Opthea Completes Recruitment in Phase 2a Clinical Trial of OPT-302 for Diabetic Macular Edema

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MELBOURNE, Australia, Jan. 07, 2020 (GLOBE NEWSWIRE) -- **Opthea Limited** (ASX:OPT), a clinical stage biopharmaceutical company developing novel biologic therapies to treat eye diseases, has completed patient recruitment into the Company's Phase 2a trial evaluating the safety and efficacy of OPT-302 administered in combination with aflibercept (Eylea®) for treatment of diabetic macular edema (DME).

"We are delighted to have completed patient enrollment into the Phase 2a DME study which marks another significant milestone in a second disease indication for the Company," said Dr Megan Baldwin, CEO of Opthea. "We are excited about the potential for OPT-302 in DME given the positive outcomes of our Phase 2b wet AMD study, as well as our earlier positive Phase 1b clinical results which showed dose escalation of OPT-302 combination therapy was well tolerated with improved visual and anatomic outcomes in patients with treatment resistant and persistent DME. The ongoing Phase 2a DME study is further evaluating OPT-302 combination therapy in a larger patient population to confirm these observations and we look forward to reporting topline data in the second quarter of 2020."

The Phase 2a trial is a randomized, dose expansion study designed to enroll at least 108 evaluable patients diagnosed with persistent centre-involved DME despite regular administration of prior anti-VEGF-A monotherapy. Participants were allocated in a 2:1 ratio to either aflibercept (2 mg) + OPT-302 (2 mg) or aflibercept monotherapy. Treatments are administered by intravitreal (ocular) injection once every 4 weeks (total of 3 doses). The primary efficacy analysis endpoint is the clinical response rate, defined as the proportion of patients receiving combination OPT-302 and aflibercept achieving a ≥5 letter gain in visual acuity at week 12 compared to baseline. Secondary efficacy measures include mean visual acuity, macular thickness, improvement in diabetic retinopathy severity score and durability of response.

DME is a complication of diabetes that is estimated to affect over 2 million people globally and is the leading cause of vision loss amongst the working-age population. Fluid from blood vessel leakage in the eye accumulates in the macula, or central portion of the retina, and the resultant swelling leads to blurred vision and blindness. Current standard-of-care treatment with anti-VEGF-A monotherapy has shown suboptimal outcomes in many patients who continue to have persistent fluid and/or impaired vision, which represents a large unmet medical need. OPT-302 blocks VEGF-C and VEGF-D, two factors involved in vessel growth and leakage in the eye, and when used in combination with a VEGF-A inhibitor, has the potential to improve clinical outcomes in DME patients.

"With the recruitment target now met for the Phase 2a DME study, Opthea's management team is now fully focused on corporate activities to progress OPT-302 into Phase 3 studies for wet AMD and preparing to report topline data from the Phase 2a DME trial in the second quarter of calendar year 2020 following the completion of patient dosing, study visits, data collection and statistical analyses," concluded Dr Baldwin.

Additional information on Opthea's technology and clinical trials in wet AMD and DME can 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 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 every 4 weeks for 24 weeks: 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 on a monthly basis over 6 months.

Opthea has also completed a Phase 1/2a clinical trial in the US investigating OPT-302 administered as monthly intravitreal injections for 3 months with and without ranibizumab 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 the Phase 1/2a trial can be found at: www.clinicaltrials.gov, Clinical trial identifier: NCT02543229. Details on the outcomes of the study can be found at: 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 over 50 years and its prevalence is increasing. 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. Chronically elevated blood glucose levels in Type 1 and Type 2 diabetics can lead to inflammation, vascular dysfunction and hypoxia, causing upregulation of the VEGF family of growth factors. VEGFs, including VEGF-A and VEGF-C, stimulate vascular permeability or leakage, leading to fluid accumulation in the macula at the back of the eye and retinal thickening which affects vision.

Standard of care treatments for wet AMD and DME include the VEGF-A inhibitors Lucentis® (ranibizumab, Roche/Novartis) and EYLEA® (aflibercept, 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 IVT injections.

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.

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