



ASX and Media Release
28 November 2018

Opthea Options Exercise Generates Proceeds of \$13.3m

- ***Strong shareholder support with 99.4% of issued options exercised***
- ***Company well-funded through clinical milestones with A\$37m cash***

Melbourne, Australia; 28 November 2018 – Opthea Limited (ASX:OPT), a late stage biopharmaceutical company developing novel biologic therapies to treat eye diseases, today announced that proceeds of A\$13.3m have been generated through the exercise of quoted options issued in November 2014.

The options, issued to investors who participated in the Company's 2014 capital raising of A\$17.4m on the basis of one for every two shares purchased, were exercisable at A\$0.27 by 25th November 2018. A total of 49,429,099 options were exercised by the expiry date, representing 99.4% of the total number of options issued and generating proceeds in excess of A\$13.3m.

Dr Megan Baldwin, CEO & Managing Director of Opthea Limited, commented "We are pleased to have delivered significant shareholder value since the 2014 capital raising which is reflected in the impressive number of options that were exercised by the expiry date. We are thankful for the support of our shareholders, many of whom participated in the 2014 capital raising and saw the potential of OPT-302 as a promising new therapy for retinal eye diseases. Since that time we have continued to advance Opthea's clinical program and have demonstrated a favourable safety profile and encouraging evidence of clinical activity of OPT-302 in both wet AMD and DME patients."

The completion of option exercise follows the receipt of a A\$12.0 million research and development (R&D) tax credit from the Australian Taxation Office for R&D costs incurred in the 2017/2018 financial year. Together, the option proceeds and R&D tax credit strengthen the Company's cash position to over A\$37m and position the Company to deliver clinical milestones, with Opthea's randomised controlled Phase 2 studies in wet AMD and DME anticipated to report results before the end of 2019.

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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