ASX and Media Release
21 November 2019

Opthea Chairman's Address to the 2019 AGM

Melbourne, Australia; 21 November 2019 – Opthea Limited (ASX:OPT)

It is a pleasure to report to our fellow shareholders following a very positive year for Opthea.

Underpinning our progress over the past 12 months was the reporting of outcomes from Opthea's Phase 2b clinical trial in wet AMD patients. This large, international study met the pre-specified primary endpoint of demonstrating significant superior vision gains in patients treated with OPT-302 (2.0 mg) combination therapy compared to standard of care Lucentis® therapy alone.

The positive outcomes of the study represent a major achievement for the company and position Opthea as a global player in ophthalmology.

Importantly, our results highlight the potential of OPT-302 to improve vision outcomes for patients suffering from serious, sight-threatening diseases that affect the back-of-the-eye, including wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME).

There are currently limited treatment options for patients with wet AMD and DME, and a large proportion of patients who, despite regular ongoing treatment with existing agents, respond sub-optimally or not at all. OPT-302 offers hope to wet AMD and DME patients that vision outcomes may be better when added to standard of care treatment for these diseases. Our conviction to progress development of OPT-302 is based on multiple factors.

Firstly, in addition to the need for new therapies for these diseases, the commercial opportunity for OPT-302 as a combination treatment for use with approved standard of care therapies is currently in excess of USD10 billion per annum and growing. Furthermore, our strategy to target VEGF-C and VEGF-D for the treatment of retinal eye diseases is based on strong scientific rationale and robust preclinical and clinical data. VEGF-C and VEGF-D are members of the Vascular Endothelial Growth Factor (VEGF) family of signals which are key drivers of vessel growth and vascular permeability, both of which are involved in the pathogenesis of wet AMD and DME.

The positive outcomes recently reported from the Phase 2b clinical trial position Opthea well-ahead in the competitive landscape of other companies developing new therapies with novel mechanisms of action for the treatment of wet AMD.

Over the past 12 months we have also made significant progress in diversification of our clinical program into a second eye disease, DME. In October 2018, we reported data from the Phase 1b dose escalation study for OPT-302 in 9 patients with persistent central-involved DME despite prior anti-VEGF-A therapy. Vision and reductions in retinal fluid were observed in patients following addition of OPT-302 to standard of care treatment, with dose responsive gains in visual acuity demonstrated with ascending dose-levels of OPT-302.

We are highly encouraged by the outcomes in this trial to date and look forward to reporting data from the larger Phase 2a clinical trial in early 2020. On the back of strong clinical data, we are now planning to rapidly advance OPT-302 into pivotal, registrational Phase 3 development, and we are in a strong financial position to undertake this planning and complete the DME trial.

The company's current cash position is A$30 million, which includes A$12.6 million received through the exercise of quoted options in late 2018 and by the receipt of an A$14.6 million tax rebate for R&D activities conducted in the 2019 financial year.

We look forward to the next stage of Opthea's corporate growth as we advance OPT-302 through late-stage clinical development and towards commercialisation. The Opthea management team and Board of Directors are truly excited about the potential of OPT-302 to change the treatment paradigm for wet AMD and DME patients.

We thank our shareholders for their continued support, many of whom have supported Opthea for many years and through the early stages of OPT-302's clinical development. Finally, I thank my fellow directors Megan Baldwin and Michael Sistenich and all of the dedicated and hard-working members of Opthea's management team for their commitment to the program and the company.

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 (e.g. Lucentis®/Eylea®). Combination therapy of OPT-302 and a VEGF-A inhibitor achieves more complete blockade of members of the VEGF family, blocking mechanisms contributing to sub-optimal responses to selective VEGF-A inhibitors and has the potential to improve vision outcomes by more completely inhibiting the pathways involved in disease progression.

Phase 2b Study Design

Opthea's Phase 2b clinical trial was an international, multi-centre, prospective, sham-controlled, double-masked, superiority study that enrolled 366 treatment-naïve patients with wet AMD who were randomized in a 1:1:1 ratio to receive one of the following treatment regimens administered every 4 weeks for 24 weeks: OPT-302 (0.5 mg) in combination with ranibizumab (0.5 mg); OPT-302 (2.0 mg) in combination with ranibizumab (0.5 mg); or sham in combination with ranibizumab (0.5 mg).

Further details on the Company's clinical trials can be found at: www.clinicaltrials.gov, Clinical trial identifiers: NCT02543229, NCT03345082 and NCT03397264.

About Wet AMD

Wet (neovascular) age-related macular degeneration, or wet AMD, is a disease characterized 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 that 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 rapid decline in visual acuity.

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 intravitreal injections. Combined administration of OPT-302 with a VEGF-A inhibitor, has the potential to improve 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 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. Therefore 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.

Company & Media Enquiries:

Megan Baldwin, PhD
CEO & Managing Director
Opthea Limited
Tel: +61 (0) 447 788 674
megan.baldwin@opthea.com

Australia:
Rudi Michelson
Monsoon Communications
Tel: +61 (0) 3 9620 3333

Join our email database to receive program updates:

Tel: +61 (0) 3 9826 0399
info@opthea.com
www.opthea.com

U.S.A. & International:
Jason Wong
Blueprint Life Science Group
Tel: +1 415 375 3340, Ext 4
Jwong@bplifescience.com