ASX and Media Release
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Opthea Completes Patient Enrolment in Phase 1/2A wet AMD Clinical Trial

Melbourne, Australia, November 21 2016 – Opthea Limited (ASX:OPT), a developer of novel biologic therapies for the treatment of eye diseases, has completed patient enrolment in the randomised dose expansion Phase 2A clinical trial of OPT-302, a novel VEGF-C/D 'Trap' therapy for wet age-related macular degeneration (wet AMD) (ClinTrials.gov ID#: NCT02543229).

The Phase 2A dose expansion study has enrolled 31 patients with wet AMD, randomised in a 1:3 ratio to two treatment groups of OPT-302 (2 mg) given either as monotherapy (n = 8, comprising 5 naïve and 3 prior-treated subjects) or in combination with standard of care Lucentis®(0.5 mg), a selective VEGF-A inhibitor (n=23, comprising 14 naive and 9 prior-treated subjects) administered by intravitreal injection on a monthly basis for 3 months. Primary analysis data is anticipated in the first quarter of 2017 when all enrolled patients have completed the week 12 follow-up visit following dosing.

Completion of enrolment in the Phase 2A clinical trial follows the recent announcements of positive results from the Phase 1 dose escalation study of OPT-302 in 20 patients with wet AMD who were either treatment naive or previously treated with standard of care.

The encouraging results from the Phase 1 study demonstrate safety and tolerability of OPT-302 administered as a monotherapy and in combination with Lucentis® and suggest that combined administration of OPT-302 + Lucentis® may lead to improved clinical outcomes over Lucentis® alone.

"We are very pleased with the progress of the Phase 1/2A clinical trial with OPT-302 and look forward to reporting clinical outcomes from the study early in 2017," commented Dr Megan Baldwin, CEO and Managing Director of Opthea.

"OPT-302 has a novel mechanism of action that differentiates our approach to address the unmet medical need for wet AMD patients from other therapies currently approved or in development for this disease. We continue to be encouraged by the results we have reported to date and are planning to initiate a large randomised controlled clinical study in wet AMD patients in 2017."

The Phase 1/2A study is being run under an Investigational New Drug (IND) program with the Food and Drug Administration (FDA) at 14 sites across the U.S.

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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 $US4.5BN in 2015. 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 $US2.6BN in 2015. 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 actively recruiting patients 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 will recruit an additional ~30 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.