ASX and Media Release
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Opthea Provides Timing Update on OPT-302 wet AMD and DME Clinical Trials

Melbourne, Australia; 22 July 2019 – Opthea Limited (ASX:OPT), a clinical stage biopharmaceutical company developing novel biologic therapies to treat eye diseases, is pleased to announce that the timing of the primary analysis from its ongoing Phase 2b trial of OPT-302 for wet age-related macular degeneration (AMD) will occur sooner than expected and be brought forward by one quarter, with the primary data now expected to be reported in the 3rd quarter of calendar year 2019.

"The reporting of top-line data from our randomised, controlled Phase 2b trial in 366 treatment naïve wet AMD patients represents a major clinical milestone for Opthea. Progress in the last few months has been excellent, such that we now expect to report primary data from this study several months earlier than originally anticipated," commented Dr Megan Baldwin, CEO and Managing Director of Opthea Limited.

Opthea is also progressing its clinical program in diabetic macular edema. The ongoing Phase 2a randomised, controlled clinical trial evaluating the safety and efficacy of OPT-302 in patients with persistent center-involved diabetic macular edema (DME) is now well advanced with the study entering its final phase of recruitment. Primary data from the Phase 2a DME trial is expected to report early in 2020.

"Whilst we remain masked to the clinical trial results of both Phase 2 studies, we are very much looking forward to reporting trial outcomes with our novel VEGF-C/D 'trap', OPT-302, which has the potential to address diseases for which there is significant unmet medical need and commercial opportunity," stated Dr Baldwin.

Dr Megan Baldwin will present the updates to the expected timing of the primary data reporting for the Phase 2b wet AMD and Phase 2a DME trials at the Ophthalmology Innovation Summit (OIS) in Chicago on Thursday, July 25th, 2019 (US Central Daylight Time). Dr Baldwin's presentation will be made in the "Innovation Showcase" session of the OIS (https://ois.net/ois-asrs-2019/agenda/). The presentation will also include an overview of clinical results from the Company's first-in-human Phase 1/2a clinical trial of OPT-302 in wet AMD and Phase 1b dose escalation of OPT-302 administered in combination with aflibercept (Eylea®) to patients with DME despite prior treatment with a VEGF-A inhibitor.

Additional information on Opthea's technology and clinical trials in wet AMD and diabetic macular edema (DME) can be 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®, and a 9 patient dose-escalation study of OPT-302 in combination with EYLEA® in patients with persistent central-involved diabetic macular edema (DME) despite prior 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 studies can be found on the Opthea website: www.opthea.com

About Wet AMD and DME

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 over 50 years and its prevalence is increasing. Without treatment, wet AMD patients often experience a chronic, rapid decline in visual acuity and increase in retinal fluid.

DME is the leading cause of blindness in diabetics and is estimated to affect approximately 2 million people globally. Chronically elevated blood glucose levels in Type 1 and Type 2 diabetics can lead to inflammation, vascular dysfunction and hypoxia, causing upregulation of members of the VEGF family of growth factors. VEGFs, including VEGF-A and VEGF-C, stimulate vascular permeability or vascular leakage, leading to fluid accumulation in the macula at the back of the eye and retinal thickening which affects vision.

Standard of care treatments for wet AMD and DME include the VEGF-A inhibitors Lucentis® (Roche/Novartis) and EYLEA® (Regeneron/Bayer), which do not inhibit VEGF-C or VEGF-D. Sales of Lucentis® and Eylea were over $US3.7BN and $US6.2BN in 2018 respectively. Approximately half of the people receiving Lucentis®/EYLEA® do not experience a significant gain in vision and/or have persistent retinal vascular leakage despite regular IVT injections. Simultaneous inhibition of VEGF-A and VEGF-C/-D, by combined administration of OPT-302 with a VEGF-A inhibitor has the potential to improve patient responses, including visual acuity, 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. Opthea's product development programs are focused on developing OPT-302 for retinal diseases.

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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