ASX and Media Release
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Opthea Receives Positive Feedback from European Regulatory Agencies for the OPT-302 Clinical Program in wet AMD

Melbourne, Australia, 20 March 2017 – Opthea Limited (ASX:OPT) Opthea Limited, a developer of novel biologic therapies for the treatment of eye diseases, has concluded positive European scientific advice meetings with the United Kingdom's (UK) Medicines and Healthcare Products Regulatory Agency (MHRA) and Sweden's Medical Products Agency (MPA) for the clinical development program of OPT-302, Opthea's novel VEGF-C/D 'Trap' therapy for the treatment of wet age-related macular degeneration (wet AMD).

Opthea sought advice from the MHRA and MPA based on their extensive ophthalmology experience including assessments of marketing authorisation applications for approved anti-VEGF-A therapies.

"We appreciate the scientific advice received from two key European regulatory agencies in support of Opthea's strategy to conduct our planned Phase 2B wet AMD clinical trial with OPT-302 in the European Union (EU)" said Dr Megan Baldwin, Chief Executive Officer and Managing Director of Opthea. "The valuable discussions and advice on our clinical program will help advance the development of OPT-302 as a combination therapy for patients suffering from wet AMD.

OPT-302 blocks signals that cause blood vessels in the back of the eye to grow and leak, and that may be associated with resistance to existing treatments for wet AMD. We are excited about the potential of OPT-302 to help improve clinical outcomes in patients suffering from this disease, many of whom experience a sub-optimal response despite ongoing therapy with selective VEGF-A inhibitors."

Following the formal regulatory and scientific advice meetings in the US and EU with the Food & Drug Administration (FDA), MHRA in the UK and MPA in Sweden, Opthea is progressing plans to initiate a Phase 2B randomised, controlled trial in wet AMD patients in 2H 2017.

The Phase 2B study will be a dose-ranging, multi-centre, randomised, parallel group, double-masked, sham-controlled study in treatment naïve patients with wet AMD. The trial will comprise three treatment groups and will investigate the clinical efficacy and safety of intravitreal OPT-302, administered monthly at two dose levels in combination with the selective VEGF-A inhibitor Lucentis® (0.5 mg), compared to monthly Lucentis® alone.

The primary endpoint of efficacy for the proposed Phase 2B study is the mean change from baseline in visual acuity, while secondary efficacy endpoints include anatomic changes in wet AMD lesion composition using spectral domain optical coherence tomography imaging.

Further details on the design of the planned Phase 2B wet AMD trial of OPT-302 will be made in 2H 2017 following finalisation of the clinical protocol and reporting of data from Opthea's ongoing Phase 1/2A clinical trial in 51 patients with wet AMD by the end of March 2017.

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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. 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).

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 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. OPT-302 is currently being investigated in a Phase 1/2A clinical trial in wet AMD patients as a monotherapy and in combination with ranibizumab (Lucentis®). The trial is being conducted under an FDA approved IND at several US clinical sites. The purpose of the trial is 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). The study is being conducted in two parts: Part 1 (Phase 1) comprises an open label, sequential dose escalation that recruited 20 patients and Part 2 (Phase 2A) a randomized dose expansion that recruited an additional 31 patients and is aimed at further characterising the safety, pharmacokinetic profile and relationship between dose/PK and clinical activity of OPT-302 (+/- ranibizumab). Further details on the Phase 1/2A trial can be found at: www.clinicaltrials.gov, Clinical trial identifier: NCT02543229.

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.