ASX and Media Release
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Opthea Doses Patients in Europe and Israel in Phase 2b Study of OPT-302 for Wet AMD

Melbourne, Australia; March 27 2018 – Opthea Limited (ASX:OPT), a developer of novel biologic therapies for the treatment of eye diseases, has dosed the first patients in Europe and Israel in the Company's ongoing Phase 2b trial of OPT-302 for wet age-related macular degeneration (AMD). The study, which is a randomised, controlled clinical trial of OPT-302, a novel VEGF-C/D 'Trap' therapy, in combination with ranibizumab (Lucentis®) for wet AMD commenced dosing at clinical sites across the U.S. in December 2017.

"The activation of clinical trial sites in Europe and Israel represents significant progress in our Phase 2b trial. It expands patient recruitment for the study into another 9 countries and follows a successful Investigators Meeting held in Barcelona, Spain, on 16th March," commented Dr Megan Baldwin, CEO and Managing Director of Opthea.

The Phase 2b study is an international trial, currently enrolling patients from over 50 clinical sites in the US and is on track to open a total of 6 trial sites in Israel and over 50 trial sites across eight European countries, consisting of the United Kingdom, France, Poland, Hungary, Spain, Latvia, Italy and the Czech Republic. All of the countries and sites have been selected based on experience with conducting ophthalmic clinical trials with anti-VEGF-A therapies. The randomisation and dosing of patients in these jurisdictions follows successful regulatory interactions with each of the participating European countries' regulatory agencies via the European Voluntary Harmonisation Process (VHP), the Ministry of Health in Israel and the US Food & Drug Administration (FDA).

The Investigators Meeting convened European and Israeli Investigators and site staff involved in the study and was an opportunity to review data from Opthea's recently completed Phase 1/2a trial in wet AMD, as well as operational aspects of the Phase 2b study, including the trial protocol and patient eligibility criteria. Opthea conducted a similar US Investigators Meeting in Dallas Texas in October 2017, prior to initiation of patient enrolment at US sites.

Opthea's Phase 2b trial will enrol ~351 patients with wet AMD who have not received prior therapy (treatment-naïve patients) and is designed to investigate whether addition of OPT-302 to Lucentis® therapy over a 6-month dosing period improves visual acuity and anatomical parameters of wet AMD lesions as assessed by imaging techniques.

Primary analysis of the data from the Phase 2b study is anticipated in early 2020.

Additional information on Opthea's technology and clinical trials in wet AMD and diabetic macular edema (DME) can 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 $US3.2BN in 2016. 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 $US5.4BN in 2016. 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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