



ASX and Media Release  
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## **Opthea Phase 1 wet AMD Clinical Trial with OPT-302 Meets Primary Safety Objective**

- **OPT-302 safe and well tolerated as monotherapy and in combination with Lucentis® in Phase 1 dose escalation clinical trial in 20 patients with wet AMD**
- **No dose limiting toxicities following 28 day safety review of high dose OPT-302 monotherapy (2 mg) and dose escalation cohorts of OPT-302 (0.3, 1.0 or 2 mg) in combination with ranibizumab (Lucentis®, 0.5 mg)**

**Melbourne, Australia** – Opthea Limited, a developer of novel biologic therapies for the treatment of eye diseases, has successfully met the primary objective of safety in the dose escalation of its ongoing first-in-human clinical trial of OPT-302, a novel VEGF-C/D ‘Trap’ therapy for wet age-related macular degeneration (wet AMD). The dose escalation trial is investigating OPT-302 administered either alone or in combination with Lucentis® on a monthly basis for three months by ocular injection. The study is being run under an Investigational New Drug (IND) program with the Food and Drug Administration (FDA) at 14 sites across the U.S. (*ClinTrials.gov ID#: NCT02543229*).

The 28 day safety assessment period has now been completed for all 20 patients in the Phase 1 dose escalation trial. OPT-302 administered by intravitreal injection as a monotherapy (2.0 mg) or at three escalating doses (0.3, 1.0 or 2.0 mg) in combination with Lucentis® (0.5 mg) was safe and well tolerated at all dose levels in 20 patients with wet AMD who were either treatment naive or previously treated with standard of care.

There were no dose limiting toxicities and a Maximum Tolerated Dose (MTD) was not reached with OPT-302. Adverse events were primarily related to the intravitreal injection procedure and were mild and manageable. There were no signs of infection inside the eye, or endophthalmitis, and no clinically significant changes in intraocular pressure, electrocardiograms, blood pressure or other vital signs during the safety assessment period at all dose levels of OPT-302.

Dr Pravin Dugel, managing partner of Retinal Consultants of Arizona and clinical professor at the University of Southern California Eye Institute, Keck School of Medicine, and member of Opthea’s Clinical Advisory Board, stated *“The investigators involved in the study are encouraged by the clinical data showing the feasibility and favourable safety profile of OPT-302 as a monotherapy and in combination with Lucentis®, particularly as a number of patients thus far have received at least two or three repeat doses on a monthly basis.”*

Dr Megan Baldwin, CEO and Managing Director, commented *“The results of the Phase 1 dose escalation study to date are very encouraging. Meeting the primary objective of the Phase 1 study by demonstrating that intravitreally administered OPT-302 is safe and well tolerated at all dose levels tested in combination with Lucentis® is a major milestone. We look forward to reporting longer term patient outcomes and secondary measures of clinical activity from the Phase 1 dose escalation study in the 3<sup>rd</sup> quarter of 2016 when all 20 patients have completed dosing on a monthly basis for 3 months.”*

With the 28 day safety assessment period complete for the patients in the Phase 1 dose escalation trial, patient recruitment for the randomised dose expansion Phase 2A study may now commence. The Phase 2A will enrol an additional ~30 subjects with wet AMD, randomised in a 1:1 ratio to two treatment groups of OPT-302 given as monotherapy or in combination with Lucentis® administered by intravitreal injection on a monthly basis for 3 months. Primary analysis data from the Phase 2A study is anticipated by the end of 2016.

*Company & Media Enquiries:*

Megan Baldwin, PhD  
CEO & Managing Director  
Opthea Limited  
Tel: +61 (0) 3 9826 0399  
[megan.baldwin@opthea.com](mailto:megan.baldwin@opthea.com)

*Join our email database to receive program updates:*

Tel: +61 (0) 3 9826 0399  
[info@opthea.com](mailto:info@opthea.com)  
[www.opthea.com](http://www.opthea.com)

*Australia:*

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

*U.S.A. & International:*

Candice Knoll  
Blueprint Life Science Group  
Tel: +1 415 375 3340, Ext 4

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## **About Opthea Limited**

Opthea (ASX:OPT; OTCQX:CKDXY) 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. The applications for the VEGF technology, which functions in regulating blood and lymphatic vessel growth, are substantial and broad. Opthea's internal product development programs are primarily 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).

## **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. In preclinical models of wet AMD, OPT-302 demonstrates significant activity as a monotherapy and additive activity when used in combination with existing agents that block VEGF-A. OPT-302 is currently being investigated in a Phase 1/2A clinical trial in wet AMD patients as a monotherapy and in combination with ranibizumab (Lucentis®). The trial is actively recruiting patients under an FDA approved IND at several US clinical sites. The purpose of the trial is 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). The study is being conducted in two parts: Part 1 (Phase 1) comprises an open label, sequential dose escalation and will recruit at least 20 patients and Part 2 (Phase 2A) a randomized dose expansion that will recruit an additional ~30 patients and is aimed at further characterising the safety, pharmacokinetic profile and relationship between dose/PK and clinical activity of OPT-302 (+/-

ranibizumab). Further details on the Phase 1/2A trial can be found at: [www.clinicaltrials.gov](http://www.clinicaltrials.gov), Clinical trial identifier: NCT02543229.

### **About Wet AMD**

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 typically affects individuals aged 50 years or older, and is the leading cause of blindness in the developed world. The prevalence of AMD is increasing annually as the population ages. Sales of the drug Lucentis® (Roche/Novartis), which targets VEGF-A but not VEGF-C, were over \$US4.5BN in 2015. Sales of EYLEA® (Regeneron/Bayer), which also targets VEGF-A but not VEGF-C first marketed in November 2011 for the treatment of wet AMD, were over \$US2.6BN in 2015. Approximately half of the people receiving Lucentis®/EYLEA® are classified as non-responders or 'poor' responders and experience no 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.

### **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.