ASX and Media Release
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Opthea Completes Patient Enrolment for OPT-302 Phase 1 Dose Escalation Trial in Patients with Wet AMD

- **Phase 1 trial fully enrolled with 20 patients accrued into 4 planned treatment cohorts of 5 patients each**
- **Primary safety data from all Phase 1 patients expected to report in April**
- **Reporting of secondary outcome measures of clinical activity anticipated in 3rd quarter 2016 following completion of repeat dosing in all patients on a monthly basis for 3 months**

Melbourne, Australia – Opthea Limited (ASX:OPT; OTCQX:CKDXY), a developer of novel biologic therapies for the treatment of eye diseases, has completed patient enrolment in its ongoing Phase 1 dose escalation clinical trial of OPT-302 as a novel therapy for wet age-related macular degeneration (wet AMD). The 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.

The phase 1 trial is a first-in-human, open-label, sequential dose escalation study designed to evaluate the safety and clinical activity of intravitreal injections of OPT-302 either in combination with standard of care ranibizumab (Lucentis®) or alone as monotherapy for patients with wet AMD. The trial enrolled the target 20 patients into four treatment cohorts that included three OPT-302 dose-escalation groups (0.3, 1.0 or 2.0 mg) in combination with Lucentis® (0.5 mg) and an OPT-302 monotherapy group (2.0 mg).

To date, OPT-302 administered at doses of 0.3 or 1.0 mg in combination with Lucentis® by intravitreal injection has been well tolerated with a promising safety profile in both treatment naïve and previously treated patients with wet AMD, allowing patient enrolment into the highest (2.0 mg) dose cohorts.

With the dose escalation trial fully enrolled, the company expects to complete the 28 day safety assessment period for the OPT-302 highest dose level (2.0 mg) subjects in April which is a primary objective of the Phase 1 study.

Additional detailed evaluation of longer term patient outcomes from the ongoing Phase 1 dose escalation study is expected in the 3rd quarter of 2016 when all of the enrolled subjects have completed dosing on a monthly basis for 3 months. The data analysis will include secondary endpoint measurements of clinical activity, such as changes from baseline in visual acuity and wet AMD lesions using optical coherence tomography and fluorescein angiography imaging, with the results to be presented at a major international clinical ophthalmology conference later in the year.

Dr Megan Baldwin, CEO and Managing Director, commented *"Full enrolment into the Phase 1 dose escalation study is an important milestone for Opthea. Our team and our investigators are excited about the progress of the study and the potential of OPT-302 to address the unmet medical need for wet AMD patients. We look forward to reporting further outcomes from the ongoing Phase 1 trial throughout 2016."*

Additional information regarding the trial is available from the U.S. National Institutes of Health (NIH) clinical trials database at www.clinicaltrials.gov, clinical trial identifier: NCT02543229.

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About Opthea Limited

Opthea (ASX:OPT; OTCQX:CKDXY) 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 internal product development programs are primarily 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 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. In preclinical models of wet AMD, OPT-302 demonstrates significant activity as a monotherapy and additive activity when used in combination with existing agents that block VEGF-A.
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 and will recruit at least 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.

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 typically affects individuals aged 50 years or older, and is the leading cause of blindness in the developed world. The prevalence of AMD is increasing annually as the population ages. Sales of the drug Lucentis® (Roche/Novartis), which targets VEGF-A but not VEGF-C, were over $US4.5BN in 2015. Sales of EYLEA® (Regeneron/Bayer), which also targets VEGF-A but not VEGF-C 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 experience no 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.

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.