ASX and Media Release

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Opthea Presents Additional Data from OPT-302 Phase 2b Wet AMD Trial at the Ophthalmology Innovation Summit in San Francisco

Melbourne, Australia; 11 October 2019 – Opthea Limited (ASX:OPT), a clinical-stage biopharmaceutical company developing novel biologic therapies to treat back-of-the-eye diseases, announced today that additional data analyses from the recently completed 366 patient Phase 2b randomised, controlled wet AMD study of OPT-302 with ranibizumab (Lucentis®) compared to ranibizumab alone, was presented at the Ophthalmology Innovation Summit (OIS) in San Francisco.

The Phase 2b study outcomes were presented for the first time in the US by Dr Megan Baldwin, the Company's Chief Executive Officer. New clinical data included prespecified subgroup and exploratory analyses showing additive benefit of OPT-302 combination therapy in patients with wet AMD lesions consisting of varying CNV classifications and composition including those with more difficult to treat morphology. The additional data supports the recent reporting of superiority with OPT-302 combination therapy over ranibizumab in mean changes in best corrected visual acuity (BCVA) from baseline to week 24 in treatment naïve patients with choroidal neovascularisation (CNV) secondary to (wet) AMD.

Dr Baldwin commented "Achieving the primary endpoint of superior visual acuity gains in the Phase 2b wet AMD study has highlighted the commercial potential of OPT-302 combination therapy, particularly given that improved efficacy is a major unmet need in retinal vascular disease. These pre-specified subgroup and exploratory data analyses not only provide insight into which patients may be more likely to respond but also suggest improved benefit of OPT-302 combination therapy over anti-VEGF-A standard of care in difficult to treat retinal lesion types where there remains an important need for more effective treatments."

The Phase 2b trial entry criteria allowed for randomisation of patients with a broad range of lesion morphology including those with CNV divided into type 1 (occult) and type 2 (classic) membranes as well as more distinct subtypes of polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP).

To assess effects of OPT-302 combination therapy compared to ranibizumab treatment in patients with different CNV lesion types, pre-specified subgroup analyses were conducted particularly in those with minimally classic (44%) or occult lesion types (44%) as these represented the majority of treated eyes whilst a smaller group had predominantly classic CNV (12%).

Additional benefit of increased mean BCVA from baseline to week 24 was observed in patients receiving OPT-302 combination treatment compared to the ranibizumab control for both occult (16.2 versus 10.2 letters, a gain of +6.0 letters, p= 0.0008, n= 53 and 51 respectively) and minimally classic (13.7 versus 11.1 letters, a gain of +2.7 letters, n = 53 per group) subgroups respectively. In addition, the proportion of patients with occult lesions receiving OPT-302 combination therapy who achieved vision gains of ≥15 letters was 55.8% versus 34% of patients with occult lesions who received ranibizumab alone. Similarly, more eyes with either occult or minimally classic lesion subtypes treated with combination therapy had ≥10 letter gains in vision and reduced vision loss at week 24 compared to ranibizumab alone. Improved anatomical changes in occult or minimally classic lesions following

OPT-302 combination therapy supported the improved visual acuity with greater reductions in retinal thickness, retinal fluid and total lesion area at week 24 compared to the control group.

In patients with PCV, which is the predominant form of wet AMD in Asian populations, the mean BCVA gain from baseline to week 24 in the OPT-302 combination group was 13.5 letters (n = 22), compared to 6.9 letters in the ranibizumab control group (n = 20), a benefit of +6.7 letters (p = 0.0253).

The majority of study patients did not have RAP present at randomisation and the mean BCVA gain from baseline to week 24 was 15.0 letters (n = 103) with OPT-302 combination therapy for these patients, compared to 10.6 letters for those treated with ranibizumab alone (n=102), a benefit of +4.4 letters (p = 0.0025). Occult patients without RAP who received OPT-302 combination therapy gained a mean of 16.7 letters at week 24 (n = 49), compared to 10.1 letters in those treated with ranibizumab alone (n = 47), a benefit of +6.5 letters (p = 0.0005). Minimally classic patients without RAP who received OPT-302 combination therapy gained a mean of 15.4 letters at week 24 (n = 39), compared to 10.7 letters who received ranibizumab alone (n = 40), a benefit of +4.7 letters (p = 0.0415).

Dr Jason Slakter, President and Medical Director at the Digital Angiography Reading Center in New York, Clinical Professor of Ophthalmology at New York University School of Medicine, and partner at Vitreous-Retina-Macula Consultants of New York commented "While VEGF-A inhibitors have been the standard of care for neovascular AMD for almost 15 years, it has been recognized that occult CNV and eyes with polypoidal lesions or PCV are less responsive to anti-VEGF-A agents. Of particular note PCV is estimated to be the most common form of wet AMD globally given that Asia currently accounts for over 60% of the world's population. The promising results with OPT-302 observed in this study suggest that combination treatment with a VEGF-C/D inhibitor may provide additive benefit and help address patient groups that are highly prevalent and challenging to treat with today's standard of care."

The newly presented data follows on from the recent reporting of the primary outcome from the study which demonstrated that patients administered 2.0 mg OPT-302 combination therapy gained a mean of 14.2 letters of vision from baseline at 24 weeks, compared to 10.8 letters in the sham + ranibizumab control group, a statistically significant vision benefit of 3.4 letters (p=0.0107). Addition of OPT-302 to standard of care ranibizumab treatment was also beneficial across multiple secondary endpoints of visual function and anatomical improvements to a greater extent than ranibizumab alone. Furthermore, OPT-302 intravitreal injections were well tolerated, with the safety profile similar to the control group.

Opthea continues to review the Phase 2b study data with its advisory group of leading retinal specialist key opinion leaders to advance OPT-302 clinical development plans.

A copy of Opthea's Ophthalmology Innovation Summit presentation is available on Opthea's website at www.opthea.com.

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 (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.

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