ASX and Media Release
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Opthea Completes FDA Meeting to Inform OPT-302 wet AMD Clinical Program

Melbourne, Australia, 9 March 2017 – Opthea Limited (ASX:OPT) Opthea Limited, a developer of novel biologic therapies for the treatment of eye diseases, has completed a Type C meeting with the U.S. Food and Drug Administration (FDA). The purpose of the meeting was to obtain regulatory guidance on the clinical development program and proposed Phase 2B clinical trial of OPT-302, Opthea's novel VEGF-C/D 'Trap' therapy for the treatment of wet age-related macular degeneration (wet AMD).

Opthea requested the meeting which was held on 8 March (US) with the FDA Division of Transplant and Ophthalmology Products, within the Center for Drug Evaluation and Research. The discussions covered the scope and design of the Phase 2B wet AMD clinical trial including patient eligibility criteria, statistical considerations including the potential sample size of the study, rationale for dose levels of OPT-302 and guidance on clinical trial endpoints to evaluate the safety and clinical efficacy of OPT-302 in wet AMD patients.

Dr Megan Baldwin, CEO and Managing Director of Opthea commented, "We are very pleased with the FDA's thorough and positive feedback and its continued support to advance the OPT-302 program for back of the eye diseases such as wet AMD. The outcomes from this meeting provide a clear path forward to Opthea as we continue to execute our plan to initiate a larger, randomised and controlled Phase 2B study in wet AMD patients in 2017."

Opthea's meeting with the FDA follows the completion of enrolment in the Phase 2A dose expansion cohorts of its ongoing Phase 1/2A clinical trial. The trial in wet AMD patients who were either treatment naïve or previously treated with anti-VEGF-A therapy, enrolled 20 patients in the Phase 1 dose escalation and 31 patients in the Phase 2A dose expansion. Patients received OPT-302 administered by intravitreal (ocular) injection either as a monotherapy (n=13) or in combination with the selective VEGF-A inhibitor Lucentis® (n=38) on a monthly basis for 3 months.

Primary analysis data from the Phase 1 dose escalation study demonstrated safety and tolerability of OPT-302 administered as a monotherapy and in combination with Lucentis®. Encouraging signs of clinical activity of OPT-302 in the Phase 1 study suggest that combined administration of OPT-302 + Lucentis® may lead to improved visual acuity and anatomical outcomes over Lucentis® alone.

Opthea anticipates the reporting of outcomes from the ongoing Phase 2A dose expansion cohorts of the clinical trial by the end of March 2017.

Wet AMD is the leading cause of blindness for people over the age of 50 in the US and Europe and is estimated to affect over 1.5 million people worldwide. The prevalence of wet AMD is increasing annually as the population ages and is forecast to rise to 3 million people globally by 2020. Wet AMD is estimated to be a $5BN per year market in the US alone. OPT-302 is a soluble receptor that blocks VEGF-C and VEGF-D and used in combination with a VEGF-A inhibitor has the potential to improve vision in wet AMD patients by targeting mechanisms of sub-responsiveness to existing approved therapies for the disease.

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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.