



ASX and Media Release
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Opthea To Present Update at the Ophthalmology Innovation Summit in Chicago

Melbourne, Australia; October 24 2018 – Opthea Limited (ASX:OPT), a clinical-stage biopharmaceutical company developing novel biologic therapies to treat back-of-the-eye diseases, announced today that Dr Megan Baldwin, the Company’s Chief Executive Officer, will present at the Ophthalmology Innovation Summit (OIS) in Chicago on Thursday, October 25th, 2018 (US Central Daylight Time).

Dr Baldwin’s presentation will be made in the “Public Company Showcase” session of the OIS (<https://ois.net/oisaaao-2018-agenda/>) together with other leading public ophthalmology companies. The presentation will include an overview of Opthea’s clinical program, including an update on the Company’s Phase 1b study in Diabetic Macular Edema (DME) investigating the dose-escalation of three ascending dose level groups for OPT-302 + Aflibercept (Eylea[®]) in nine patients with persistent central-involved DME. OPT-302 is a novel VEGF-C/D ‘Trap’ therapy for the treatment of retinal eye diseases, which is currently being investigated in Phase 2b and Phase 1b/2a clinical trials in wet age-related macular degeneration (wet AMD) and DME respectively.

Dr Baldwin commented “I look forward to participating in this must-attend event and to have the opportunity to present an update on Opthea’s clinical program to a broad ophthalmology and investor audience. Our Phase 2 programs have advanced significantly over the last 12 months and continue to build on the very encouraging safety profile and activity observed in our first-in-human Phase 1/2a trial in wet AMD patients.”

The OIS is being held in conjunction with the annual meeting of the American Academy of Ophthalmology (AAO), which is one of the largest gatherings of ophthalmology healthcare specialists globally, and will be attended by professionals from the investor, pharmaceutical and clinical ophthalmology community.

A copy of the presentation will be made available on Opthea’s website at www.opthea.com.

Additional information on Opthea’s technology and clinical trials in wet AMD and 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®. The trial was conducted under an FDA approved IND at 14 US clinical sites. The purpose of the trial was 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). Of the 51 patients enrolled, 25 were treatment naïve and 26 had received prior intravitreal anti-VEGF-A therapy.

Further details on Opthea's clinical trials can be found at www.clinicaltrials.gov, clinical trial identifiers: NCT02543229 (Phase 1/2a wet AMD); NCT03345082 (Phase 2b wet AMD) and NCT03397264 (Phase 1b/2a DME). Additional information on Opthea's technology and clinical trials can be found on Opthea's 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 50 years or older. The prevalence of AMD is increasing annually as the population ages. 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^{1,2,3}. 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. Existing standard of care treatments for DME are limited and include inhibitors of VEGF-A (Lucentis®, Eylea®), steroids and laser therapy. Despite these treatments, many patients remain refractory and have a sub-optimal response to therapy with persistent fluid and impaired vision. OPT-302 blocks VEGF-C and VEGF-D, which cause vessels to grow and leak. Used in combination with a VEGF-A inhibitor, OPT-302 has the potential to improve clinical outcomes in DME patients.

Existing standard of care treatments for DME and wet AMD include agents that inhibit VEGF-A, but not VEGF-C or VEGF-D. Sales of the drug Lucentis® (Roche/Novartis), which targets VEGF-A, were over \$US3.4BN in 2017. Sales of Eylea® (Regeneron/Bayer), which also targets VEGF-A but not VEGF-C/-D were over \$US5.9BN in 2017. Many patients receiving Lucentis®/Eylea® are classified as non-responders or 'poor' responders and do not experience a 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.

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. The applications for the VEGF technology, which functions

in regulating blood and lymphatic vessel growth, are substantial and broad. Opthea's product development programs are 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) and Diabetic Macular Edema (DME).

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.

- ¹ Ding J, Wong TY. Current epidemiology of diabetic retinopathy and diabetic macular edema. *Curr Diab Rep.* 12: 346-354, 2012.
- ² Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Eye and Vision.* 2:17, 2015.
- ³ Managing Diabetic Eye Disease in Clinical Practice. Singh RP (ed). Springer International Publishing 2015.

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