ASX and Media Release
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Opthea Confirms Final Patient Enrolment in Phase 2b Wet AMD Clinical Trial

Melbourne, Australia; 26 November 2018 – Opthea Limited (ASX:OPT), a clinical stage biopharmaceutical company developing novel biologic therapies to treat eye diseases, is pleased to report that the last patient has been enrolled in the Company's ongoing Phase 2b trial of OPT-302 for wet age-related macular degeneration (AMD) and the final number of patients is confirmed as 366.

Today's announcement follows the randomization of an additional 15 patients who were undergoing eligibility screening when the Company recently successfully achieved its target enrolment of 351 treatment naïve patients into the study. With patient enrolment into the Phase 2b trial now closed, Opthea is currently focused on the completion of all patient dosing and data collection. The Company expects to report top-line primary outcome results from this study in the fourth quarter of 2019, significantly ahead of the original projected timelines.

Professor Guna Laganovska, Head of Department Ophthalmology at Riga Stradiņš University and Pauls Stradiņš Clinical University Hospital in Riga, Latvia, and leading recruiter in the Phase 2b clinical trial, stated "We are delighted to be involved in Opthea's Phase 2b wet AMD clinical trial and to be a part of a program advancing a promising clinical candidate, OPT-302, that may offer patients additional clinical benefit over standard of care anti-VEGF-A therapies."

"More complete blockade of the VEGF/VEGFR pathway, by combined administration of OPT-302 with a VEGF-A inhibitor, may be an effective strategy to address the significant unmet medical need for patients with wet AMD, DME and other retinal diseases. With a scarcity of novel combination approaches in development and encouraging clinical data to date, we look forward to the outcomes from Opthea's ongoing Phase 2 clinical trials with OPT-302."

Opthea's Phase 2b trial is a double-masked, randomized, controlled clinical study of 366 patients randomized in a 1:1:1 ratio to each of three treatment groups to investigate the clinical efficacy and safety of OPT-302 administered at 0.5 mg or 2.0 mg in combination with the VEGF-A inhibitor ranibizumab (Lucentis®, 0.5 mg) compared to ranibizumab (0.5 mg) alone. Patients randomized to the ranibizumab alone group also receive a sham injection to mask the patient to the treatment group. Treatments are administered on a monthly basis for 6 months via intravitreal (ocular) injection. The study is being conducted at 113 clinical sites in the US, Israel and eight European countries.

Dr Megan Baldwin, CEO & Managing Director of Opthea Limited commented "We are very pleased to have completed this patient enrolment clinical milestone ahead of schedule and are looking forward to completing the 6-month treatment phase of this study and then releasing top-line data in the fourth quarter of next year. We are grateful to the individuals, their families and physicians who are participating in the study."

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).

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 (eg. Lucentis®/Eylea®). Combination therapy of OPT-302 and a VEGF-A inhibitor achieves more complete blockade of members of the VEGF family, blocks mechanisms contributing to sub-optimal response to selective VEGF-A inhibitors and has the potential to improve vision outcomes by more completely inhibiting the pathways involved in disease progression.

Opthea has completed a Phase 1/2a clinical trial in the US investigating OPT-302 wet AMD patients as a monotherapy and in combination with Lucentis®. The trial was conducted under an FDA approved IND at 14 US clinical sites. The purpose of the trial was to evaluate the safety, pharmacokinetics (PK) and pharmacodynamics of OPT-302 administered as monthly intravitreal injections for 3 months with and without Lucentis® in patients with wet age related macular degeneration (AMD). Of the 51 patients enrolled, 25 were treatment naïve and 26 had received prior intravitreal anti-VEGF-A therapy.

Further details on the Phase 1/2a trial can be found at: www.clinicaltrials.gov, Clinical trial identifier: NCT02543229. Details on the outcomes of the study can be found on the Opthea website: www.opthea.com

About Wet AMD

Wet (neovascular) age-related macular degeneration, or wet AMD, is a disease characterised 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 and leads to severe and rapid loss of vision.

Wet AMD is the leading cause of blindness in the developed world in individuals aged 50 years or older. The prevalence of AMD is increasing annually as the population ages. Without treatment, wet AMD patients often experience a chronic, rapid decline in visual acuity and increase in retinal fluid. Sales of the drug Lucentis® (Roche/Novartis), which targets VEGF-A but not VEGF-C or VEGF-D, were over $US3.4BN in 2017. Sales of EYLEA® (Regeneron/Bayer), which also targets VEGF-A but not VEGF-C/-D first marketed in November 2011 for the treatment of wet AMD, were over $US5.9BN in 2017. Approximately half of the people receiving Lucentis®/EYLEA® are classified as non-responders or 'poor' responders and do not experience a significant gain in vision and/or have persistent retinal vascular leakage. There is great opportunity to improve patient responses by targeting more than one factor involved in disease progression. Existing therapies, such as Lucentis® and EYLEA®, target VEGF-A that promotes blood vessel growth and leakage through its receptor VEGFR-2. VEGF-C can also induce angiogenesis and vessel leakage through the same receptor as well as through an independent pathway. Combined inhibition of VEGF-A and VEGF-C/-D, has the potential to improve patient response 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 Vascular Endothelial Growth Factor (VEGF)-C, VEGF-D and VEGFR-3. Opthea's intellectual property is held within its wholly-owned subsidiary Vegenics Pty Ltd. The applications for the VEGF technology, which functions in regulating blood and lymphatic vessel growth, are substantial and broad. Opthea's product development programs are focused on developing OPT-302 (formerly VGX-300, soluble VEGFR-3) for 'back of the eye' disease such as wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME).

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. Thus 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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