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 August 2023

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 ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101 (b) (1):
Yes ☐ No ☒

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101 (b) (7):
Yes ☐ No ☒

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.
Yes ☐ No ☐

EXHIBIT INDEX

Exhibit	Description
99.1	Press Release - ASRS Presentation 2023 - PK and safety of sozinibercept (OPT-302)

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.

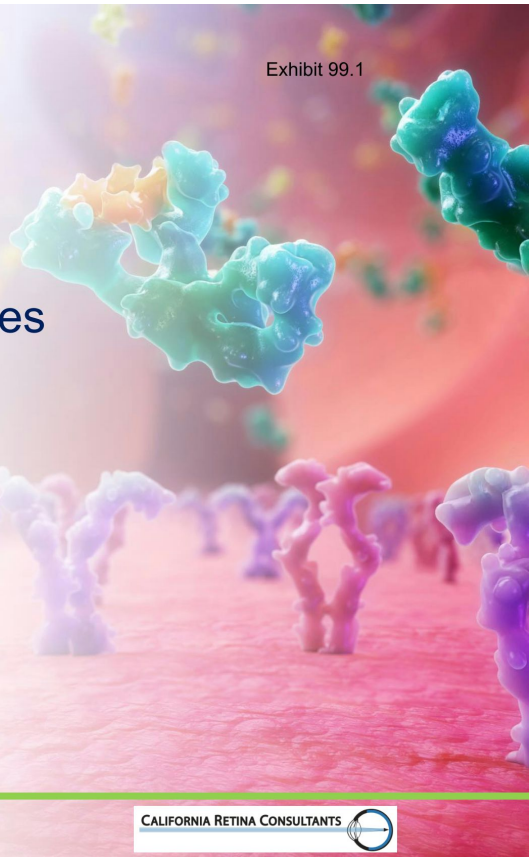
OPTHEA LIMITED
(Registrant)

By: /s/ Megan Baldwin
Name: Megan Baldwin, Ph.D.
Title: Chief Executive Officer and Managing Director

Date: 8/1/2023

Exhibit 99.1

Population Pharmacokinetics and Safety of sozinibercept (OPT-302), an anti-VEGF-C/-D 'trap' in Patients with Retinal Vascular Diseases



Dante J. Pieramici, MD

California Retina Consultants, Santa Barbara, CA

ASRS, Seattle, 2023

CALIFORNIA RETINA CONSULTANTS

Disclosures

Presenter's Financial Disclosures:

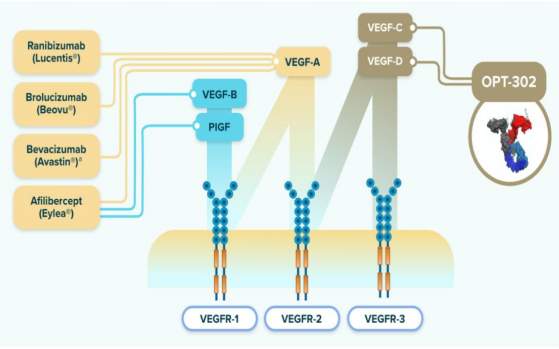
- Adverum (C), Gemini, Genentech, Inc., Iveric Bio, NGM, Opthea (C), Regeneron, Regenxbio

• This presentation will discuss IRB/IEC approved research of an investigational product.

(C): Consultant; (S): Stock/shareholder; (R): Grants/Research Support

Sozinibercept (OPT-302): A novel “Trap” Inhibitor of VEGF-C/-D

When used in combination is complementary/agnostic with anti-VEGF-A molecule used



	Sozinibercept (OPT-302)	LUCENTIS RANIBIZUMAB INJECTION	EYLEA (aflibercept) Injection For Intravitreal Injection
Molecule type	‘Trap’ fusion protein	Antibody fragment	‘Trap’ fusion protein
Structure			
MW	140 kDa	48 kDa	115 kDa
Dose	2 mg	0.5 mg	2 mg
IVT injection volume	0.05 mL	0.05 mL	0.05 mL
VEGF-A inhibition	NO	YES	YES
VEGF-C/-D inhibition	YES	NO	NO

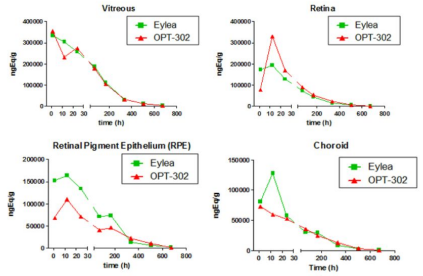
OPT-302 can also be potentially combined with Bevacizumab, Faricimab, Biosimilars, HD Eylea

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

*Dugel et al 2019, Ophthalmology Retina; †Lashkari et al , 2013 ARVO Annual Meeting, 4999-A0128; Bevacizumab used “off-label”; *Faricimab also targets Angiopoietin 2*

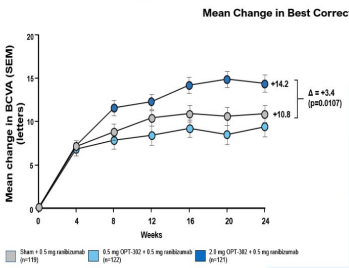
Sozinibercept (OPT-302) combination therapy for retinal vascular diseases

Similar ocular biodistribution & PK of intravitreal Sozinibercept to Aflibercept

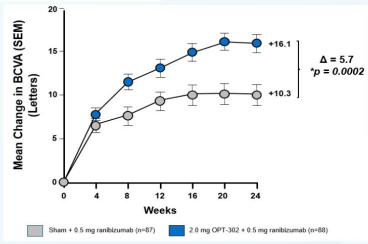


[^{125}I]OPT-302, or [^{125}I]aflibercept IVT injection of 500 µg/eye) (rabbit)

Superiority in BCVA gains with Sozinibercept (2 mg) combination therapy vs anti-VEGF-A monotherapy in Phase 2b study of treatment naïve patients (n=366) with nAMD



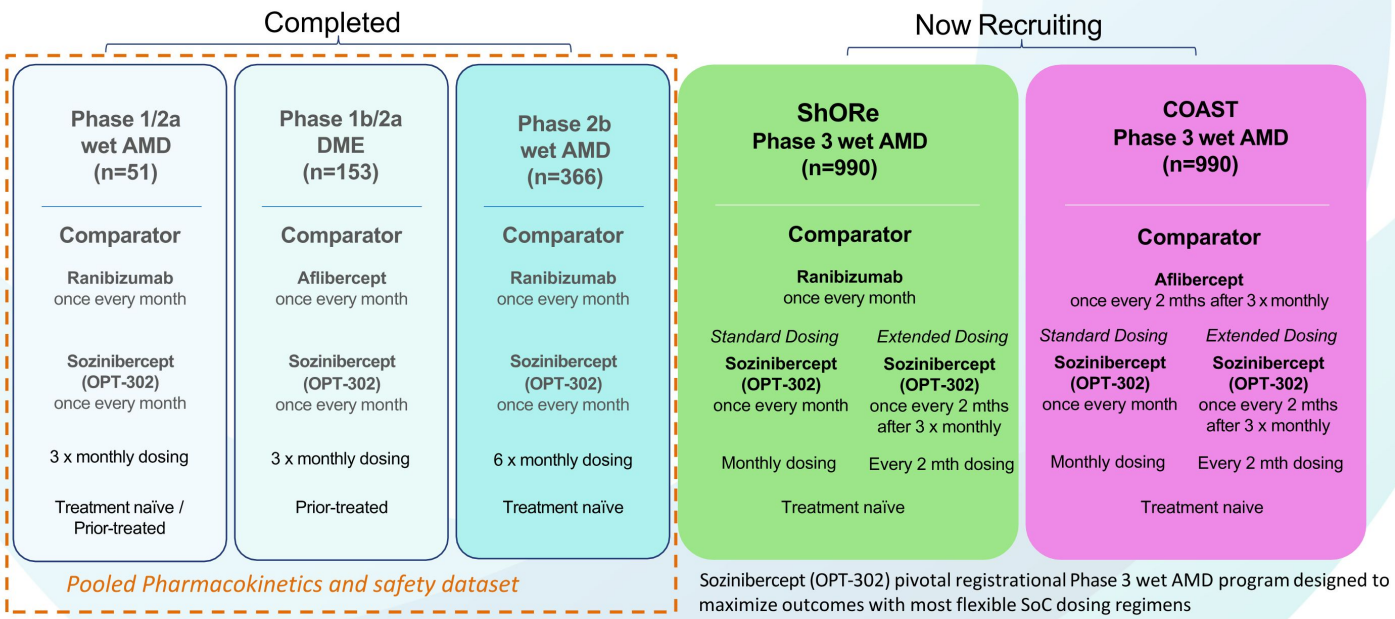
Additional +3.4 letter gain (p=0.0107) over ranibizumab in total population



Additional +5.7 letter gain in high responder subgroup (minimally classic & occult lesions)

- Currently two ongoing global pivotal registrational Phase 3 studies in wet AMD
- Analysis of OPT-302 serum pharmacokinetics (PK) of completed studies is important for interpreting safety and efficacy results and informing dosing for phase III trials
- A population PK model and pooled data analysis from clinical studies in patients with wet AMD and DME were used to describe PK parameters and safety following intravitreal (IVT) OPT-302 administration

Sozinibercept (OPT-302) Combination Therapy Clinical Program



Sozinibercept (OPT-302) pivotal registrational Phase 3 wet AMD program designed to maximize outcomes with most flexible SoC dosing regimens

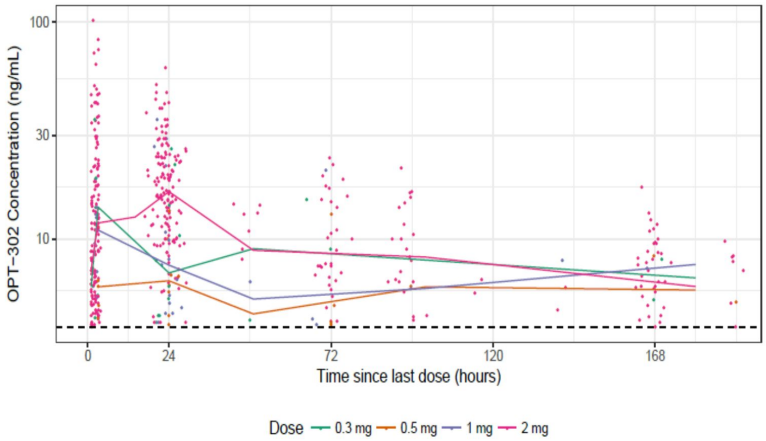
Exposure and demographics of pooled PK / safety dataset

Pooled data from a total of 1,853 intravitreal injections of sozinibercept (OPT-302: 0.3, 0.5, 1 or 2 mg)

- includes 1,130 IVT injections of 2.0 mg OPT-302
- PK samples in human serum were mostly collected at pre-dose, then ≥ 1 to 168 hours post-dose
- The PK bioanalytical method used a ELISA assay for determination of total OPT-302 serum concentrations (VEGF-C and -D bound and free OPT-302), the lower limit of quantitation of the assay was 3.91 ng/mL

	Age (years)	Weight (kg)	BMI (kg^2/m^2)	CrCL (mL/min)	eGFR ($ml/min/1.73m^2$)	Sex	Race	Pr Tx	Disease
N	394	394	394	394	394	Male: 176 (44.7%)	White: 375 (95.2%)	No: 265 (67.3%)	nAMD: 291 (73.9%)
Mean	73.8	78.4	28.6	81.1	77.8				
SD	11.3	18.4	5.58	40.4	26	Female: 218 (55.3%)	Black: 10 (2.5%)	Yes: 129 (32.7%)	DME: 103 (26.1%)
CV%	15.3	23.5	19.5	49.9	33.4				
Median	76	75	27.9	72.6	76.8		Asian: 1 (0.3%)		
Min	39	47	18.8	17.7	18.5				
Max	95	178	61.6	318	178		Other: 8 (2%)		

Sozinibercept (OPT-302) systemic PK profile & noncompartmental parameters



The solid lines show the median, with the filled circles representing the observed data, dashed black line = LLOQ (3.9 ng/mL). Plots truncated at 180 hours post-dose. Data below the LLOQ (3.9 ng/mL) excluded. Y-axis on log-scale.

Pooled systemic serum PK data:

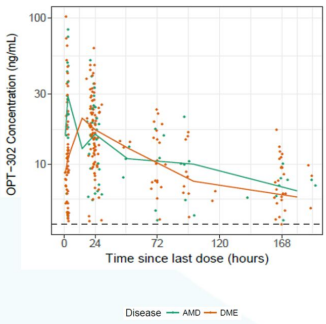
- C_{max} ~20 ng/mL [4 - 83]
- T_{max} ~30 hrs [1.8 - 96]
- $T_{1/2}$ ~7 days [2 -12]

The majority of the PK data for OPT-302 was collected following an IVT dose of 2 mg, where serum (C_{max}) occurs ~30 hours after administration.
Quantifiable concentrations remained in some subjects at 168 hours post- dose.
The interpretation of linear kinetics across dose range studied is challenging given the limited data from low dose groups ≤ 1 mg due to BLQ. .

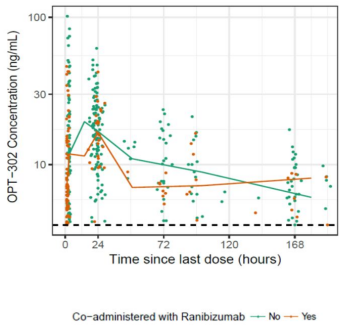
Sozinibercept (OPT-302) PK profiles by:

(A) ranibizumab co-therapy (nAMD); or (B) disease indication, nAMD vs DME; or (c) age group; or (d) renal impairment classification

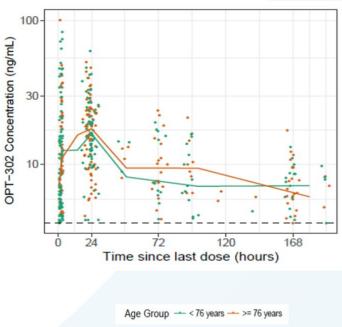
(A) ± ranibizumab co-therapy (nAMD)



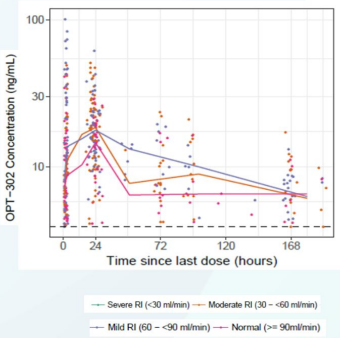
(B) nAMD vs DME



(C) age group

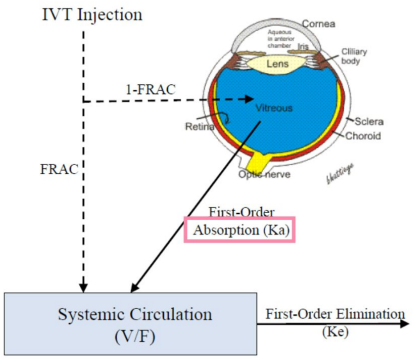


(D) renal impairment



No evidence of altered sozinibercept (OPT-302) PK by co-variates, as the profiles are comparable irrespective of (A) ranibizumab co-administration or (B) disease indication or (C) Age or (D) renal impairment classification

Vitreous Parameter Estimates from sozinibercept (OPT-302) Population PK Model



Parameter	Estimate (%RSE)	95% CI
Elimination $t_{1/2}$ (days)	0.145 (12.8)	0.113 – 0.189
Volume of Distribution (V/F, L)	3.52 (15.9)	2.65 – 4.96
Absorption $t_{1/2}$ (days)	4.64 (10.5)	3.62 – 5.78
Fraction absorbed directly into systemic circulation (%)†	6.94 (12.8)	3.10 - 12.1
Between subject variability on elimination $t_{1/2}$ (%CV)	26.4 (36.6)	0.26 – 44.3
Between subject variability on V/F (%CV)	50.3 (13.5)	36.4 – 67.0
Between subject variability on FRAC (variance)‡	0.342 (47.7)	3.42E-05 – 1.57
Between occasion variability on absorption $t_{1/2}$ (%CV)	40.7 (19.3)	24.5 – 56.1
Residual unexplained variability (proportional, %CV)	43.5 (10.7)	31.6 – 53.4
Residual unexplained variability (additive SD, ng/mL)	1.63 (13.9)	1.10 - 2.27

†$V/F = 3.2 \cdot (1\text{-}0.391)^{SEX}$, where SEX = 0 for males and 1 for females. ‡$FRAC = \exp(-2.596+\eta)/(1+\exp(-2.596+\eta))$, where η followed a normal distribution with a mean of zero and a variance of 0.342. 95% CI from bootstrap analysis of 1000 samples.

The PK model retained the single distribution compartment and linear elimination. Absorption from the vitreous space was described by a first-order process.
During selected dosing occasions, a small fraction, (≈7%) of the administered OPT-302 bypassed the vitreous compartment into the systemic circulation.
This phenomena has previously been described for IVT ranibizumab using a population PK approach.
The absorption of OPT-302 was the rate-limiting step, with the PK of OPT-302 via IVT administration described by 'flip-flop' kinetics.
The model assumes no clearance of OPT-302 in the vitreous compartment. The M3 method was used during estimation given the BLQ data.

Pooled safety for completed sozinibercept (OPT-302) Trials

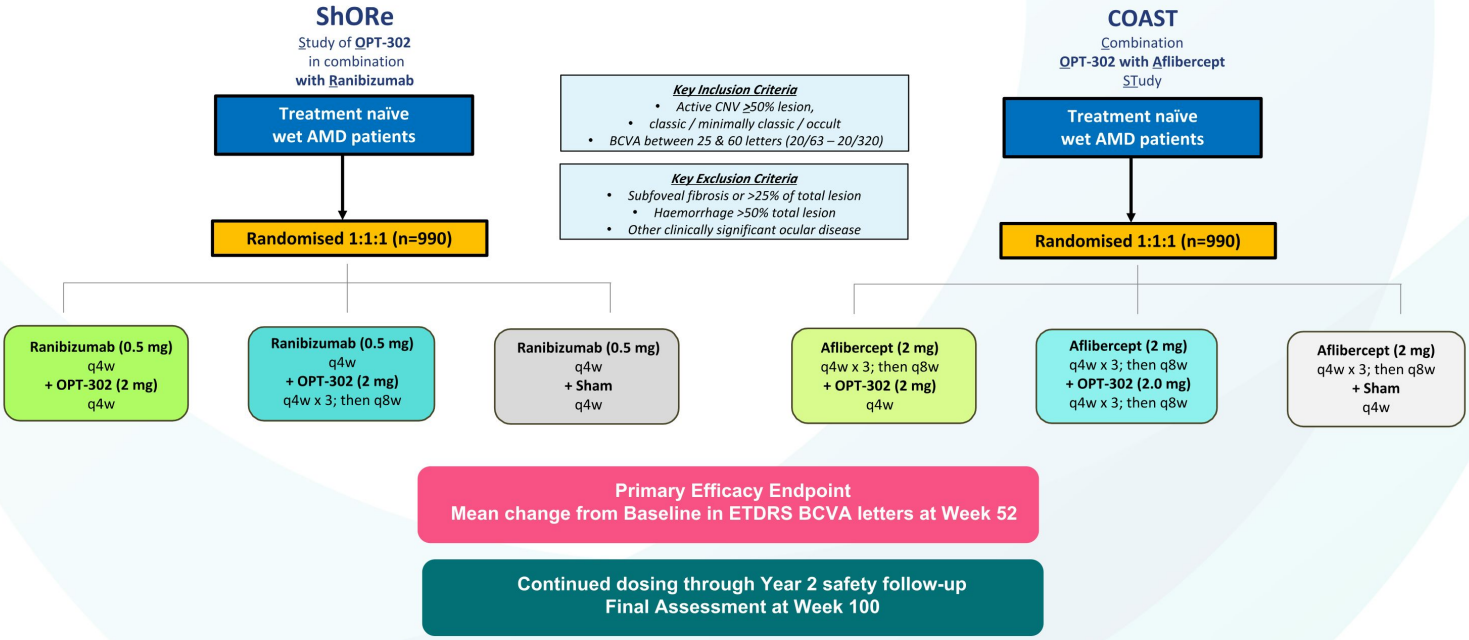
Combination therapy well-tolerated and comparable to standard of care monotherapy

N Participants (%)	OPT-302 Any dose* N=399 (N=1,842 injections)	OPT-302 2.0 mg N=263 (N=1,121 injections)	Sham + anti-VEGF-A control N=169 (N=854 injections)
Ocular TEAEs - Study Eye – related to study product(s)	41 (10.2%)	22 (8.4%)	20 (11.8%)
Ocular TEAEs - Study Eye – Severe	4 (1.0%)	2 (0.8%)	2 (1.2%)
Intraocular inflammation – Study Eye	7[1,2,3] (1.8%)	3[1] (1.1%)	3[1] (1.8%)
Participants with AEs leading to treatment discontinuation	4[2,4-6] (1.0%)	1[4] (0.4%)	2[7,8] (1.2%)
Any APTC event	4[4,5,9,10] (1.0%)	3[5,9,10](1.1%)	2[11,12] (1.2%)
Deaths	2[10,13] (0.5%)	2[10,13] (0.8%)	2[14,15] (1.2%)

[1]Transient anterior chamber cell (trace 1-4 cells); [2] SAE of endophthalmitis, with AE's of hypopyon and anterior chamber cell (n=1; 0.5 mg); [3] SAE of vitritis (n=1; 0.5 mg); [4]Non-fatal myocardial infarction; [5]Cerebrovascular accident; [6]Enteritis; [7]Abdominal pain; [8]Increased IOP; [9] Non-fatal angina pectoris; [10]Fatal congestive heart failure/myocardial infarction; [11]Non-fatal arterial embolism; [12]Embolic stroke; [13]Metatstaic ovarian cancer; [14] Pneumonia; [15] infective endocarditis

** Any dose (OPT-302 0.3 mg, 0.5 mg, 1 mg or 2 mg)*

Phase 3 trials of Sozinibercept (OPT-302) Combination therapy (*ongoing*)



- **Design:** Multi-centre, double-masked, randomised (1:1:1), sham control
- **Regulatory quality:** 90% power, 5% type I error rate

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

Summary: Sozinibercept (OPT-302) pooled PK and safety

- The PK profiles of intravitreal sozinibercept (OPT-302) from completed studies in patients with nAMD and DME indicated:
  - low systemic exposure
  - within one week drug levels were mostly no longer detectable in serum
  - estimated vitreous absorption half-life was ~4.6 days [95% CI 3.6-5.8] comparable to other IVT biologics
  - the PK profile was unaltered by anti-VEGF-A co-therapy, disease indication (nAMD vs DME), age or renal function
- Pooled safety analysis shows soziniberept (OPT-302) combination therapy has a favourable safety and tolerability profile
  - comparable to standard of care anti-VEGF-A monotherapy
- Promising treatment option for wet AMD currently in two pivotal registrational Phase 3 studies
  - pooled PK and safety data support ShORe and COAST dosing regimens of 2 mg sozinibercept q4w or q8w following 3 loading doses