ASX and Media Release

27 July 2020

Opthea Reports New Data of OPT-302 in Diabetic Macular Edema at the 2020 Annual Meeting of the American Society of Retina Specialists

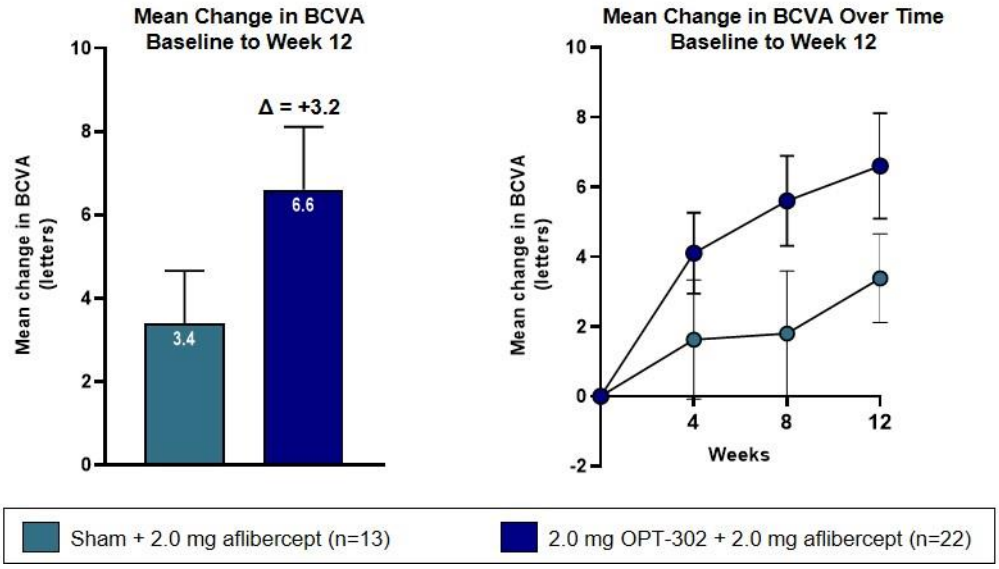
Company to host Key Opinion Leader Symposium on Wet AMD & DME on Aug 6 AEST

Melbourne, Australia; 27 July 2020 – Opthea Limited (ASX:OPT), a clinical stage biopharmaceutical company developing a novel therapy to treat highly prevalent and progressive retinal diseases, is pleased to announce that new data from the Phase 1b/2a clinical study of OPT-302 in patients with treatment refractory diabetic macular edema (DME) has been presented at the 2020 American Society of Retina Specialists (ASRS) Virtual Annual Meeting (24-26 July 2020).

The presentation titled "*Switching to combination OPT-302 with aflibercept from prior anti-VEGF-A monotherapy in eyes with persistent diabetic macula edema (DME)*" was presented by Dr David Boyer, MD, Senior Partner Retina Vitreous Associates Medical Group, Los Angeles, and Clinical Professor at the University of Southern California Roski Eye Institute, Keck School of Medicine. The presentation was part of the "Diabetic Retinopathy Symposium" and provided an overview of the scientific rationale for targeting VEGF-C/-D for the treatment of DME and new data from Opthea's Phase 1b/2a clinical trial of OPT-302, including subgroup analyses to evaluate outcomes in patients with a more homogeneous prior treatment history of previous aflibercept (Eylea) therapy.

In the subset of patients who received a minimum of at least three consecutive aflibercept intravitreal injections on a regular basis immediately before enrollment into the Phase 2a trial (n=35), a mean improvement in best corrected visual acuity (BCVA) of +6.6 letters (n=22) from baseline to week 12 was observed following OPT-302 + aflibercept combination treatment, compared to +3.4 letters (n=13) for patients continuing on aflibercept monotherapy.

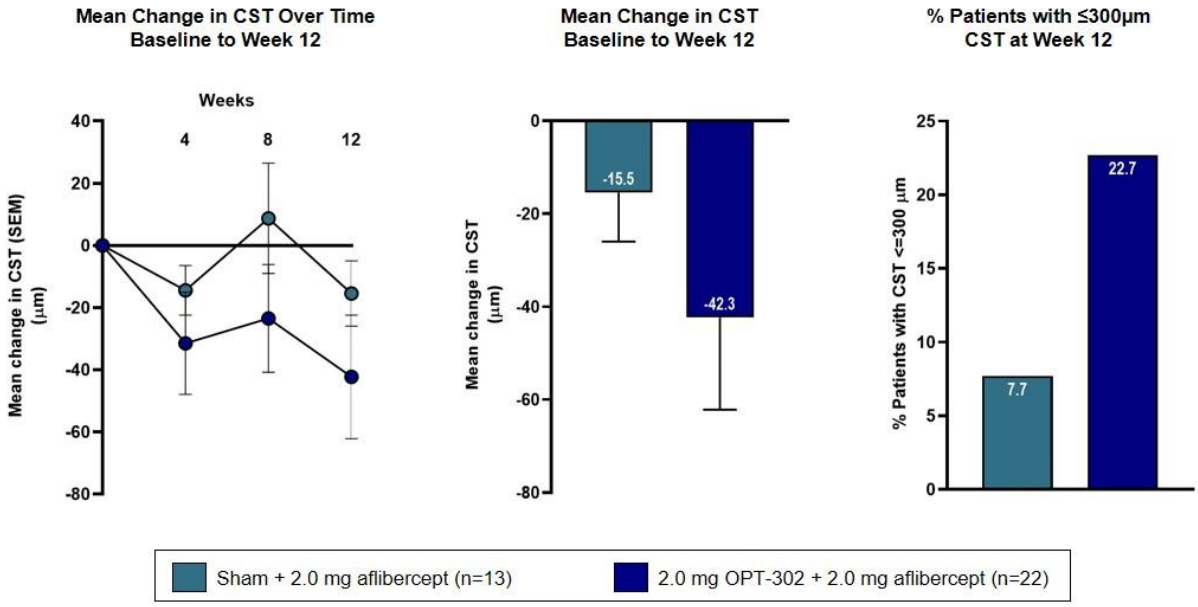
Greater Gains in Visual Acuity following OPT-302 Combination Therapy in Patients with a Treatment History of Prior Aflibercept*



In addition, the proportion of patients gaining ≥10 letters from baseline to week 12 in the OPT-302 combination group was 27.3% compared to 0% in the aflibercept monotherapy group. The proportion of patients gaining ≥15 letters from baseline to week 12 was 9.1% in the OPT-302 combination group, compared to 0% patients in the aflibercept monotherapy group. Furthermore, the proportion of patients who lost ≥1 letter of BCVA from baseline to week 12 was 9.1% in the OPT-302 combination therapy group and 23.1% in the aflibercept monotherapy group.

Improved anatomical changes were consistent with these functional visual acuity outcomes, as the mean reduction in retinal thickness, measured as central subfield thickness (CST) from baseline to week 12, was -42.3 µm in the OPT-302 combination therapy group and -15.5 µm in the aflibercept monotherapy group. The proportion of patients with improved CST of ≤300 µm at week 12 was 22.7% in the OPT-302 combination therapy group and 7.7% in the aflibercept monotherapy group. In addition, improved underlying diabetic retinopathy by 2 or more steps was observed in 13.6% of patients in the OPT-302 combination therapy and 7.7% in the aflibercept monotherapy group.

Greater Mean Reduction in Retinal Thickness following OPT-302 Combination Therapy in Patients with a Treatment History of Prior Aflibercept*



Per Protocol population, patients with a treatment history of prior aflibercept (n=35), must have received all 3 intravitreal study treatments and and be sufficiently compliant with the protocol. Error bars (± SEM); BCVA: Best Corrected Visual Acuity; CST: Central Subfield Thickness measured by Spectral Domain-Optical Coherence Tomography (SD-OCT)

"We are very pleased to report favorable visual function and anatomical outcomes following OPT-302 combination therapy in DME patients with persistent disease despite prior treatment with standard-of-care anti-VEGF-A therapy. The new data presented at ASRS includes a subgroup analysis of approximately one third of patients enrolled into the study with a treatment history of prior aflibercept. This patient population represents a more stringent and less variable patient population in which to investigate the ability of OPT-302 to provide additional benefit, particularly as aflibercept is considered the optimal first-line standard of care treatment to achieve maximal VEGF-A suppression in DME" said Dr Megan Baldwin, CEO and Managing Director, Opthea Limited.

Dr Baldwin also commented "The positive outcomes with OPT-302 combination therapy in these patients is very encouraging, particularly given that treatment refractory patients are considered difficult-to-treat and that outcomes were assessed after only three monthly doses at week 12. Our DME trial results support further investigation in this indication in larger, randomized, controlled clinical trials."

In addition, the overall safety profile of OPT-302 combination therapy has continued to be favorable and has now shown consistent tolerability alone or in combination with anti-VEGF-A standard of care therapy across two eye indications with over 1850 intravitreal injections administered to nearly 400 patients with wet AMD and DME.

The Phase 2a DME trial is ongoing with additional analyses and the final outcomes for longer term safety and treatment durability to be completed in the second half of calendar year 2020. In addition to the ongoing Phase 2a trial, Opthea continues to undertake planning for its Phase 3 program in wet AMD, including regulatory engagement in the US and Europe, and to progress its manufacturing of OPT-302 for Phase 3 clinical trials.

A copy of the data presented at the ASRS 2020 Virtual Meeting has been posted to the ASX and is available on the Opthea website at www.opthea.com

Opthea plans to host a Key Opinion Leader symposium focused on providing insights into the current treatment landscape and an overview of Opthea's clinical programs in both wet AMD and DME. The virtual online event will be held from 9am – 10:30am AEST on Thursday 6th August 2020 (7PM EST on Wednesday 5th August) and additional details will provided closer to the event.

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 wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME). 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.

The OPT-302 DME trial was a prospective, proof-of-concept, clinical study consisting of a dose escalation (Phase 1b) followed by a randomized dose expansion (Phase 2a) in treatment refractory participants with the aim to evaluate the safety, visual function and anatomic outcomes of switching from anti-VEGF-A monotherapy to combination therapy of OPT-302 with aflibercept. In the Phase 1b, patients received escalating doses of OPT-302 (either 0.3, 1 or 2 mg) + aflibercept (2 mg) across 3 cohorts. In the Phase 2a, 144 patients were randomized in a 2:1 ratio to either 2 mg aflibercept + 2 mg OPT-302 or aflibercept + sham. Aflibercept ± OPT-302 was given once every 4 weeks for a total of 3 doses, and patients then assessed through week 12 for outcomes including safety, effects on BCVA, and anatomic changes. A total of 115 patients enrolled in the study complied sufficiently with the protocol and were included in the Per Protocol population.

Opthea has also reported outcomes from an international, multi-centre, prospective, sham-controlled, double-masked, superiority study that enrolled 366 treatment-naïve patients with wet AMD. Participants in the study were randomized in a 1:1:1 ratio to receive one of the following treatment regimens administered once every 4 weeks for 24 weeks (six treatments in total): OPT-302 (0.5 mg) in combination with ranibizumab (Lucentis®) (0.5 mg); OPT-302 (2.0 mg) in combination with ranibizumab (0.5 mg); or sham in combination with ranibizumab (0.5 mg). The study met the primary endpoint demonstrating superior vision gains in participants who received OPT-302 (2.0 mg) in combination with ranibizumab at week 24. Opthea is also investigating OPT-302 in a Phase 2a clinical trial in patients with persistent, centre-involved DME. Further details on the Company's clinical trials can be found at: www.clinicaltrials.gov, Clinical trial identifiers: NCT02543229, NCT03345082 and NCT03397264.

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.

Authorised for release to ASX by Megan Baldwin, CEO & Managing Director

Company & Media Enquiries:

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

Join our email database to receive program updates:

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

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

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