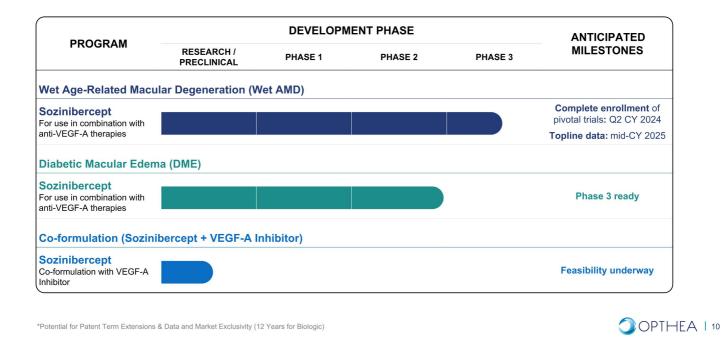
Jackson, Timothy L., et al. "A randomized controlled trial of OPT-302, a VEGF-C/D inhibitor for neovascular age-related macular degeneration." Ophthalmology, vol. 130, no. 6, June 2023, pp. 588–597, https://doi.org/10.1016/j.ophtha.2023.02.001.; MOA – Mechanism of Action

Sozinibercept Builds on Wet AMD Market as a Potential Combination Therapy with Any VEGF-A Inhibitor



### Long-term Value Opportunities for Sozinibercept

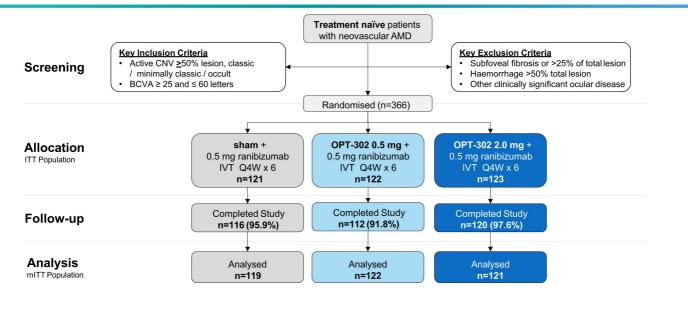
Main Patent Family Extends through 2034, with Expansion Opportunities Beyond 2034\*



### Near-term Focus Is on Sozinibercept Phase 3 Execution Pivotal Program Design Informed by Phase 2b and Optimized for Success

		Phase 3 Trials rials anticipated in mid-CY 2025
Completed Phase 1-2 Trials	Enrollment Complete	Anticipated CY 2Q 2024
Phase 2b (n=366) Treatment <b>naïve</b> wet AMD <b>OPT-302:</b> 6 x monthly dosing <b>Comparator: Ranibizumab (monthly)</b>	COAST Phase 3 - wet AMD (treatment naïve) n=~990	<b>ShORe</b> Phase 3 - wet AMD (treatment naïve) n=~990
Phase 1b/2a (n=153) Prior-treated DME <b>OPT-302</b> : 3 x monthly dosing <b>Comparator: Aflibercept</b> (monthly)	Comparator: Aflibercept (Eylea®) once every two months after three monthly doses	Comparator: Ranibizumab (Lucentis®) once every month
Phase 1/2a: (n=51) Treatment Naïve/Prior-treated wet AMD <b>OPT-302 + Ranibizumab</b> : 3 x monthly dosing	Standard Dosing         Extended Dosing           OPT-302         OPT-302           once every month         OPT-302           once every month         once every two months after three monthly doses	Standard Dosing         Extended Dosing           OPT-302         OPT-302           once every month         OPT-superior           once every month         once every two months after three monthly doses

### Phase 2b Wet AMD Trial Overview



CNV – choroidal neovascularisation; IVT – intravitreal; Q4W – once very 4 weeks; ITT – Intent to Treat Population, all participants who were randomised into the study irrespective of whether study medication was administered or not; Safety Population - all participants in the ITT but excluding those who did not receive at least one dose of study medication; mITT – Modified ITT Population, all participants in the Safety Population but excludes any participant whon at Baseline VA score and/or any participant who did not return for at least one post-baseline visit



#### **Primary Endpoint**

Mean change from baseline in BCVA at week 24

#### **Key Secondary Endpoints**

Proportion of patients gaining  $\geq$ 15 letters from baseline at week 24

Change in central subfield thickness (CST) from baseline at week 24

Change in intra-retinal and sub-retinal fluid from baseline to week 24

Safety and tolerability

#### **Select Pre-specified Subgroups**

Predominantly classic, minimally classic, & occult lesions (Stratification Factor)

Retinal Angiomatous Proliferation (RAP) detected/not detected at baseline

Polypoidal Choroidal Vasculopathy (PCV) detected/not detected at baseline

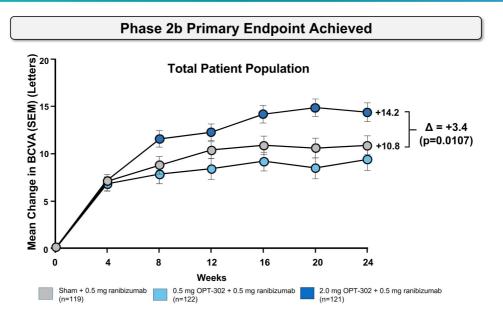


### Phase 2b Trial Demographics and Baseline Characteristics

Demographic/Baseline Disease Characteristic		Sham + ranibizumab n=121	0.5 mg OPT-302 + ranibizumab n=122	2.0 mg OPT-302+ ranibizumab n=123
Mean Age – years ± S	SD	76.1 ± 9.48	78.8 ± 8.16	77.8 ± 8.82
0	Male	48 (39.7%)	49 (40.2%)	45 (36.6%)
Sex – n (%)	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 <sup>2</sup> ± SD		6.08 ± 3.21	6.48 ± 3.30	6.62 ± 3.39
	Predominantly classic – n (%)	15 (12.4%)	15 (12.3%)	16 (13.0%)
	Minimally classic – n (%)	53 (43.8%)	51 (41.8%)	53 (43.1%)
Lesion Type	Occult - n (%)	53 (43.8%)	56 (45.9%)	54 (43.9%)
	PCV detected <sup>1</sup> -n (%)	20 (16.5%)	24 (19.7%)	22 (17.9%)
	RAP detected <sup>2</sup> -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%

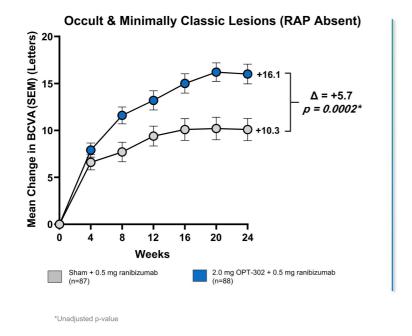
Intent-to-Treat (ITT) population; SD: standard deviation; BCVA: Best Corrected Visual Acuity. <sup>1</sup>PCV - polypoidal choroidal vasculopathy, detected by SD-OCT, FA and fundus OPTHEA 1 14 photography. <sup>2</sup>RAP - retinal angiomatous proliferation, detected by SD-OCT, FA and fundus photography.

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



Jackson, Timothy L., et al. "A randomized controlled trial of OPT-302, a VEGF-C/D inhibitor for neovascular age-related macular degeneration." Ophthalmology, vol. 130, no. 6, June 2023, pp. 588–597, https://doi.org/10.1016/j.ophtha.2023.02.001.





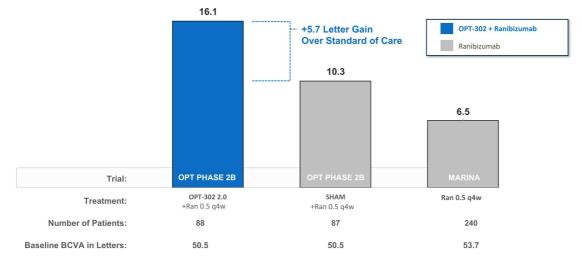
Phase 2b demonstrated **superior efficacy** of +5.7 letter gain over standard of care, based on a pre-determined analysis

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



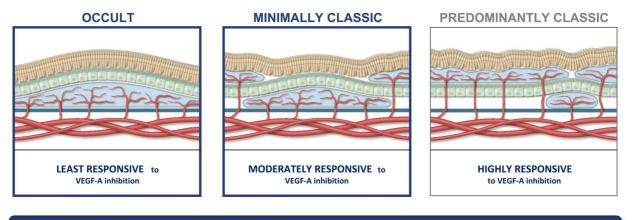
## Control Arm in Phase 2b Overperformed MARINA Trial at Week 24 in in Similar Lesion Type Patient Population

#### Mean Change in BCVA from Baseline at Week 24 – OPT-302 Phase 2b vs. MARINA Trial Occult and Minimally Classic Lesions



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

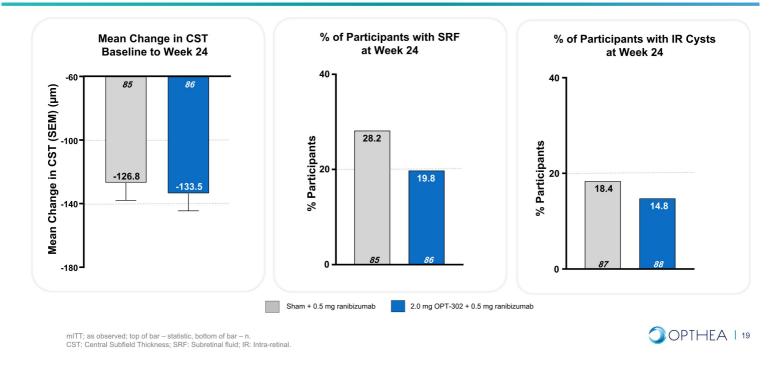




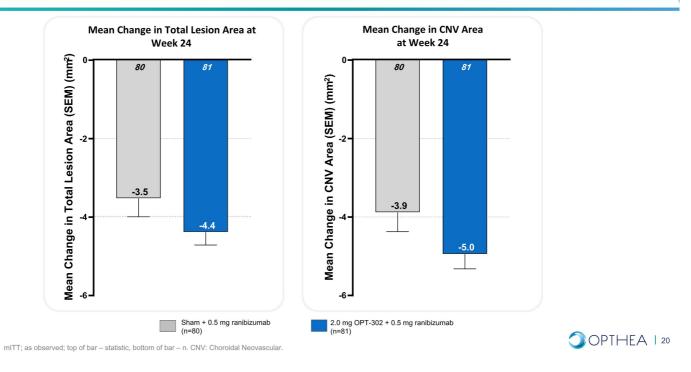
~75% of Wet AMD Patients Have Occult or Minimally Classic Lesions



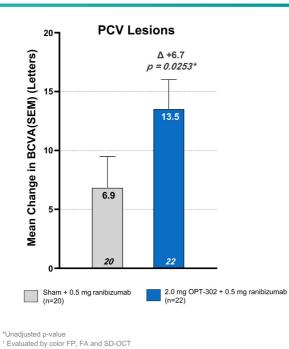
## Reduced Retinal Thickness and Better Retinal Drying With Combination Therapy in Occult & Minimally Classic (RAP Absent) Patients

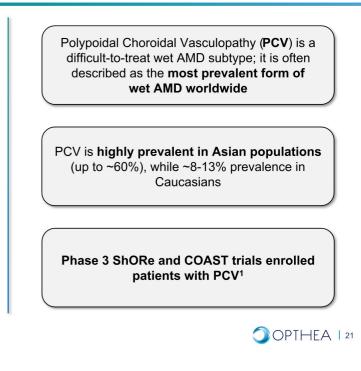


### Greater CNV and Lesion Regression With Combination Therapy in Occult & Minimally Classic (RAP Absent) Patients



## Sozinibercept Further Demonstrated Superior Vision Gains in a Pre-Specified Subgroup of PCV Lesion Patients





N Participants (%)	OPT-302 Any dose* N=399 (N=1,842 injections)	OPT-302 2.0 mg N=263 (N=1,121 injections)	Sham + anti-VEGF-A control N=170 (N=854 injections)
Ocular TEAEs - Study Eye – related to study product(s)	41 (10.2%)	22 (8.4%)	20 (11.8%)
Ocular TEAEs - Study Eye – Severe	4 (1.0%)	2 (0.8%)	2 (1.2%)
Intraocular inflammation – Study Eye	71,2,3 (1.8%)	31 (1.1%)	31 (1.8%)
Participants with AEs leading to treatment discontinuation	42,4-6 (1.0%)	14 (0.4%)	27,8 (1.2%)
Any APTC event	44,5,9,10 (1.0%)	35,9,10(1.1%)	211,12 (1.2%)
Deaths	210,13 (0.5%)	210,13 (0.8%)	214,15 (1.2%)

<sup>1</sup>Transient anterior chamber cell (trace 1-4 cells); <sup>2</sup> SAE of endophthalmitis, with AE's of hypopyon and anterior chamber cell (n=1; 0.5 mg); <sup>3</sup> SAE of vitritis (n=1; 0.5 mg); <sup>4</sup>Non-fatal myocardial infarction; <sup>6</sup>Cerebrovascular accident; <sup>6</sup>Enteritis; <sup>7</sup>Abdominal pain; <sup>6</sup>Increased IOP; <sup>9</sup> Non-fatal angina pectoris; <sup>10</sup>Fatal congestive heart failure/myocardial infarction; <sup>11</sup>Non-fatal arterial embolism; <sup>12</sup>Embolic stroke; <sup>13</sup>Metatstaic ovarian cancer; <sup>14</sup> Pneumonia; <sup>15</sup> infective endocarditis. \* Any dose (OPT-302 0.3 mg, 1 mg or 2 mg)



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

N Participants (%)	OPT-302 Any dose* N=399 (N=1,842 injections)	OPT-302 2.0 mg N=263 (N=1,121 injections)	Sham + anti-VEGF-A control N=170 (N=854 injections)
Intraocular Inflammation <sup>1</sup>	7 (1.8%)	3 (1.1%)	3 (1.8%)
OPT-302-1001 (Phase 1/2a wet AMD)	2	0	0
Uveitis with anterior chamber cell 1+	1	0	0
Uveitis with anterior chamber cell 2+	1	0	0
OPT-302-1002 (Phase 2b wet AMD)	3	1	2ª
Endophthalmitis with anterior chamber 1+ and hypopyon	1	0	0
Vitritis	1	0	0
Anterior chamber cell, trace	1	1	2ª
OPT-302-1003 (Phase 1b/2a DME)	2 <sup>b</sup>	2 <sup>b</sup>	1
Iritis with keratic precipitates and anterior chamber cell 2+	1	1	0
Iritis with anterior chamber cell 2+	0	0	1
Anterior chamber cell 4+, associated with cataract extraction/ intraocular lens	1 <sup>b</sup>	1 <sup>b</sup>	0

Safety population <sup>1</sup>AEs observations considered to be indicative of intraocular inflammation, defined prior to database lock <sup>a</sup>Observed during ophthalmic examination, but not reported as TEAEs <sup>b</sup>Considered associated with lens extraction and not reported as TEAEs





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



Two robust pivotal trials studying sozinibercept in combination with Eylea<sup>®</sup> and Lucentis<sup>®</sup> in treatment naïve patients with wet AMD



**Phase 3 designed to support broad label** for use in combination with any VEGF-A inhibitor for all wet AMD patients (treatment naïve and prior treated)



Sample Size       • ~990 per trial         • ~330 patients per arm: 2 mg sozinibercept q4w & q8w, or sham control         Comparators       • 2 mg Eylea® q8w (COAST) & 0.5 mg Lucentis® q4w (ShORe)         Regulatory Quality       • ~90% power, 5% type I error rate	Design	<ul> <li>Multi-center, double-masked, randomized (1:1:1), sham control</li> <li>Treatment naïve wet AMD patients</li> </ul>
	Sample Size	· ·
Regulatory Quality • ~90% power, 5% type I error rate	Comparators	<ul> <li>2 mg Eylea<sup>®</sup> q8w (COAST) &amp; 0.5 mg Lucentis<sup>®</sup> q4w (ShORe)</li> </ul>
	Regulatory Quality	<ul> <li>~90% power, 5% type I error rate</li> </ul>



#### **Primary Endpoint**

#### Mean change from baseline in BCVA at week 52

#### Key Secondary Endpoints (Baseline to Week 52)

Proportion of participants gaining ≥15 letters

Proportion of participants gaining ≥10 letters

Change in choroidal neovascularization area

Proportion of participants with absence of both sub-retinal fluid and intra-retinal cysts



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



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

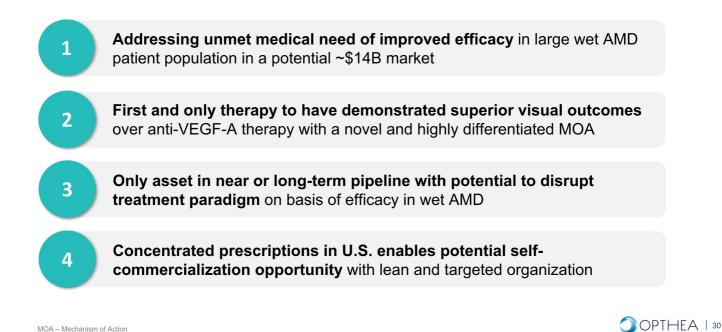
	We are dedicated to advancing sozinibercept to improve patients' visual outcomes				
Next Steps	Clinical Milestones	<ul> <li>Complete enrollment in 2<sup>nd</sup> Phase 3 trial (ShORe) in Q2 CY2024</li> <li>Mid-CY2025 topline data from both pivotal Phase 3 studies</li> </ul>			
	Manufacturing Scale- up	<ul> <li>Production of validation batches supportive of BLA filing and launch</li> </ul>			
	Regulatory Preparations	FDA Fast Track designation allows rolling submission of completed BLA modules			
	Commercial Readiness	<ul> <li>Strengthen medical expert engagement and develop market access strategy</li> <li>Complete development of product launch plan</li> </ul>			
	Readiness	Complete development of product launch plan			



Financial Overview		Development Funding Agreement (DFA)	
Ticker	OPT (ASX/NASDAQ)	<ul> <li>Total funding drawn under DFA: US\$170M</li> </ul>	
Shares Outstanding <sup>1</sup>	662.8M (Ordinary)/ 82.9M (ADSs equivalents)	<ul> <li>Provides non-dilutive funding for development of sozinibercept</li> <li>If sozinibercept is approved, repayment split between fixed payments and variable payments at 7% of revenues, capped at 4x investment</li> <li>No amounts owed if the clinical trials do not meet the primary endpoint or if regulatory approval is not received</li> </ul>	
Cash/Cash Equivalents <sup>1</sup>	US\$157.1M		
Offices	Melbourne, Australia Princeton, NJ		

<sup>1</sup> As of December 31, 2023





### Thank you!

For IR and BD contacts: info@opthea.com

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