ASX and Media Release

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Opthea Presents Positive Data from OPT-302 Phase 2b Wet AMD Trial at EURETINA Congress

Melbourne, Australia; 6 Sept 2019 – Opthea Limited (ASX:OPT), a clinical biopharmaceutical company developing novel biologic therapies for eye diseases, announced today that new clinical data from its completed 366 patient Phase 2b randomised, controlled study of OPT-302 with ranibizumab (Lucentis®) compared to ranibizumab alone, was presented at the European Society of Retina Specialists EURETINA 2019 Congress in Paris. The Phase 2b study data was presented for the first time at an international ophthalmology congress by Professor Tim Jackson, Chief Investigator of the study, and Consultant Ophthalmic Surgeon at King's College London.

Additional analysis of the clinical data from the Phase 2b study further supports the primary outcome of the trial, which demonstrated superior vision gains following OPT-302 + ranibizumab combination therapy compared to sham + ranibizumab (control) ($p = 0.0107$). Addition of OPT-302 to standard of care anti-VEGF-A therapy was associated with improved anatomical changes of retinal lesions, including reduced CST, and reduced sub-retinal fluid and intra-retinal cysts. OPT-302 combination therapy also reduced total lesion area and choroidal neovascularisation (CNV) area compared to ranibizumab alone.

"We are pleased to report additional results from our Phase 2b clinical trial at EURETINA. Together with the previously reported superiority in visual acuity gains, the further data analyses support the primary outcome of the study and demonstrate that OPT-302 has direct mechanistic effects on wet AMD lesion pathology," commented Dr Megan Baldwin, CEO and Managing Director of Opthea Limited.

In the 2.0 mg OPT-302 + ranibizumab treatment group, 18.5% of patients had sub-retinal fluid present at week 24 versus 29.3% in the ranibizumab + sham group. In addition, the relative proportion of patients with intra-retinal fluid cysts was 16.8% for the 2.0 mg OPT-302 combination group and 21.6% for ranibizumab alone.

In patients who received 2.0 mg OPT-302 combination therapy, the mean wet AMD total lesion area at week 24 decreased from baseline by 4.33 mm^2, compared to 3.11 mm^2 in the control group, a relative benefit of 39% ($p = 0.0137$). Similarly, the mean CNV area was also reduced from baseline to week 24 in the OPT-302 combination treatment group by 4.97 mm^2, compared to 3.59 mm^2 in the control group, a relative benefit of 38% ($p = 0.0052$).

The safety profile of OPT-302 intravitreal injections was similar to the control group. There were two ocular serious adverse events (SAEs) reported in the study eye, one case of endophthalmitis and one case of vitritis, both in the 0.5 mg OPT-302 + ranibizumab group. The incidence of intraocular inflammation in the study eye was very low across all treatment groups. There was one AE that lead to study discontinuation and one APTC* event of non-fatal myocardial infarction in the ranibizumab + sham and 0.5 mg OPT-302 + ranibizumab groups respectively. There were two patient deaths whilst on study, both deemed to be unrelated to study drugs and both in the ranibizumab control group. Overall, intravitreal administration of OPT-302 in combination with ranibizumab was well tolerated with no safety concerns identified.

Dr Megan Baldwin, CEO & Managing Director, Opthea Limited added "We continue to be encouraged by the positive outcomes of the further analyses of the Phase 2b trial. We anticipate reporting additional outcomes from the study over the following months at international ophthalmology meetings."

A copy of the data included in the EURETINA presentation is available on Opthea's website at www.opthea.com.

Additional information on Opthea's technology and clinical trials in wet AMD and diabetic macular edema (DME) can be found at www.opthea.com and ClinicalTrials.gov (ID#: NCT03345082 and ID#: NCT03397264, respectively).

** Anti-platelet Trialists' Collaboration (APTC) events classified as non-fatal myocardial infarction, non-fatal stroke, or vascular death*

About OPT-302

OPT-302 is a soluble form of vascular endothelial growth factor receptor 3 (VEGFR-3) or 'Trap' molecule that blocks the activity of two proteins (VEGF-C and VEGF-D) that cause blood vessels to grow and leak, processes which contribute to the pathophysiology of retinal diseases. Opthea is developing OPT-302 for use in combination with inhibitors of VEGF-A (e.g. Lucentis®/Eylea®). Combination therapy of OPT-302 and a VEGF-A inhibitor achieves more complete blockade of members of the VEGF family, blocking mechanisms contributing to sub-optimal responses to selective VEGF-A inhibitors and has the potential to improve vision outcomes by more completely inhibiting the pathways involved in disease progression.

Phase 2b Study Design

Opthea's Phase 2b clinical trial was an international, multi-centre, prospective, sham-controlled, double-masked, superiority study that enrolled 366 treatment-naïve patients with wet AMD who were randomized in a 1:1:1 ratio to receive one of the following treatment regimens administered every 4 weeks for 24 weeks: OPT-302 (0.5 mg) in combination with ranibizumab (0.5 mg); OPT-302 (2.0 mg) in combination with ranibizumab (0.5 mg); or sham in combination with ranibizumab (0.5 mg).

Further details on the Company's clinical trials can be found at: www.clinicaltrials.gov, Clinical trial identifiers: NCT02543229, NCT03345082 and NCT03397264.

About Wet AMD

Wet (neovascular) age-related macular degeneration, or wet AMD, is a disease characterized by the loss of vision of the middle of the visual field caused by degeneration of the central portion of the retina (the macula). Abnormal growth of blood vessels below the retina, and the leakage of fluid and protein from the vessels, causes retinal degeneration that leads to severe and rapid loss of vision. Wet AMD is the leading cause of blindness in the developed world in individuals aged over 50 years and its prevalence is increasing. Without treatment, wet AMD patients often experience a rapid decline in visual acuity.

Standard of care treatments for wet AMD and DME include the VEGF-A inhibitors Lucentis® (Roche/Novartis) and Eylea® (Regeneron/Bayer), which do not inhibit VEGF-C or VEGF-D. Sales of Lucentis® and Eylea were over $US3.7BN and $US6.2BN in 2018 respectively. Approximately half of the people receiving Lucentis®/Eylea® do not experience a significant gain in vision and/or have persistent retinal vascular leakage despite regular intravitreal injections. Combined administration of OPT-302 with a VEGF-A inhibitor, has the potential to improve visual acuity by more effective inhibition of the pathways involved in disease progression.

About Opthea Limited

Opthea (ASX:OPT) is a biologics drug developer focusing on ophthalmic disease therapies. It controls exclusive worldwide rights to a significant intellectual property portfolio around VEGF-C, VEGF-D and VEGFR-3. Opthea's intellectual property is held within its wholly-owned subsidiary Vegenics Pty Ltd. Opthea's product development programs are focused on developing OPT-302 for retinal diseases.

Inherent risks of Investment in Biotechnology Companies

There are a number of inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Opthea are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Therefore investment in companies specialising in drug development must be regarded as highly speculative. Opthea strongly recommends that professional investment advice be sought prior to such investments.

Forward-looking statements

Certain statements in this ASX announcement may contain forward-looking statements regarding Company business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavour of building a business around such products and services. Opthea undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Actual results could differ materially from those discussed in this ASX announcement.

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