OPT-302-1003 Clinical Trial Summary – Phase 1b/2a DME

Protocol Number	OPT-302-1003
Title	Phase 1b/2a study of OPT-302 in combination with aflibercept for persistent central-involved diabetic macular edema
Sponsor	Opthea Limited
Indication	Diabetic macular edema (DME)
Study Phase	1b/2a
Primary Endpoints	Phase 1b and Phase 2a: Safety: Subject incidence of adverse events, DLTs and clinically significant changes in vital signs, ECGs and clinical laboratory tests Phase 2a: Efficacy: Response rate as defined by proportion of participants receiving combination OPT-302 and aflibercept achieving at least a 5 letter gain in BCVA compared to baseline at week 12 according to ETDRS criteria
Secondary Endpoint(s)	• Mean change in BCVA from baseline to week 12 using ETDRS criteria • Mean change from baseline to week 12 in CST and macular volume on SD-OCT • Percent of eyes with ≥ 50% reduction in excess foveal thickness from baseline to week 12 on SD-OCT • Percent of eyes with CST < 300 µm on SD-OCT through week 12 • Percent of participants with a ≥ 2 step improvement from baseline to week 12 in ETDRS Diabetic Retinopathy Severity Score • The mean time to, and number of, retreatment injections of aflibercept anti-VEGF-A therapy based on protocol specified criteria during week 12 to week 24 follow-up • OPT-302 pharmacokinetics parameters • Incidence of anti-OPT-302 antibody formation
Study Design	Two part multi-centre study consisting of a Phase 1b open-label, sequential dose escalation followed by a Phase 2a randomized, controlled, dose expansion evaluating intravitreal OPT-302 in combination with aflibercept in patients with persistent central-involved DME
Investigational Product	OPT-302
Comparator	Aflibercept (Eylea®)
Control	Sham control
Dose Regimens	Phase 1b dose escalation: The dose regimens for the 3 sequential, escalating treatment cohorts in the Phase 1b are as follows: Cohort 1: OPT-302 0.3 mg and aflibercept 2 mg Cohort 2: OPT-302 1 mg and aflibercept 2 mg Cohort 3: OPT-302 2 mg and aflibercept 2 mg OPT-302 and aflibercept will be administered as separate intravitreal injections (each 0.05 mL) once every 4 weeks for 3 treatment cycles.

	Phase 2a dose expansion: At least 108 patients will be randomized in a 2:1 ratio between one of the following two treatment groups: Cohort 4: OPT-302 (*dose from Phase 1b*) and aflibercept 2 mg Cohort 5: Sham intravitreal injection and aflibercept 2 mg OPT-302 (or sham) and aflibercept will be administered as separate intravitreal injections (each 0.05 mL) every 4 weeks for 3 treatment cycles. Following the dosing period, in the Phase 1b and Phase 2a there will be a 4 week treatment free follow-up to week 12 and then a follow-up to week 24 during which the subject will receive as needed standard of care IVT aflibercept based on retreatment criteria for persistent DME if BCVA or CST worsens.
Clinical Trial Sites	Approximately 15-25 ophthalmology sites in the USA and Australia
Key Eligibility Criteria	• Males and females, ≥ 18 years of age • Diabetes mellitus (type 1 or type 2) • Edema that involves the center of the macula as confirmed by the reading center • Eyes with recurrent / persistent DME despite prior intravitreal anti-VEGF-A therapy with a suboptimal response • History of macular edema ≤ 12 months • An ETDRS BCVA letter score ≤ 73 and ≥ 24 (approximate Snellen equivalent 20/40 to 20/320), inclusive, in the study eye